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Актуальні питання створення нових лікарських засобів : тези доповідей XXIII Міжнародної науково-практичної конференції молодих вчених та студентів (21 квіт. 2016 р.). В 2-х.т., Т.1. – Х. : Вид-во НФаУ, 2016. – 433 с.

Збірка містить матеріали науково-практичної конференції молодих вчених та студентів «Актуальні питання створення нових лікарських засобів». Матеріали згруповано за провідними напрямками науково-дослідної та навчальної роботи Національного фармацевтичного університету. Розглянуто теоретичні та практичні аспекти синтезу біологічно-активних сполук і створення на їх основі лікарських субстанцій; стандартизації ліків, фармацевтичного та хіміко-технологічного аналізу; вивчення рослинної сировини та створення фітопрепаратів; сучасної технології ліків та екстемпоральної рецептури; біотехнології у фармації; досягнень сучасної фармацевтичної мікробіології та імунології; доклінічних досліджень нових лікарських засобів; фармацевтичної опіки рецептурних та безрецептурних лікарських препаратів; доказової медицини; сучасної фармакотерапії, соціально-економічних досліджень у фармації, маркетингового менеджменту та фармакоекономіки на етапах створення, реалізації та використання лікарських засобів; управління якістю у галузі створення, виробництва і обігу лікарських засобів; інформаційниих технологій у фармації та медицині; основ педагогіки та психології; суспільствознавства; філології. Для широкого кола наукових і практичних працівників фармації та медицини.

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Editorial board: academician of NAS of Ukraine Chernykh V.P., ass. prof. Krutskyh T.V., Danylchenko S.Yu.
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Topical issues of new drugs development : Abstracts of XXIII International Scientific And Practical Conference Of Young Scientists And Student (April 21, 2016). In 2 vol. Vol.1. – Kharkiv : Publishing Office NUPh, 2016. – 433 P.

Book of Abstracts includes materials of Scientific and Practical Conference of Young Scientists and Students «Actual questions of development of new drugs». Materials are groupped according to the main directions of scientific, research and educational work of the National University of Pharmacy. Teoretical and practical aspects of the synthesis of biologically active compounds and development of medicinal substances on their basis; standardization of drugs, pharmaceutical and chemical-technological analysis, the study of raw materials and herbal remedies development, modern drug technology and extemporal recipe; biotechnology in pharmacy, modern advances in pharmaceutical microbiology and immunology, clinical trials of new drugs, pharmaceutical care for prescription and OTC-drugs, evidence-based medicine, modern pharmacotherapy, socio-economic studies in pharmacy, marketing management and pharmacoeconomics during the development, implementation and use of drugs, quality management in development, production and traffi cking of drugs; information technologies in pharmacy and medicine; basics of pedagogy and psychology; social science; philology are presented. For a wide audience of scientists and pharmaceutaical and medicinal employees.

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Dear colleagues and our talented youth!

The development of science has always been one of the most important tasks for our university. Because we are both the greatest pharmaceutical educational institution in our country, and the developed research structure, we want to provide not only good specialists, but also new and safe medicines. Of course, nowadays we already have powerful scientific basement – well-known scientists, professors and their achievements. Today 371 medicines with wide range of pharmacological activities are in various stages of implementation. But in order to continue the development of current research areas in the future we need you – students and young scientists with a strong desire to make our life better, healthier, happier.

Different Student Scientific Societies have been fruitfully working in every department for 70 years already. Nowadays they unite more than 700 students, among them – students from foreign countries too. Student Scientific Societies are

the first step for students and young scientists on the way of improving their skills. You can choose the most interesting for you research area in pharmacy: from synthesis of new biologically active molecules and their analysis to preclinical and clinical testing, industrial aspects or marketing research. You have brilliant opportunity to test yourself in order to find your own way in science during students' years. And your supervisors will surely help you and lead you on this way to success. Because altogether we are working for our main goal – development of new, safe and efficient medicines.

Thus our Conference «Topical issues of new drugs development» is the first step for you today. The Conference became International five years ago. Nowadays publication of abstracts is carried out entirely in English, as well as our plenary sessions. The Conference is an important part of your scientific work – an interesting and challenging pathway that leads to PhD degree, then to the degree of Doctor of Science, to professorship. And it begins as a rule in our Student Scientific Societies. Almost 90 % of our teaching staff, as well as I'm myself, has started their scientific career the same way.

Someone can say that scientific work isn't always easy and straight, that it needs lots of energy and even money. But we must understand that without the development of national science it's just impossible to make our country strong and independent, as it will be for sure in the nearest future.

That's why the main goal for us is making science fashionable for talented youth and creating all necessary conditions for your scientific work. And I'm proud that so many of our students are deeply interested in it nowadays.

I wish you to achieve all your goals, to become famous and successful. And, of course, I wish everyone good health, happiness and love!

Rector of National University of Pharmacy,
Academician of NAS of Ukraine,
prof. Valentyn P. Chernykh

SECTION № 1

SYNTHESIS OF PHYSIOLOGICALLY ACTIVE SUBSTANCES

SYNTHESIS AND STRUCTURE OF ETHYL 1-HYDROXY-3-OXO-5,6-DIHYDRO-3*H*-PYRROLO[3,2,1-*ij*]QUINOLINE-2-CARBOXYLATE

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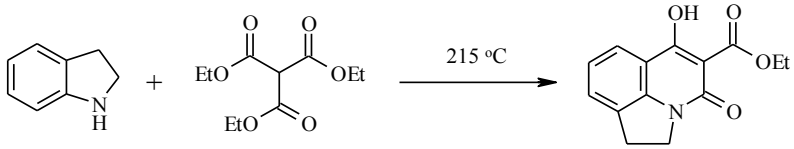
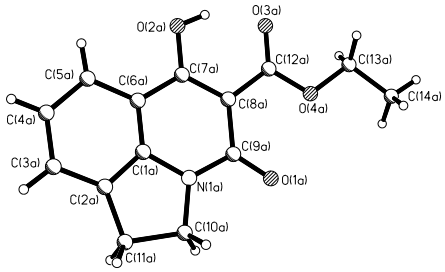
Introduction. Ethyl ester of 1-hydroxy-3-oxo-5,6-dihydro-3*H*-pyrrolo[3,2,1-*ij*]quinoline-2-carboxylate is of interest as the starting material for obtaining a potentially biologically active of tricyclic analogues of 4-hydroxyquinolone-2.

Aim. The aim of this work was to synthesis ethyl ester of 1-hydroxy-3-oxo-5,6-dihydro-3*H*-pyrrolo[3,2,1-*ij*]quinoline-2-carboxylic acid and study of the structure. **Materials and Methods.** Its quinoline synthesized by a condensation of indoline **1** with diethyl ester metantricarboxylic acid **2**:



1 **2** **3**

Results and discussions. The symmetrically independent cells of elementary ester **3,** there are two molecules (**A** и **B**), which differ by some peculiarities of structure. All non-hydrogen atoms of molecule **A**, excluding atoms $C_{(11A)}$ and $C_{(14A)}$, lay in one plane accurate within 0.02 Å. Atoms $C_{(11A)}$ and $C_{(14A)}$ deflect from a root-mean-square plane of the rest non-hydrogen atoms to -0.08 and 0.25 Å respectively. In the molecule **B** atom $C_{(11B)}$ only deflects from a root-mean-square plane of the rest non-hydrogen atoms (accuracy 0.02 Å) to - 0.11 Å.



In the molecule **A** bonding $C_{(7)}$-$C_{(8)}$ 1.414 (7) Å is extended comparing to its average value 1.326 Å, that is explained by the result of creation of quite strong intermolecular hydrogen bonds $O_{(2)}$-$H_{(2O)}$…$O_{(3)}$ (H…O 1.76 Å, O-H…O 149°). In analysis of a bond length, in a molecule **B** [bonding $O_{(1)}$-$C_{(9)}$ 1.249(7) Å and $C_{(7)}$-$C_{(8)}$ 1.404(8) Å are extended (average values 1.210 and 1.326 Å), but bonding $O_{(2)}$-$C_{(7)}$ 1.304(6) Å and $C_{(8)}$-$C_{(9)}$ 1.432(8) Å are shorten (average values 1.333 and 1.464 Å)]. This is proved by pretty weak character of intramolecular hydrogen bond in a molecule **B** $O_{(2)}$-$H_{(2O)}$…$O_{(3)}$ (H…O 1.94 Å, O-H…O 126°), that excludes a possibility of proton transferring from 4-hydroxygroup to a carboxylic atom of oxygen $O_{(3)}$. Between molecules **A** and **B** обнаружены shorten intramolecular contacts $H_{(11C)}$…$C_{(9A)'}$ (*x, y, z*) 2.78 Å, $H_{(10B)}$…$C_{(3B)'}$ (*x, y, z*) 2.84 Å have been discovered.

Conclusions. The structure of ethyl ester 1-hydroxy-3-oxo-5,6-dihydro-3*H*-pyrrolo[3,2,1-*ij*]quinoline-2-carboxylic acid was confirmed by ^{1}H NMR spectroscopy and was proved by X-ray structural analysis.

SYNTHESIS AND PHYSICO-CHEMICAL PROPERTIES NEW BIOLOGICALLY ACTIVE SUBSTANCES DERIVATIVES 5-R-1,3,4-OXADIAZOL -2-IL-THIOACETIC ACID AS POTENTIAL ANTICONVULSANT

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Introduction. A number of synthetic drugs are available to treat epilepsy. But these drugs are produces more side effects. Based on the foregoing the research of anticonvulsants is actual now. Analysis of the literature shows that among the derivatives of 1,3,4-oxadiazole, there are a lot of promising compounds in terms of pharmacy, but at the same time, their biological properties have been insufficiently studied.

Aim. Purpose of the work is synthesis of potential biologically active substances on the bases 5-(3-pyridil)-2-mercapto- 1,3,4-oxadiazoles, prediction of biological activity and study of their anticonvulsive activity.

Material and methods. The synthesis of new amides of 5-(3-pyridil) -1,3,4-oxadiazole-2-yl- thioacetic acid has been carried out. The high reactivity of starting substances of 5-(3-pyridil)-2-mercapto-1,3,4-oxadiazoles makes it possible quite easy modify their structure by alkylation, which extends the probability of finding new effective compounds in this series. Reactions were monitored by thin layer chromatography carried out using pre-coated silica gel plates. By the PASS program the prognosis of their pharmacological activity is carried out for a next planning of pharmacological skreening. Anticonvulsive activity of new compounds was studied.

Results and discussions. The series new derivatives 5- (3-pyridyl)- 1,3,4-oxadiazoles -2-ilthioacetic acid by interaction 5-(3-pyridil)-2-mercapto-1,3,4-oxadiazoles and amide chloracetic acid was synthesized. The structure was improved by the method of UV- and ^{1}H NMR-spectroscopy. The structure of substances synthesized was proved by spectral methods. The purity of the obtained compounds determined by TLC. By the computer program PASS *online* we can make the presumption that all compounds of the group may exhibit high anticonvulsive activities (Pa from 0.5 to 0.7).

Conclusions The series new derivatives 5- (3-pyridyl)- 1,3,4-oxadiazoles -2-ilthioacetic acid was synthesized. The structure was improved by the method of UV- and ^{1}H NMR-spectroscopy. Received experimental data show that all 10 synthesized substances have moderate anticonvulsive activity, and one compound exceed depakine activity.

SYNTHESIS AND PROPERTIES OF 2-(BENZOYILAMINO)(1-R-2-OXOINDOLIN-3-YLIDENE)ACETIC ACID ETHYL ESTERS

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Introduction. Analysis of scientific and patent literature testifies that research of biologically active compounds among derivatives of 2-oxoindoline is promising. They include the well-known amino acids (tryptophane), neurohormone serotonine, series of natural alkaloids and synthetic drugs (indomethacin, dimecarbin).

Aim. The aim of the research is the synthesis of a new group of chemical compounds – 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethyl esters as potentially biological active substances.

Materials and methods. While studying of the research objects in order to prove the structure and purity of the substances synthesized the physical and chemical methods given in the State Pharmacopeia of Ukraine were applied.

Melting points were determined by the capillary method at "PTM (M)" apparatus. The elemental analysis of Nitrogen content was carried out the help of an automatic analyser "CNH", model EA 1108 "Carlo Erba".

IR-spectra were registered by a "Tensor 27" device in KBr tablets, the concentration of the substance − 1%.

^{1}H NMR spectra of the compounds synthesized were recorded on a Varian Mercury VX-200 (200 MHz) spectrophotometer. The solvent is DMSO-D_6, the internal standard is tetramethylsilane (TMS).

Data of elemental analysis correspond to the calculated ones.

2-(Benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acid ethyl ester (3a).

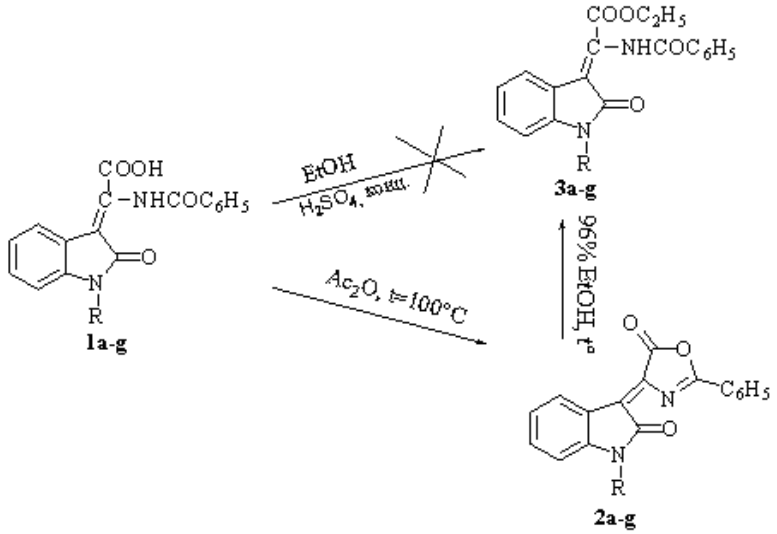
Method A. Boil 2.9 g of the solution of (0.01 Mole) of 1-R-3-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)-1,3-dihydro-2*H*-indole-2-one (**2a**) in 200 ml of absolute ethanol for 6 hours. Then add 100 ml of water to the reaction mixture and continue to heat for 30 minutes. Filter the precipitate obtained, wash with water, dry and recrystallize from ethanol. The yield is 3.10 g (92.5%). The melting point is 176-177^{o}C. Compounds (**3b-g)** were obtained in the same manner.

Method B. Boil 2.9 g of the solution of (0.01 Mole) of 1-R-3-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)-1,3-dihydro-2*H*-indole-2-one (**2a**) in 50 ml of 96% ethanol on water bath for 1 hour. In 2 hours filter the precipitate obtained, wash with ethanol, dry and recrystallize from ethanol. The yield is 3.29 g (98%). The melting point is 176-177^{o}C. Compounds (**3b-g)** were obtained in the same manner.

The mixed sample of compounds obtained by methods A and B does not lead to melting point depression, their ^{1}H NMR spectra are identical.

Results and discussion. An attempt to obtain 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethyl esters through esterification was unsuccessful. Even after a long boiling of the appropriate acids in absolute ethanol in the presence of concentrated sulphuric acid the starting compounds were isolated from the reaction mixture.

Taking into consideration alternative ways to obtain 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethyl esters, for their synthesis interaction of ethanol with 1-R-3-(5-oxo-2-phenyl-1,3-oxazol-4(5H)-ylidene)-1,3-dihydro-2*H*-indole-2-ones (**2a-g)** was proposed, in their turn, they were synthesized by heating of acids (**1a-g)** on boiling water bath with the excess of acetic anhydride (Scheme).



Based on the method described in scientific literature, alcoholysis of 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids azlactone is carried out with its long-term boiling (not less than 6 hours) using 10 times excess of absolute ethanol. We have proposed a preparative method for synthesis of 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethylic esters; it has significant advantages comparing to the current method, namely the use of 96% ethanol in the ratio of 1:4 and heating of the reaction mixture for one hour.

Ethyl esters of 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids (**3a-g)** after crystallization from ethanol are yellow crystalline substances with precious melting points that are soluble while heating in ethanol, dioxane, DMFA, DMSO.

Conclusions. 1. A new method for 2-(benzoyilamino)(1-R-2-oxoindolin-3-ylidene)acetic acids ethylic esters has been developed and their synthesis has been performed.

2. The structure of the compounds synthesized has been confirmed by IR-, ^{1}H NMR – spectroscopy.

SYNTHESIS OF SPIRO-2-OXINDOLE DERIVATIVES AS POTENTIAL SODIUM CHANNEL BLOCKERS

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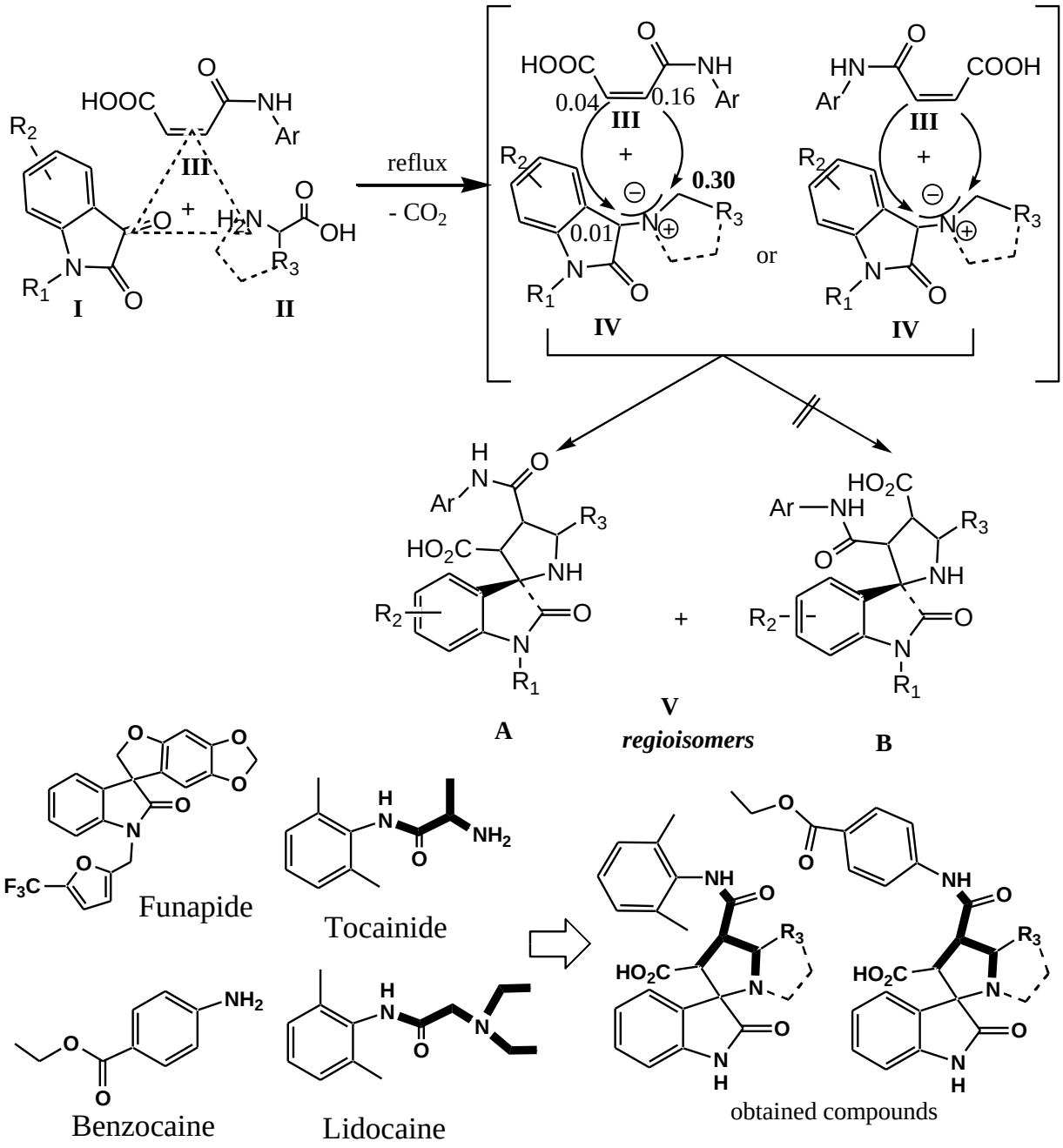
Introduction. Voltage-gated sodium channels (Na_vs) are an important family of transmembrane ion channel proteins and Na_v drug discovery is an exciting field. Sodium channel blockers are used as local anesthetics, in the treatment of cardiac arrhythmia and anticonvulsants. The study of literature dates showed that spiro-2-oxindole derivatives may be promising Na_v-inhibitors, for example, funapide is a novel analgesic. As part of an ongoing work on the research of potent and selective sodium channel blockers among small-molecule inhibitor of the sodium channels.

Aim. Synthesis of spiro-2-oxindole derivatives and search potential sodium channel blockers among them. For the design of the synthesized molecules, we used the structural design and incorporated in their molecules pharmacophores of benzocaine and tocainide, lidocaine.

Materials and methods. ^{1}H NMR spectra were recorded on instruments Varian Mercury VX-200 (200 MHz) in DMSO-d_6 solution, TMS internal standard. The COSY, NOESY, HSQC, and HMBC spectra were recorded using the standard procedure with gradient separation of the signal. Mass spectrum obtained on the instrument GC-MS Varian 1200L with ionizing voltage of 70 eV. Elemental analysis was performed on the elementary analyzer EA 3000 "Eurovektor" (CHNS-analysis). Commercially available reagents and solvents were used without further purification.

3V web server was employed to predict the channel through comprehensive analyses of the internal volumes considering difference as large as possible probe radius and the solvent radius (typically 1.5 Å for water). LAZAR online server was used to predict *in silico* toxicity. T.E.S.T software (2012, U.S. Environmental Protection Agency) and Molinspiration web server (Molinspiration Cheminformatics 2016) were respectively used for predicting LC_{50} and bioactivity of the compound. ADMET profiles were calculated using admeSAR (Laboratory of Molecular Modeling and Design. Copyright 2012, East China University of Science and Technology, Shanghai Key Laboratory for New Drug Design).

Results and discussion. The regioselective three-component condensation of azomethine ylides derived from isatins (I) and α-amino acids (II) with N-arylmaleaminic acids (III) as dipolarophiles (IV) has been realized through a one-pot 1,3-dipolar cycloaddition protocol in boiling aqueous alcohols afforded to the spirooxindoles (V) (possible regioisomers A and B both in racemic) in moderate to excellent yields.



New (V) cyclo-adducts obtained by the above method were characterized by mass-spectrometry, ^{1}H and ^{13}C NMR, and elemental analyses. The regiochemical outcome of the cycloaddition was unam-biguously confirmed by NOE experiments in ^{1}H NMR.

Conclusions. The 1,3-dipolar cycloaddition of azomethine ylides (IV) generated *in situ* from isatins and sarcosine or cyclic amino acids to N-arylmaleaminic acids afforded regio- and stereoselectively the spirooxindoles (V) in moderate to good yields. By using computational chemistry *in silico* methods we have found, that the obtained compounds are potentially non-toxic, does not have mutagenic and carcinogenic properties, and are a potential sodium channel blockers.

CHEMISTRY IN WONDERLAND

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Introduction. One and the same molecule can exist in two different stereoisomers (enantiomers). Stereochemistry studies the relative spatial arrangement of atoms which forms the structure of stereoisomers. This type of isomerism has been found as the most common among organic molecules. It is of great interest for chemical synthesis and pharmaceutical analysis as enantiomers have potentially different effects on the body.

Aim. Determination the difference in the biological effects on the body of S – and R –isomers of Penicillamine, Thalidomide and Ibuprofenum. The establishment of absolute configuration of molecules by using the experimental study of anomalous X-ray diffraction on nucleus of heavy atoms and the theoretical calculation of optical rotation.

Materials and methods. Standard solutions for introduction of Penicillamine, Thalidomide and Ibuprofenum. A polarimeter was used to measure the angle of rotation caused by passing polarized light through the optically active enantiomers.

Roentgenograms were recorded on the X-ray diffractometer Dron-7. Trans-2,3-epoxybutane was used in order to determine the relative rotation of optical isomers which was correlated with the configuration of tartaric acid and then with glycerin aldehyde.

Results and discussion. There is only one stereoisomer in any biological organism so it is not surprising that all the enzymes in our body are stereospecifically, id est react only to one optical isomer. Our research has shown that S – isomers of Penicillamine, Thalidomide and Ibuprofenum have positive effects on a biological organism and can be used as anti-inflammatory and immunosuppressive agents. However, R – isomers of these molecules have quite different effects on a biological organism, moreover these forms are toxic and can lead even to blindness and other negative consequences. Many well-known drugs contain the racemate – an equimolar mixture of a pair of enantiomers. The rotation of one enantiomer in this mixture is compensated by the rotation of the second isomer and their total rotation is equal to 0 that is why a large number of pharmaceutical drugs which contain R – isomers continue to be issued.

Conclusions. We prepared standard solutions for introduction and determined S – and R –isomers of Penicillamine, Thalidomide and Ibuprofenum and established their effects on a biological organism. In conclusion we can say that stereoisomers can show both positive and negative effects and pharmacists should be vigilant while making medicines.

SELECTIVE SYNTHESIS OF ANTICONVULSANT VIA DIRECT ALDOL REACTION OF ISATIN WITH CYCLOHEXANONE

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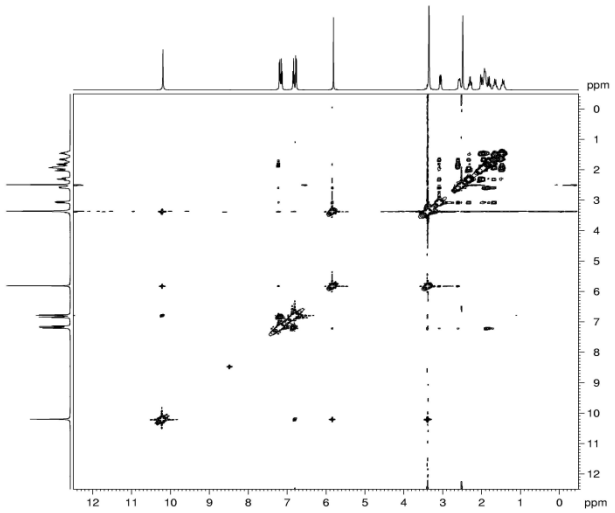
Introduction. 3-Hydroxy-3-substituted oxindole's motifs have gained deal of pharmacological interest over the years. There substituted oxindoles are present in many biologically active molecules, ranging from naturally occurring to synthetically produced ones. The inflexibility of the quaternary carbon locks the adjoined the stereogenic center at the C-3 position into a fixed conformation such that it must receive some responsibility for its interaction with a given receptor. Popp F.D *et al* (*J. Pharm. Science*, 1983, 72, 318-321) reported that cyclohexanone have been condensed with isatin to give racemic the 3-hydroxy-3-substituted oxindole with anticonvulsant activity in the maximal electroshock seizure screen. In connection with our ongoing research towards the synthesis of both natural products and industrially relevant molecules, we are interested in the enantioselective synthesis of the 3-hydroxy-3-(2-oxocyclohexyl)indolin-2-one as anticonvulsant.

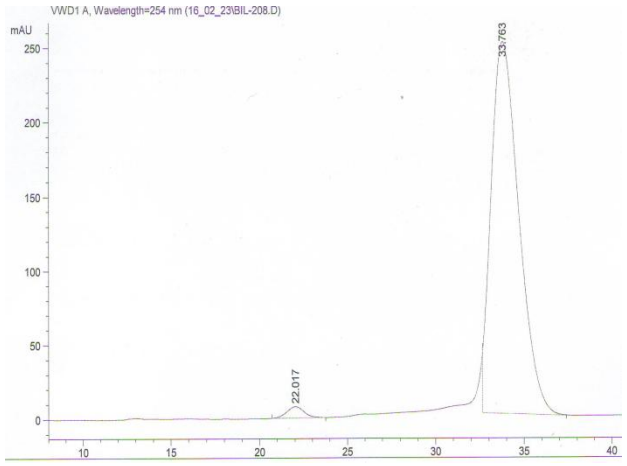
Aim. The aim of this investigation dedicated to demonstrate the selective formation of (-)(*R*)-3-hydroxy-3-[(*R*)-2-oxocyclohexyl]indolin-2-one. Our attention is to employ the resulting isatin and cyclohexanone as acceptors in cross-aldol additions, for the preparation of target molecule in aqueous medium.

Materials and methods. Commercially available and inexpensive chiral 1,2-amino alcohols cross-condensation reaction at room temperature, using both electron rich and poor ketones, have been achieved in good yield. Enantioselectivity of the asymmetric direct aldol reaction has been confirmed by chiral-phase HPLC analyses using Agilent Technologies 1100 series, a ChiralCel OD column: 0,46cm I.D. X 25cm, temp. 20^{o}C (95:5 hexanes/i-PrOH at 1,5ml/min), UV-VIS 254nm, results in parentheses refer to the minor diastereoisomer.

Results and discussion. Our experiments shown that isatine and cyclohexanone in presence of 10 mol % catalysts have been converted into adduct. All reactions were performed at room temperature in mixture CH_2Cl_2/H_2O and under completely heterogeneous conditions. Its structure has been elucidated by 2D-NMR.

A clear NOE difference interaction was observed between OH and CH, which suggests structure as (*R*)-3-hydroxy-3-[(*R*)-2-oxocyclohexyl]indolin-2-one. Absolute configurations assigned by comparison with literature data.





Enantioselectivity (up to 99% ee) and diastereoselectivity (98:2) of the direct aldol reaction has been confirmed by chiral-phase HPLC analyses using Agilent Technologies 1100 series, a ChiralCel OD column: 0,46cm I.D. X 25cm, temp.20^{o}C (95:5 hexanes/i-PrOH at 1,5ml/min), UV-VIS 254nm, results in parentheses refer to the minor diastereomer.

Conclusions. We describe here synthetic route to enantiomerically pure 3-hydroxy-3-(2-oxocyclohexyl)indolin-2-one, which previously have been reported as potent anticonvulsant.

METHODS OF ANALYSIS OF AFLATOXINS IN FOOD

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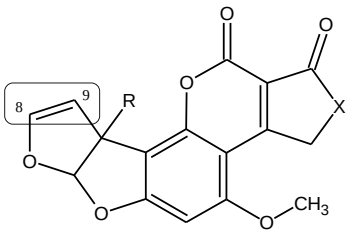
Introduction. One of the factors to increase the population life expectancy is the improvement of the food quality. This demands a continuous improvement of the system of food monitoring for the content of harmful substances like aflatoxins and other toxic substances. Aflatoxins can occur in food, such as groundnuts, tree nuts, maize, rice, figs and other dried food, spices, crude vegetable oils and cocoa beans, as a result of fungal contamination before and after harvesting. Besides, aflatoxins can be found in milk and eggs if the animals consume the infected forage.

Aim. We have tried to study and generalize information on modern requirements for the aflatoxins content in various products accepted in the EU, the USA and Ukraine. Besides, it was necessary to systematize the methods of express-detection and aflatoxins quantitative analysis.

Material and methods. We have used the variety of the information available over the internet and the data of the specialized text-books and periodicals within the framework of our work. The methods of the analysis the most valuable information selection and scientific induction method were applied for this study.

Results and discussion. Aflatoxins are a number of derivatives of the furo[2,3-*h*]-coumarine which are produced by *Aspergillus flavus*. Aflatoxins cause sharp and chronic toxicoses for a human. At a chronic aflatoxicosis (the use with food in a regular dose of 500 μg/kg of body weight) the development of primary cancer of liver is possible for a human. Aflatoxin M1 is a major metabolite of aflatoxin B1 for humans and animals, which may be contained in milk derived from animals fed with aflatoxin B1 contaminated food. In the EU the extreme content of aflatoxin B1 is set at the level of 2-5 μg/kg for grain and nuts. UV detection in long-wave region either TLC are used as screening methods for grains and nuts. Concentration of suspected samples is performed through extraction or special sorbents use. The methods of quantitative determination of aflatoxins can foresee immunoassay or radioimmunoassay, and chromatography such as HPLC. Immunologic methods are based on obtaining antisera to mycotoxins conjugate with bovine serum albumin and have the most sensitivity.



X = CH_2 **B1** R = H; **B2** R = H, 8H,9H;
M1 R = OH; **M2** R = OH, 8H,9H;
X = OCH_2 **G1** R = H; **G2** R = H, 8H,9H

Conclusions. Bringing legal environment in line with the EU directives and the introduction of the modern methods of detection and quantification of aflatoxins for food products is an actual task for Ukraine with respect to the ambition to place leading positions at the world's agro-industrial competition.

SYNTHESIS, PHYSICO-CHEMICAL PROPERTIES AND PHARMACOLOGICAL ACTIVITY OF BIOLOGICALLY ACTIVE SUBSTANCES IN A RANGE OF 2-HYDROXY-4-OXO-4H-PYRIDO [1,2-α] PYRIMIDINE-3-CARBOXYLIC ACID DERIVATIVES

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Introduction. Nowadays one of the important problems of pharmaceutical industry of Ukraine is a problem of import substitution of various drugs and pharmacologically active agents that will reduce dependence on import on the pharmaceutical market, and can expand the range of products of domestic pharmaceutical companies production.

From this point of considerable interest and of perspective application are the derivatives of 2-hydroxy-4-oxo-4H-pyrido[1,2α]-pyrimidine-3-carboxylic acid. As established earlier, unsubstituted derivatives showed relatively high diuretic activity, some substances were promising and currently undergoing extensive pharmacological studies. Taking it into consideration, carrying out the synthesis of analogues of the compounds described before is very interesting.

Materials and methods. For synthesis we have taken as a starting materials 2-amino-pyridine that will result in appropriate esters after interaction with triethylmethane tricarboxylate. The logical subsequent conversion of esters have been obtained is the synthesis of their amides of various nature.

The literature describes a process for obtaining for aryl and alkylamides of 2-hydroxy-4-oxo-4H- pyrido[1,2 α] pyrimidine-3-carboxylic acid by reaction with ethyl ester of 2- hydroxy-4-oxo-4H-pyrido[1,2 a] pyrimidine-3-carboxylic acid with a double, but better - triple number of excess of the corresponding alkylamine in the boiling ethanol. We have taken the synthesis of previously undescribed corresponding amides of 2-hydroxy-4-oxo-4H-pyrido[1,2 α] pyrimidine-3-carboxylic acid.

As substituents in the amide function we have planned radicals, which allow to get the aimed products in this reaction without especial synthetic complications – alkyl, aryl and heterylalkyl.

Results and discussion. The method of the synthesis for 2-hydroxy-4-oxo-4H-pyrido [1,2-α] pyrimidine-3-carboxylic acid has been elaborated. It has been stated, that the technique elaborated is reproducible, yield is up to 85%.

Conclusions. The technique of synthesis can be used in fallowing researches in the range of search 2-hydroxy-4-oxo-4H-pyrido [1,2-α] pyrimidine-3-carboxylic acid using as potential biologically active compounds.

DEPENDENCE OF MICROBIAL ACTION ON THE SUBSTITUENTS IN THE MOLECULES OF N-, R-ALKYL AMINES

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Introduction. The most common gram-positive pathogens of nosocomial infections are Staphylococcus aureus, coagulase-negative staphylococci and enterococci. This tendency creates significant problems since the choice of antimicrobial agents intended to combat drug resistant gram-positive microorganisms is limited.

Aim. The aim of this work was to determine the effect of various functional groups containing in the molecules of N-, R-alkylamines derivatives on their antibacterial activity in relation to some gram-positive strains of microorganisms.

Materials and methods. In order to determine dependence of the microbiological action on the nature of substituents in the molecules of N-, R-alkylamines the following groups were tested: alkylamines, aminoalcohols, N-hydroxymethyl-N-carboxymethylamines, and N-methyl-N-carboxymethylamines. 1% Aqueous solutions of compounds were tested. In accordance with the WHO recommendations to assess the antibacterial activity of N-, R-alkylamines the gram-positive test strains – Staphylococcus aureus ATCC 25923 and Bacillus subtilis ATCC 6633 were used.

Results and discussion. A low sensitivity of the set of microorganisms used to the action of aliphatic amines was determined. The antimicrobial activity of aminoalcohols was slightly higher, and its enhancement is observed with increasing the number of hydroxyethylene radicals in the molecule. Compounds containing a carboxyl and hydroxymethyl group in the molecule was more active, with the increasing number of hydroxyethylene groups the inhibition zones were 20-21 mm for Staphylococcus aureus and 17-25 mm for Bacillus subtilis. Compounds containing a carboxyl group and methyl radicals appeared to be the most promising among the compounds tested. Increase of the number of methyl radicals in the molecules of compounds leads to a significant increase in activity – the inhibition zones are 39-42 mm.

Conclusions. The effect of various functional groups containing in the molecules of N-, R-alkylamines derivatives on their antibacterial activity in relation to some gram-positive strains of microorganisms has been determined. The aliphatic amines and aminoalcohols studied show a weak or moderate activity in relation to strains of Staphylococcus aureus ATCC 25923 and Bacillus subtilis ATCC 6633. Compounds containing a carboxyl group and methyl radicals in the molecule exhibit the greatest antimirobial activity in relation to the gram-positive strains of microorganisms under research.

HISTORY OF DRUGS: IBUPROFEN

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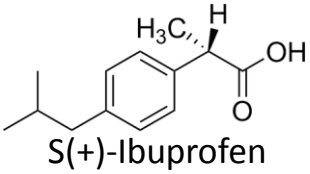
Introduction. Currently, more than 20% of the world's population is constantly using non-steroidal anti-inflammatory drugs (NSAID) - available and effective drugs, which include over 70 biologically active molecules of different chemical structure. Derivatives of salicylic, anthranilic, indolacetic, phenylacetic, propionic acids, pyrazolones and medicines of other chemical groups are among them. However, their main drawback is the ulcerogenic effect on the gastrointestinal tract. This problem in 1969 allowed scientists to discover one of the world's famous drug – "Ibuprofen". It's chemistry and properties were studied in our work.

Aim. The aim of is work is the study of chemical structures, mechanisms of action of NSAID, analysis of available methods of synthesis, search and study of dependencies in the field of "structure-biological activity" of drugs.

Materials and methods. We used original protocols and studied procedures and reports of initial design of NSAID from the group of propionic acids. Methods of scientific-bibliographic research were also applied.

Results and discussion. In this work, we studied basic precondition of origin and milestones of the development of NSAID chemistry from qinin to ibuprofen. The last one was used as an example for detailed study of its properties, methods of synthesis, protocols of clinical trials. We found historical documents, the first research and stages of synthesis of the drug, analyzed all available schemes of industrial synthesis of ibuprofen. The most rational among them is the "green synthesis". Also we generalized some dependencies "structure-activity".

Conclusions. It was that ibuprofen exists in two isomers. One of them is biologically active substance - S(+)-Ibuprofen. The drug is a weak acid (pK_a=5.2), that allows it to bind to plasma proteins and to accumulate in inflammated tissues, acting longer and more effective, in such a manner. Ibuprofen has a weak ulcerogenic effect, because of selectivity to COX- 2 inhibitor. As it has a methyl group, bonded to α-carbon atom, it possesses lower hepatotoxicity. However, this is true when the dose is low. Ibuprofen has side effects too, but in comparison with other NSAIDs they are expressed weakly. That's why Ibuprofen is one of the most popular and well-sold drug all over the world.



S(+)-Ibuprofen

ANTIOXIDANT ACTIVITY BY DPPH RADICAL SCAVENGING METHOD OF (1S,3S,4S,6R)-4-(1*H*-IMIDAZOL-1-YL)-3,7,7-TRIMETHYLBICYCLO[4.1.0]HEPTAN-3-OL DERIVATIVES

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Introduction. Monoterpenes, which are the main components of essential oils, act as allelopathic agents, attractants in plant-plant or plant-pathogen/herbivore interactions or repellants. Their antioxidative capacity is believed to be responsible for the health promoting properties of fruits and vegetables. Several investigations have studied the antioxidant activity of number of monoterpenes in vitro but it not any data about monoterpene (+)-3-carene and its derivatives. On the other side monoterpenes have been recently used to prepare the cationic or anionic moiety of room-temperature ionic liquids. In many cases, these new solvents, based on modifications of monoterpenes, contain chiral centres and/or specific functional groups. Well known, one of the tasks of the synthesis of a bioactive compound is preparation of required enantiomer in optically pure form. Bicyclic monoterpene (+)-3-carene with 3,7,7-trimethylbicyclo[4.1.0]heptane framework is widely used for resolving this type of problems. A structural future of (+)-3-carene is the presence of the reactive C=C double bond and bicyclic bridging system and opens perspectives for synthesis with retention of the natural framework.

Aim. The research aims to indicate which of the structural elements of monoterpene (+)-3-carene are responsible for their antioxidant activity. In this study we have synthesized several (1S,3S,4S,6R)-4-(1*H*-imidazol-1-yl)-3,7,7-trimethylbicyclo[4.1.0]heptan-3-ol derivatives.

Materials and methods. In order to determine the reaction stoichiometry, different molar ratios, expressed as moles of antioxidant per mole of DPPH▪, were tested, ranging from 0.1 to 10. For each molar ratio, the remaining concentration of DPPH▪ at the plateau was determined and graphed, and EC50 was read on the graph as the molar ratio which reduces half of the initial DPPH▪ concentration, was determined from the graph. A lower EC50 value is associated with a stronger DPPH radical scavenging capacity under the same testing conditions. These results for clarity were also expressed in terms of antiradical power (ARP) calculated as ARP=1/EC50 in which larger ARP values represented a larger scavenging capacity. The number of reduced DPPH▪ molecules per one molecule of antioxidant was

defined as σ = 1/(2 x EC50). The results obtained for EC50, σ and ARP of the studied compounds were compared to those of ascorbic acid as well as ionol (control).

Results and discussion. It was observed that 1-{(1R,3S,4S,6S)-4-hydroxy-4,7,7-trimethylbicyclo[4.1.0]heptan-3-yl}-3-methyl-1*H*-imidazol-3-ium (S)-2-[(S)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate **2** shows a similar radical scavenging capacity to that of ascorbic acid, which is probably due to the presence of AscH in its structure. It was observed that 3-ethyl-1-{(1R,3S,4S,6S)-4-hydroxy-4,7,7-trimethylbicyclo[4.1.0]heptan-3-yl}-1*H*-imidazol-3-ium (S)-2-[(S)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate **4** shows a greater radical scavenging capacity than ascorbic acid, which allows us to conclude that the ethyl- group contributes to a greater dislocation of the hydrogen atoms and contributes to their greater readiness to react with the DPPH radical. The radical scavenging capacity of remaining compounds decreases in the range: ionol > 1-{(1R,3S,4S,6S)-4-Hydroxy-4,7,7-trimethylbicyclo[4.1.0]heptan-3-yl}-3-methyl-1*H*-imidazol-3-ium iodide **1** > 1-{(1R,3S,4S,6S)-4-hydroxy-4,7,7-trimethylbicyclo[4.1.0]heptan-3-yl}-3-propyl-1H-imidazol-3-ium iodide *5* > 3-ethyl-1-{(1R,3S,4S,6S)-4-hydroxy-4,7,7-trimethylbicyclo[4.1.0]heptan-3-yl}-1H-imidazol-3-ium iodide **3**. In terms of stoichiometry it was observed that one molecule of compound 4 deactivates two radical molecules, suggesting that the 2 hydrogen atoms of -OH groups in the structure of AscH are responsible for compound 4 radical scavenging activities. Ionol shows a 1:1 stoichiometry, which is in accordance with its chemical formula (one -OH group attached to the aromatic ring capable of donating the H atom). All compounds are characterized by more complex reaction mechanisms, according to fractional σ numbers. It may be seen that compound **2** has σ=1.46 which is the highest σ value among remaining compounds, probably due to the presence of AscH in its structure. **1, 3** and **5** have σ values less than 1, suggesting that it takes more than one molecule of studied compound to deactivate one molecule of DPPH, which is probably due to the fact that an active form capable of donating an H atom has to be formed in the reaction medium prior to the DPPH scavenging step.

Conclusions. It was identified which of the structural elements of (1S,3S,4S,6R)-4-(1*H*-imidazol-1-yl)-3,7,7-trimethylbicyclo[4.1.0]heptan-3-ol is responsible for their antioxidant activity.

THREE-COMPONENT SYNTHESIS OF 2-AMINO-4-(2-O-R-PHENYL)-3-CYANO-6-ETHYL-4,6-DIHYDROPYRANO[3,2-*C*][2,1]BENZOTHIAZINE 5,5-DIOXIDES

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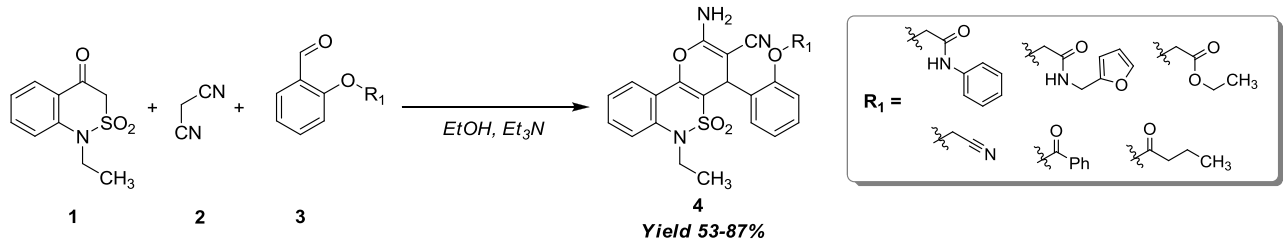
Introduction. 2-Amino-4*H*-pyran core represents a «privileged scaffold». A lot of promising biologically active compounds comprise it within its structure. A common approach toward 2-amino-4*H*-pyrans is three-component interaction of enol-nucleophiles with aldehydes and active methylene nitriles. Various types of aldehydes were introduced in the reaction. Despite this, series of *O*-substituted salicylic aldehydes, which were used in such interaction, is very poor and it is limited to the simplest derivatives. Moreover, salicylic aldehydes being embedded in the 2-amino-4*H*-pyran molecule give 4-(2-*O*-R)phenyl residue. The latter allows to vary the biological properties by introducing different *O*-R-functions into the molecule of salicylic aldehyde.

Aim. Our research was focused on the three-component 2-amino-3-cyano-4*H*-pyrans synthesis based on the various *O*-alkylated and *O*-acylated salicylic aldehydes, 1-ethyl-1*H*-2,1-benzothiazin-4(3*H*)-on 2,2-dioxide and malononitrile. We also aspired to determine the structure of synthesized compounds.

Materials and methods. We used different methods of organic synthesis. Also we used ^{1}H NMR spectroscopy to confirm the structure of synthesized compounds.

Results and discussion. We showed, that the three-component interaction of 1-ethyl-1*H*-2,1-benzothiazin-4(3*H*)-on 2,2-dioxide **1** with malononitrile **2** and *O*-substituted salicylic aldehydes **3** led to the target 2-amino-4*H*-pyrans **4** irrespective of R_1 residue. In general, the reactions were carried out in ethanol in the presence of triethylamine as a catalyst. The products **4** are high-melting solids which can be recrystallized from EtOH/DMF mixture.



1 **2** **3** **4**

Yield 53-87%

Conclusion. In this research we synthesized 2-amino-4-(2-*O*-R-phenyl)-3-cyano-6-ethyl-4,6-dihydropyrano[3,2-*c*][2,1]benzothiazine 5,5-dioxides via three-component interaction of 1-ethyl-1*H*-2,1-benzothiazin-4(3*H*)-on 2,2-dioxide with *O*-substituted salicylic aldehydes and malononitrile.

SYNTHESIS AND DEHYDRATION OF N'-AROYLHYDRAZIDES OF (±)-CIS-3-DICHLOROMETHYL-1,2,2-TRIMETHYLCYCLOPENTANCARBOXYLIC ACID

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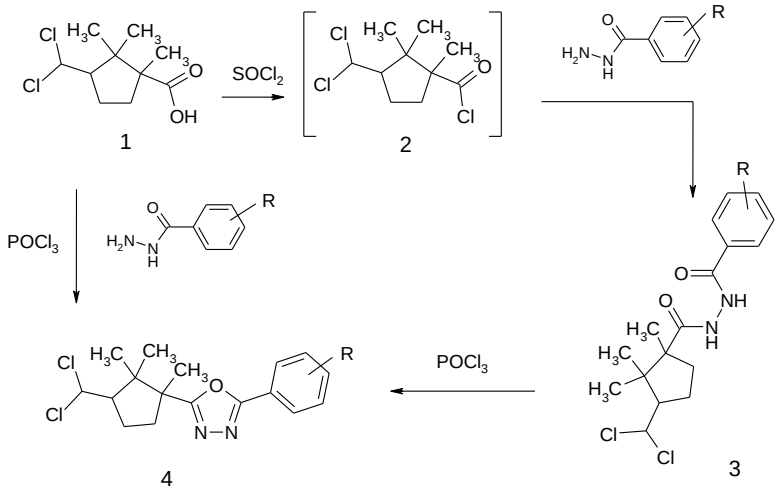
Introduction. (±)-Cis-3-dichloromethyl-1,2,2-trimethylcyclopentancarboxylic acid 1 (scheme) and (±)-camphoric acid have the same 1,2,2-trimethylcyclopentane moiety. The acid 1 was used by us in the synthesis of 1,3,4-oxadiazole derivatives with mentioned moiety, which could not be obtained from (±)-camphoric acid. Camphoric acid derivatives show hypoglycemic, anticonvulsant and diuretic activity and 1,3,4-oxadiazoles are known as compounds with antiproliferative, anticonvulsant, anti-inflammatory, antimicrobial and other activities.

Aim. The aim of work is elaboration method allowed to obtaine new potential biologically active substances which containe 1,3,4-oxadiazole and 1,2,2-trimethylcyclopentane pharmacophores.

Result and discussion. In previous studies the method of synthesis of (1R,3S),(1S,3R)-1,2,2-trimethyl-3-{[2-(R-benzoyl)hydrazinyl]-carbonyl}cyclopentanecarboxylic acids 3 has been developed. In this work we have extended the row of compounds 3 by using new hydrazides and carried out their dehydration. As a result, 2-[(1S,3R),(1R,3S)-3-(dichloromethyl)-1,2,2-trimethylcyclopentyl]-5-(R-phenyl)-1,3,4-oxadiazoles 4 have been obtained. It was managed to obtained oxadiazoles 4 by one-pot reaction from acid 1. The purity of synthesized compounds was proved by TLC, and their structure was confirmed by methods ^{1}NMR spectroscopy and elemental analysis.

Scheme



Conclusions. A one-pot method for the synthesis of oxadiazoles 4 from acid 1 has been developed.

CATALYSIS IN MODERN ORGANIC SYNTHESIS

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Introduction. Modern life is characterized by permanent development of different areas of science, industry, pharmacy, health protection, c.x. etc. These calls stimulate development of modern organic synthesis, by means of that it maybe to get natural connections, their analogues and practically any organic molecules. A catalysis fundamentally changed the state of chemical science of 21 century and is a basis of most synthetic processes.

Aim. Our aim was to select existing problems in realization, application of catalysis and exposure of basic methods of catalysis used in modern organic synthesis.

Materials and methods. We used the searching system Google, special scientific editions, reference sources on a synthesis and catalysis. The materials were systematized by the methods of classification of informative analysis, deduction.

Results and discussion. In a modern organic synthesis most distribution was purchased by 2 types of catalysis: 1 is a homogeneous catalysis by means of metallic complexes. A homogeneous catalysis is applied in a thin organic synthesis, synthesis of pharmaceutical substances and medical preparations; 2 - the heterogeneous catalysis carried out by nano-particles of metals is used in processing of hydrocarbons, natural raw material in a multitonnage synthesis. In addition, there are clusters of transitional metals, it is a border between a heterogeneous and homogeneous catalysis. For catalytic reactions in solution there are 2 border cases: 1 is a catalysis by the particles of one type of metal-ligand, in this case the structure of catalyst during a catalytic cycle is saved; 2 is a catalysis through the "cocktail of catalysts" (of metal-complexes, clusters, nano-particles). For this system a dynamic interconversion is characteristic. To date in an organic synthesis the reaction of cross-coupling (aimed at formation of connections of C-C and carbon-heteroatom) is most often used and as an alternative way of formation of connections a carbon-heteroatom is used reaction of joining. To the catalysts certain requirements are produced: they must be effective, selective, stable. Similarly optimization of criterion matters cost \ efficiency, creation of catalysts suitable to the repeated use without the loss of catalytic activity, creation of adaptive catalytic systems.

Conclusions. It is possible to say as a result of realization of work, that a catalysis will improve in parallel with development of scientific methods, technologies and economic factors, and is the major constituent of synthetic processes.

ISATIN-BASED BIGINELLI-LIKE REACTIONS

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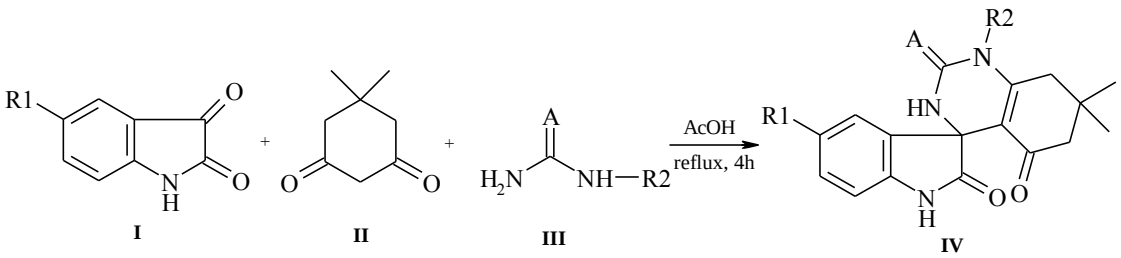
Introduction. More than 100 years ago Italian chemist Pietro Biginelli discovered the acid-catalyzed three-component interaction of ethyl acetoacetate with benzaldehyde and urea that led to 3,4-dihydropyrimidin-2(1*H*)-ones. At first it didn't draw a lot of attention, but later the products were considered to reveal such valuable biological activities as anticancer, anti-inflammatory, antibacterial, antiviral, calcium channel blocking etc. Therefore the scope of this reaction has been extended broadly. Nowadays literature data include different structural variations of initial compounds, catalysts applied and reaction modes of classical Biginelli reaction. Nevertheless the selection of the most suitable conditions for each type of possible interactions remains a challenging task.

Aim. Our research was dedicated to the study of Biginelli-like interaction of isatins with dimedone and (thio)ureas (or their N-substituted derivatives) in acetic acid medium. We also aimed to determine the structure of the obtained compounds.

Materials and methods. Isatins, dimedone, (thio)ureas and their N-substituted derivates were used as starting materials. In order to achieve the research goals, the methods of organic synthesis and ^{1}H NMR spectroscopy were also used.

Results and discussion. Previously the reaction between isatin, dimedone and urea was reported to pass smoothly in ethanol using HCl as a catalyst. We applied a new reaction conditions for such type of interaction, namely glacial acetic acid was used as solvent and acidic catalyst simultaneously. In general the studied interaction of isatins (I) with dimedone (II) and (thio)ureas (III) (the molar ratio 1:1:1.25) was carried out in refluxing AcOH for 4 hours. As a result compounds IV were isolated in high yields. The products are yellow precipitates, which can be recrystallized from ethanol. The structures of obtained compounds were confirmed using ^{1}H NMR spectroscopy.



I II III IV

R_1 = H, CH_3 ; R_2= H, Ph, Ac ; A = O, S

Conclusions. Thus, we have demonstrated convenient and beneficial novel reaction mode for the Biginelli-like interaction of isatins with dimedone and (thio)ureas, which led to the formation of compounds IV in high yield.

SYNTHESIS AND BIOLOGICAL ACTIVITY OF 2-HYDROXY-4-OXO-4*H*-PYRIDO[1,2-*a*]PYRIMIDINE-3-CARBOXAMIDES

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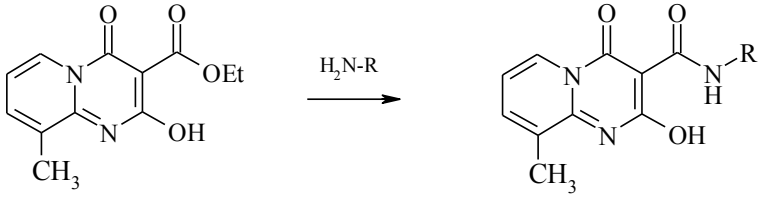
Introduction. The spectrum of nitrogen-containing heterocyclic compounds exhibiting biological and pharmaceutical activity is increasing every year. Despite the fact that drugs are known in medical practice, there is a considerable amount pyrido-pyrimidine derivatives, the biological activity of these compounds are poorly understood.

Aim. The aim of this work was synthesize and to search of antiviral activity for new amidated derivatives of 2-hydroxy-4-oxo-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acids.

Materials and Methods. Based on the results of preliminary forecast for the PASS program showed a high enough probability (not less than 60%) of antiherpes properties as objects of research we selected N-R-amides 2-hydroxy-4-oxo-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acids **2**, which were obtained by amidation of the corresponding esters **1** with primary amines.



1 **2**

***2**: R = 2-dimethylaminoethyl; 2-ethylaminothyl; 2-(2-hydroxyethylamino)-ethyl; 2- diethylaminoethyl; 1-ethylpyrrolidine-2-ilmethyl; 2-piperasine-1-ilethyl; 2-morpholine-4- ilethyl*

Results and discussions. The chemical structure of synthesized compounds is confirmed by ^{1}H NMR spectrum. Percularities of spatial structure and character inside and of intermolecular hydrogen bindings were defined on a certain sample by X-ray spectral analysis method. Study of antiviral activity of amidated derivatives of 2-hydroxy-4-oxo-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidine-3-carboxylic acids allowed to discover in the examined line compounds, which in therapeutic dosages did not exhibit a cytotoxic activity on the processes of microorganism's cells action and, in the meantime, effects high activity (to keep reproduction down significantly) onto herpes simplex virus type I as in vitro, as in vivo.

Conclusions. The ^{1}H NMR spectroscopy we used in the study of the structure of the obtained derivatives. The studied compounds **2** show a high activity onto herpes simplex virus type I.

SYNTHESIS AND ANTI-MICROBIAL ACTIVITY OF N-DERIVATIVES OF PYROLIDIN-5-OH-2(3)-CARBOXYLIC ACIDS AND THEIR AMIDES

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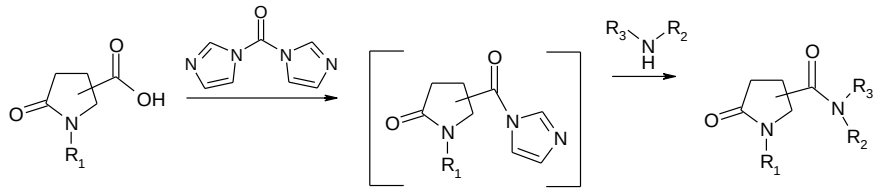
Introduction. It is known from literature sources, that pyrolidoncarboxylic acids are perspective objects for scientific research, and among them compounds have been discovered, which experimentally in vivo displayed stimulating activity on biochemical processes in cells of micro- and macroorganisms, reduced features of stress-syndrome, increased the organism's adaptogenic activity. The compounds have also found with significant anticonvulsant, antitumoral, antimicrobial and many other types of activity.

Aim. To conduct synthesis of new biologically active compounds, to define their physical and chemical properties, to screen microbiologically so that to reveal types and levels of the antimicrobial activity.

Matherials and methods. As the object of our research, N-substituted pyrolidin-5-он-2(3)-carboxylic acids and their amides were applied, which synthesis is presented in the scheme.



Within the synthesis, as precursors N-arylsubstituted pyrolidin-5-он-2(3)-carboxylic acids were used, which amidated upon activation of carboxylic group by force of carbodiimidazole. Structures of synthesized compounds were proved by the current instrumental methods.

Trials of antimicrobial activity of N-substituted pyrolidin-5-он-2(3)-carboxylic acids and their amides were conducted on a sample of serial two-folds dilution in a liquid environment and by diffusion method of water solutions to agar. Тест-microorganisms were the following: Staphylococcus aureus, Bacterium subtilis, Echerichia coli, Pseudomonas aeruginosa, beside this Candida were applied.

Results and discussion. Within experiment, the minimum overwhelming concentration of N- substituted pyrolidin-5-он-2(3)-carboxylic acids and their amides was displayed in the dosages of 5-20 mg/ml.

Conclusions. Compounds that have been obtained are quite interesting scientifically as potential antimicrobial preparations.

INTERACTIONS OF TRYPTANTHRIN ANALOGUE WITH B-CYCLODEXTRIN IN SOLID BINARY SYSTEMS

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Introduction. Thryptanthrin (6,12-dihydro-6,12-dioxoindolo-(2,1-b)-quinazoline) – natural alcaloid contained in various medicinal indigo plants (*Isatis indigotica*, *Strobilanthes cusia* and others) was reported in numerous scientific papers as antimicrobial, antiinflammatory, antitumor, antituberculous compound, etc. Based on this results were synthesized many derivatives and structural analogues, which reproduce partially or completely thryptanthrin structure and effects. One of these compounds is thryptanthrin analogue (TA) – 2-(propylsulfanyl)-5*H*-[1,3,4]thiadiazolo[2,3-*b*]quinazolin-5-one (Fig.1), synthesized by Macaev et al. in 2015, at the Institute of Chemistry (Academy of Sciences of Moldova), demonstrated antituberculosis properties.

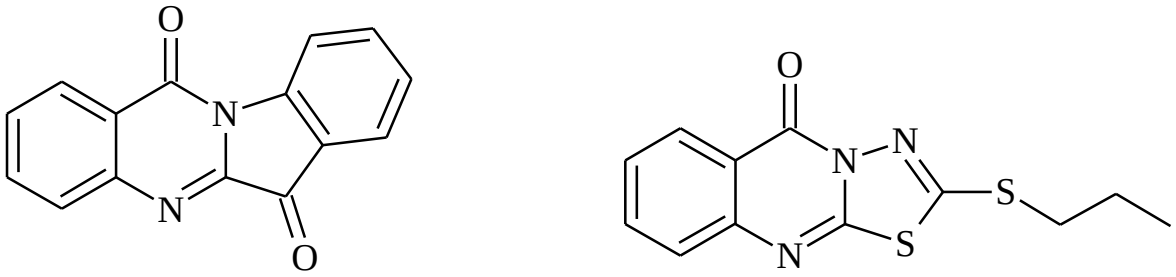

Fig.1 Structural formulas of thryptanthrin (left) and its synthetic analogue (right)

In attempt to amplify antituberculosis effect of thryptanthrin analogue were obtained solid binary systems with β-cyclodextrin (β-CD) – cyclic oligosaccharide consisting of 7 glucopyranose units.

Aim. Study of intermolecular interactions between thryptanthrin analogue – 2-(propylsulfanyl)-5*H*-[1,3,4]thiadiazolo[2,3-*b*]quinazolin-5-one and β-cyclodextrin.

Materials and methods. The following reagents were used: β-cyclodextrin, molecular formula $C_{42}H_{70}O_{35}$, molecular weight 1134.98, was purchased from Sigma; 2-(propylsulfanyl)-5*H*-[1,3,4]thiadiazolo[2,3-*b*]quinazolin-5-one, molecular formula $C_{12}H_{11}N_3OS_2$, molecular weight 277.36, was synthesized and purified in our laboratory.

FT-IR spectra of TA, β-CD and of binary systems were obtained using KBr pellet technique and were colected with PerkinElmer spectrometer „Spectrum 100 FT-IR" in the 4000 to 650 cm^{-1} spectral range with the resolution of 1 cm^{-1}.

Solid binary systems were obtained through kneading method: equimolar amounts of β-CD and TA were weighed and passed in agate mortar. Obtained

mixtures were wetted with appropriate quantity of distilled water so as to obtain a paste. The paste was blended for 60 minutes once in a while adding water to keep paste consistency. Then it was milled for 30 minutes without addition of water. Obtained systems were stored in sealed with parafilm sample tubes, at room temperature (20±2°C).

Results and discussion. In order to study intermolecular interactions between β-CD and TA were colected IR spectra of individual compounds and of binary system (Fig.2).

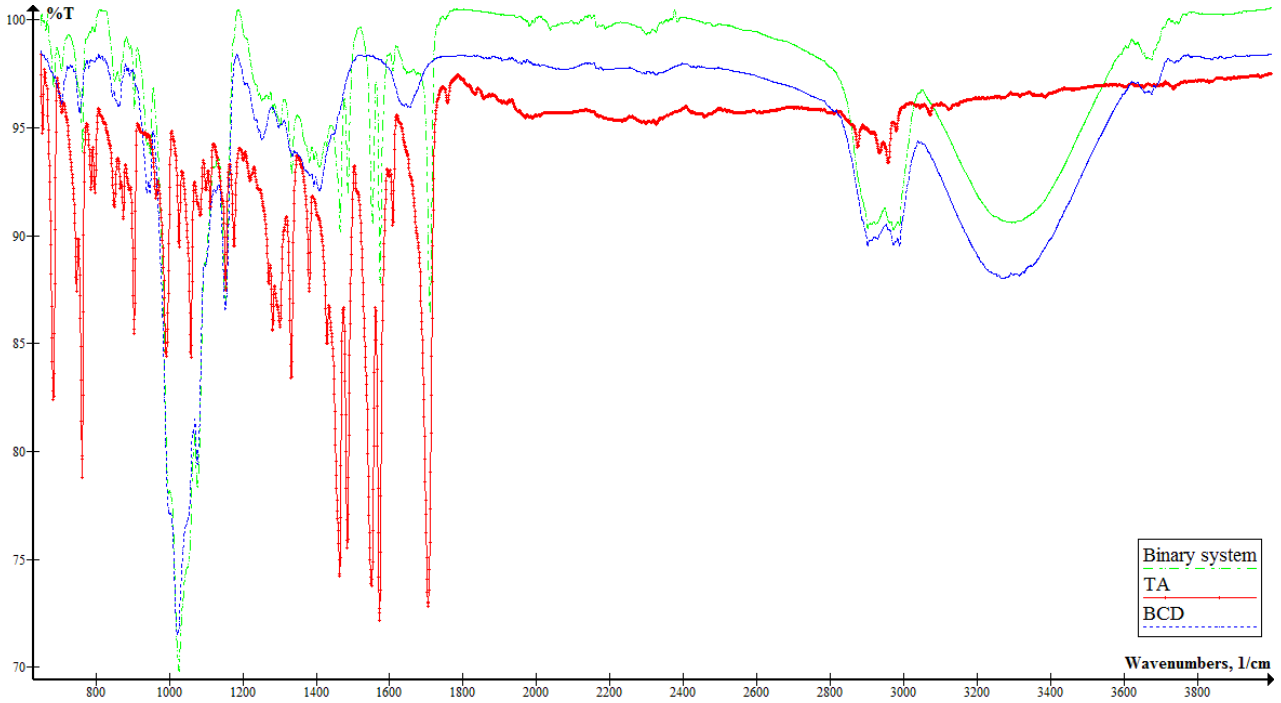

Fig.2 IR spectra of β-CD, TA and binary systems (β-CD – TA)

As can be clearly seen, new bands not occur in binary system spectre, in comparison with TA and β-CD spectra. Occur shifts of binary system peaks comparing with: TA peaks positions (1463 (to 1455) cm^{-1}, 1571 (to 1575) cm^{-1} and 1704 (to 1709)cm^{-1}, corresponding to bending vibrations of ν[C-H], stretching vibrations of $\nu[C=C]_{aromatic}$ and stretching vibrations of ν[C=O], respectively) and β-CD peak position (3265 (to 3300) cm^{-1} corresponding to stretching of ν[OH]). Also we can see changes in the intensities of some binary systems peaks (at 1027 cm^{-1} (bending vibration of ν[O–H]) – binary system peak intensity is higher than intensity of β-CD peak; at 1455, 1575, 1709 and 3300 cm^{-1} binary system peak intensity is lower than intensity of TA and β-CD peaks, respectively). Based on experimental and theoretical data in this area it can be assumed that β-CD interacts with TA through hydrogen bonds formed between the carbonyl functional groups of TA and hydroxyl groups of β-CD.

Conclusions. β-cyclodextrin interact with 2-(propylsulfanyl)-5*H*-[1,3,4]-thiadiazolo[2,3-*b*]quinazolin-5-one in the solid binary systems predominantly through hydrogen bonds.

SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 3-ALKYLSUBSTITUTED 4-CHLORO-2-METHYLQUINOLINES AND THEIR SALTS

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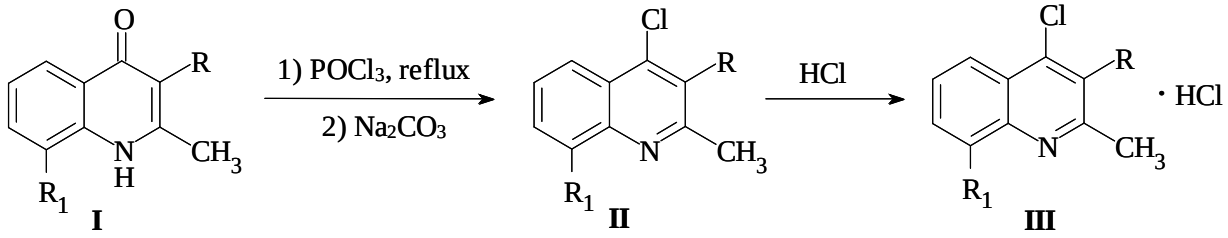
Introduction. In recent times humanity was faced with the problem of antimicrobial resistance occurrence. This problem has rapidly escalated and became threatening. Because of this, the research of novel classes of antibacterial drugs actual more that ever.

Aim. Synthesis and study of the antibacterial activity of novel 3-alkylsubstituted 4-chloro-2-methylquinolines and their hydrochlorides were the aim this research work.

Materials and methods. The target compounds **II** and **III** have been synthesized with yields 55-82% by reaction of corresponding 3-alkyl-2-methylquinolin-4-ones **I** with phosphorus oxychloride under the reflux.



The structure of the compounds obtained was confirmed by ^{1}H NMR spectroscopic method and the Beilstein test.

The study of antimicrobial activity of the compounds **II** and **III** have been carried out using the agar diffusion screening method known as “well method”. Test-strains of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Bacillus subtilis* and *Candida albicans* recommended by WHO were used. The serial dilution method has been used for determination of the minimum inhibitory concentration (MIC) for the most promising compounds.

Results and discussion. The results of antimicrobial activity screening have shown that novel 4-chloro-2-methylquinolines **II** and their hydrochlorides **III** have a moderate broad-spectrum activity but hydrochlorides **III** tested were more active against all test-strains. It may be explained by higher water-solubility of these compounds.

Conclusions. According to the results, 4-chloro-3-hexyl-2-methylquinoline hydrochloride was chosen as promising antibacterial compound with MIC 0.5-1.0 mg/ml for *Staphylococcus aureus* and 1.0-2.5 mg/ml for *Escherichia coli*.

SYNTHESIS OF NEW [1,2,4]TRIAZOLO[4,3-a]PYRIDINE-3-YL]ACETAMIDE DERIVATIVES WITH AN 1,2,4-OXADIAZOLE CYCLE

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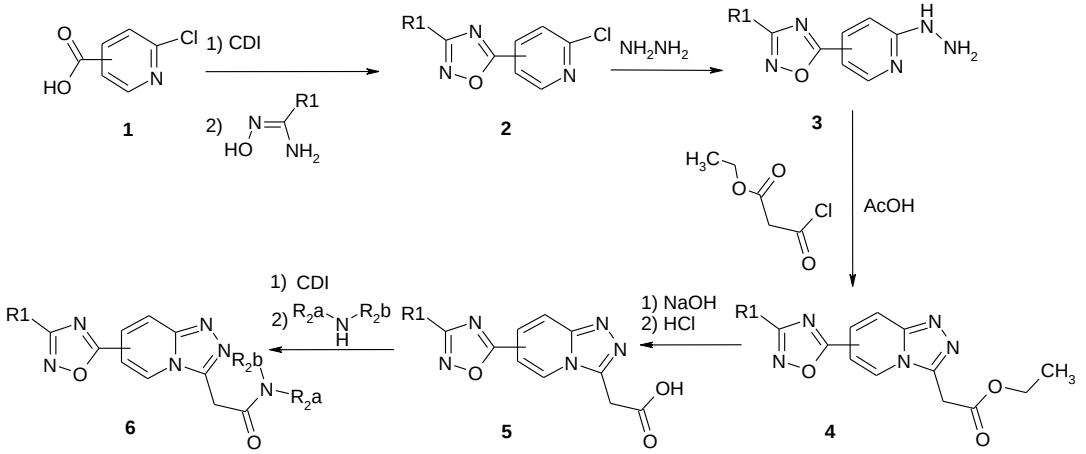
Introduction. Triazole derivatives often exhibit broad biological activities in medicine and agriculture. Pyridine derivatives have also displayed various biological activities. The chemistry of 1,2,4-triazoles and their fused heterocyclic derivatives have received considerable attention owing to their synthetic and effective biological importance. [1,2,4]triazolo[4,3-a]pyridine derivatives possess diverse pharmaceutical and biological activities, i.e., as antibacterial, antithrombotic, anticancer, anti-inflammatory, herbicidal, antifungal, anticonvulsant, anxiolytic, antipsychotic, and antidepressant agents. The incorporation of an [1,2,4]-oxadiazole cycle into the main scaffold is considered to be a good way to produce novel active compounds.

Aim. In view of all these facts, and as a continuation of research on bioactive heterocycles, herein a series of novel 1,2,4-triazolo[4,3-a]pyridines with an [1,2,4]-oxadiazole cycle were synthesized. Prognosis and study of their pharmacological activity was also carried out.

Materials and methods. Our new target compounds 2-[(1,2,4-oxadiazol-5-yl)-[1,2,4]triazolo[4,3-a]pyridine-3-yl]acetamides were prepared following the process presented in Scheme.

Scheme



The reaction sequence starts from known 2-chloropyridine carboxylic acids 1 dissolved in anhydrous DMF (N,N-Dimethylformamide) with an excess of CDI (carbonyldiimidazole). Adding an excess of corresponding amidoxime resulted in the

formation of corresponding 2-chloro-[3-R_1-1,2,4-oxadiazol-5-yl]pyridine 2. 2-hydrazine-[3-R_1-1,2,4-oxadiazol-5-yl]pyridines 3 have been synthesized by hydrazinolysis with hydrazine hydrate and subsequent heating until the end of reaction in dioxane. Further synthesis of ethyl 2-[(3-R_1-1,2,4-oxadiazol-5-yl)-1,2,4-triazolo[4,3-a]pyridine-3-yl]acetates 4 were performed following a procedure of the addition of ethyl malonylchloride to the solution of 2-hydrazine-[3-R_1-1,2,4-oxadiazol-5-yl]pyridines 3 in acetic acid with reflux for 2h. The obtained products 4 then were hydrolysed by sodium hydroxide in aqueous methanol during 12h and then was acidified with hydrochloric acid to obtain corresponding 2-[(3-R_1-1,2,4-oxadiazol-5-yl)-1,2,4-triazolo[4,3-a]pyridine-3-yl]acetic acids 5. The products 5 were further reacted with CDI, in order to activate the carboxyl group for direct reaction with corresponding amines via amide bond formation. As a result, we have obtained novel 2-[(1,2,4-oxadiazol-5-yl)-[1,2,4]triazolo[4,3-a]pyridine-3-yl]acetamides 6.

The purity and structures of the synthesized compounds were confirmed by elemental analysis and ^{1}H NMR spectroscopy data.

In order to predict the pharmacological activity of 2-[(1,2,4-oxadiazol-5-yl)-[1,2,4]triazolo[4,3-a]pyridine-3-yl]acetamides, we performed a pharmacophore-based parallel *in silico* screening experiments. Our collection of structure- and ligand-based interaction models was used, which revealed potential inhibitory activity of the compounds against Cytochrome P 450 (CYP) known to be a heme containing protein superfamily of enzymes metabolizing a broad variety of xenobiotics, including drugs and toxic chemicals. In addition, our experiment also revealed potential inhibitory activity against 5-HT2C (G-protein coupled receptor), known to be a potential target for the treatment of central nervous system (CNS) disorders.

Antimicrobial activity (bacterial and fungal) of some of the synthesized compounds was studied *in vitro*. Antimicrobial screening was performed by CO-ADD (The Community for Antimicrobial Drug Discovery), funded by the Wellcome Trust (UK) and The University of Queensland (Australia). The inhibition of growth was measured against 5 bacteria: *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, and 2 fungi: *Candida albicans* and *Cryptococcus neoformans*.

Results and discussion. New target compounds 2-[(1,2,4-oxadiazol-5-yl)-[1,2,4]triazolo[4,3-a]pyridine-3-yl]acetamides have been synthesized and obtained with satisfactory yields. Unfortunately, the compounds deemed active in the Primary Screen (≤32 μg/mL) were not confirmed hits (≤16 μg/mL) in the dose response assay, therefore further development was not prioritized.

Conclusions. However knowing that such type of scaffold could possess wide range of pharmacological activity we would continue searching new biologically active substances among [1,2,4]triazolo[4,3-a]pyridine-3-yl]acetamide derivatives.

SYNTESIS, CHARACTERIZATION AND SURFACE STRUCTIURE OF $Ag@Fe_3O_4$ CORE-SHELL *NANOCOMPOSITE*

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Introduction. Magnetite nanoparticles are the most used magnetic material for biomedical applications. Surface modification of the magnetite particles can be used to prevent aggregation, improve stability, exhibit many interesting properties that can be exploited in a variety of biomedical applications such as drug delivery, magnetic resonance imaging, magnetic hyperthermia, cell separation and many others.

For systems such as core-shell is a very important issue for determining the structure of the surface. One of the modern methods used to study the surface is an optical spectrometry – surface plasmon resonance spectroscopy (SPR). SPR is the basis of many standard tools for measuring adsorption of material onto planar metal (typically gold or silver) surfaces or onto the surface of metal nanoparticles. It is the fundamental principle behind many color-based biosensor applications and different lab-on-a-chip sensors.

Silver nanoparticles have unique properties for biomedical application and plasmonic properties of silver nanoparticles have been studied, and they are extraordinarily efficient at absorbing and scattering light. Such properties make the silver nanoparticles ideal for numerous technologies, including biomedical, materials, optical, and antimicrobial applications.

Aim. Optimize the process for the synthesis of $Ag@Fe_3O_4$ magnetic nanocomposite of the "core-shell" type with the islet cover with preservation of the magnetic properties. To get more information about silver nanoparticles and to improve their applications or develop new ones, careful study related to their stability, functionality, particle sizes and also their materials and physical behaviors are essential.

Materials and methods. Magnetite with the islet silver coating obtained by the original single-phase method of chemical co-precipitation with the temperature increasing up to 60 – 70°C. The studies were conducted by the following methods: X-ray analysis, semi-quantitative phase analysis, scanning electron microscopy. The specific surface area of the samples was determined by thermal desorption of argon. The specular reflectance measurements of the nanoparticles were measured using a UV-visible spectrophotometer.

Results and discussions. In the diffraction pattern the silver peaks at 44.6°, 52° and 76.65° were registered, while magnetite peaks did not disappear. It may indicate the islet surface of the magnetic cores. According to the data of scanning

electron microscopy the average particle sizes of $Ag@Fe_3O_4$ they were 23 nm. $Ag@Fe_3O_4$ compared to the Fe_3O_4 one has a slightly larger specific surface area. Magnetization of saturation for the sample with a silver coating it is 62.5 emu/g.

The UV-Visible spectra of the samples measured in the range 100 – 1200 nm, using a double beam UV-Vis spectrophotometer. The strong broad reflection bands located between 250 and 710 nm for both samples with the *minimum value* ~440 nm assigned to a surface plasmon resonance typical of silver nanoparticles, is well-documented for various metal nanoparticles with sizes from 2 to 100 nm. Hyperchromic effect observed in the band of $Ag@Fe_3O_4$ nanocomposites. Such effect in the case of continuous nanoshells is more significant. It can be assumed, that the maximum shift caused by the influence of magnetite.

Clusters of surface layer are sensitive to changes of the metal core, such as the oxidation state and the number of metal atoms in the cluster. The plasmon width increases with decreasing cluster size for typical cluster shape distributions. The peak appears in the band of $Ag@Fe_3O_4$ nanocomposites at ~265 nm, indicating the formation of sub-*nanometer silver clusters* (*smaller than 1 nm*). The peak at ~770 nm can be attributed to an *increase in* the *thickness* or/and surface area of silver clusters. The location of this resonant peak matches to a flat silver clusters.

Among the samples it is apparent that there is a general increase in the measured surface area as the silver coat appears. This fact suggesting that the coverage of magnetite by silver is not complete. It can be assumed, that the silver atoms form “island-like” structures on the surface of magnetite. Such organization of surface layer will increase the contact area of the silver nanocomposite with bacteria or viruses, greatly improving its bactericidal effect. It is known that particles with a large specific surface area have a high chemical and biochemical activity.

Conclusion. The method of one-pot synthesis of $Ag@Fe_3O_4$ nanoparticles consisting of a spherical core of magnetite and silver islet shell has been developed. The particles are almost monodispersed with the average size <d> ~ 23 nm. The silver nanoparticles form of islands (20-100 atoms) on the surface of magnetite. As-synthesized core-shell nanocomposities $Ag@Fe_3O_4$ have good *perspectives* of applications, including chemical and biological sensing, due to the broad absorption in the optical region associated with localized surface plasmon resonance. Formation of $Ag@Fe_3O_4$ composite structures such as "core-shell" will allow combining magnetic controllability of the magnetite core with bactericidal and bacteriostatic properties of the silver shell. This effect is very interesting from the perspective of using particles with the "core-shell" structure in pharmacy and medicine to create new medicines.

SYNTHESIS AND ANTIMICROBIAL PROPERTIES OF 3-ALKYL-2-METHYLQUINOLIN-4-THIONES

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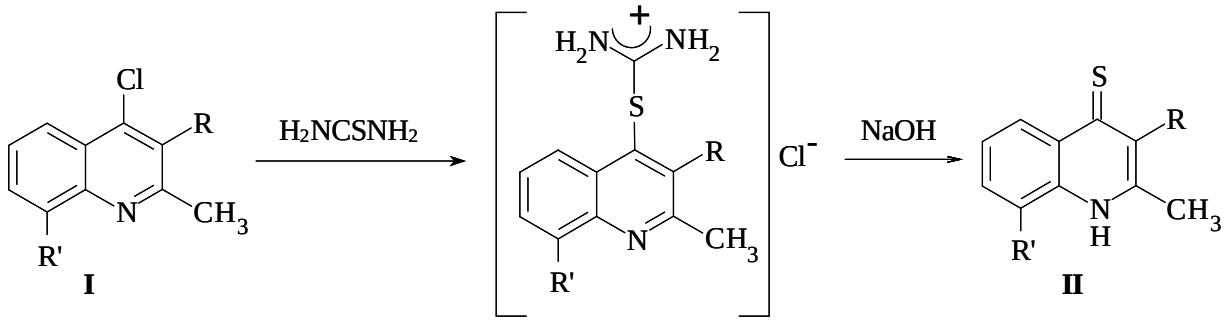
Introduction. The need for novel antimicrobial drugs is greater than ever because of the emergence of multidrug resistance in common pathogens and the rapid emergence of new infections.

Aim. Development of versatile method of synthesis of 3-alkyl-2-methylquinolin-4-thiones and study of their antimicrobial properties were the aim our research work.

Materials and methods. The 3-alkyl-2-methylquinolin-4-thiones **II** have been synthesized *via* reaction of corresponding 4-chloro-2-methylquinolines **I** with thiourea and further alkaline hydrolysis of isothiuronium salts obtained. The structure of the compounds **II** was confirmed using ^{1}H NMR spectroscopy.



yields 53-80%

The study of antimicrobial properties of novel 3-alkyl-2-methylquinolin-4-thiones **II** have been performed using the agar diffusion screening method ("well method") and the serial dilution method for determination of the minimum inhibitory concentration (MIC) for the most promising compounds. Test-strains of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Bacillus subtilis* and *Candida albicans* recommended by WHO were used.

Results and discussion. The results of antimicrobial activity screening of 2-methylquinolin-4-thiones **II** have shown that most of 3-alkylsubstituted derivatives are more active against all test-strains than 3-unsubstituted analogues. Moreover, they have anticandidal activity. The exception was 3-benzyl-2,8-dimethylquinolin-4-thione that displayed the weakest antibacterial activity. It may be explained by high lipophilicity of this compound.

Conclusions. Based on the results, 3-ethyl-2-methylquinolin-4-thione was chosen as promising antimicrobial compound with MIC 1.0-2.5 mg/ml for *Staphylococcus aureus* and 1.0-2.5 mg/ml for *Escherichia coli*.

THE DERIVATIVES OF 4-R-PHENYL(BENZYL-, ALLIL-)-5-(R^1)-PHENYL(OXY-, THIO-, AMINE)-METHYL-1,2,4-TRIAZOL(4*H*)- 3-THIONS AS POTENTIAL ANTIULCER AGENT

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Introduction. In recent years, great attention of scientist in many countries of world is devoted to the synthesis of derivatives of 1,2,4-triazole. This is due to several factors – wide opportunities of introducing radicals into the heterocyclic ring, which allows you to vary widely series of compounds, as well as the high potential of the derivatives as potential pharmacological agents.

Aim. The work devoted to the synthesis and researches about physical-chemical properties of the newly synthesized compounds the derivatives of 4-R-phenyl(benzyl-, allil-)-5-(R^1)-phenyl(oxy-, thio-, amine-)-methyl-1,2,4-triazol(4*H*)- 3-thions and the study of their antiulcer activity. Analysis of the literature shows that among the derivatives of 1,2,4-triazol(4*H*) there are a lot of promising compounds in terms of pharmacy, but at the same time, their biological properties have been insufficiently studied.

Materials and methods. In order to search for new bioactive substances - potential antiulcer 4-R-phenyl(benzyl-, allil-)-5-(R^1)-phenyl(oxy-, thio-, amine-)-methyl-1,2,4-triazol(4*H*)-3-thions were synthesized. Therefore, as the starting materials for the formation of the 5-substituted triazoles nucleus, we selected anilines - unsubstituted and 4-substituted ones, phenols and thiophenols. Resulting from the alkylation of ethyl chloroacetate and subsequent hydrazinolysis hydrazides were involved into interaction with phenyl(benzyl-, allil-) isothiocyanates. Reaction was carried out in an alcohol in the presence of alkali solution. Target products have been obtained with satisfactory yields. The structure of obtained 4-R-phenyl(benzyl, allil)-5-(R^1)-phenyl(oxy, thio, amine)-methyl-1,2,4-triazol(4*H*)-3-thions was proved by modern physical and chemical methods of ^{1}H NMR-spectroscopy, the purity was confirmed by the method of thin-layer chromatography. The computer prognosis of biological activity spectrum of all new compound by program PASS has set that the several substances are able to show the antiulcer and antihelicobacter activity (activity indexes of compounds are in the range for 0.5 to 0.6). It was determined also by PASS program high possibility such pharmacological activities as analgesic, sedative and antineurotic. Pharmacological screening for antiulcer activity has been carried out. **Results and discussion**. New R-phenyl(benzyl, allil)-5-(R^1)-phenyl(oxy, thio, amine)-methyl-1,2,4-triazol(4*H*)-3-thions were synthesized. The structure of the compounds obtained was proved by methods NMR-spectroscopy and their purity and individuality was determined by thin-layer chromatography.

Conclusions. The results of studying an antiulcer activity have shown that the compounds synthesized are antagonists against the ulcer activity of mixture of ethanol-prednizolone. Performed researches have allowed to select two leading compounds for in-depth researches.

THE PURPOSEFUL SYNTHESIS OF ANTIULCER SUBSTANCES IN THE SERIES OF 4-(R-PHENYL)-5-PHENOXYMETHYL-3-THIO-1,2,4-TRIAZOLES (4 *H*) DERIVATIVES

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Introduction. Now gastric ulcer is one of the leading diseases in gastroenterology, because this pathology is mostly affects people most able-bodied and active-age, causing severe complications, reduced work capacity, worsening the quality of life. About 10% of people develop a peptic ulcer at some point in their life. They resulted in 301,000 deaths in 2015 down from 327,000 deaths in 1990. The growing population with diseases of the gastrointestinal tract is considered to be a problematic issue of the XXI century, which is increasingly attracting the attention of scientists and practitioners in many countries. A number of synthetic drugs are available to treat ulcers. But these drugs are expensive and produce more side effects. The ideal aims of treatment of peptic ulcer disease are to relieve pain, heal the ulcer, and delay ulcer recurrence. Based on the foregoing the research of anti-ulcer drugs is actual now. Analyzing published data we found that the 1,2,4- triazoles (4*H*) derivatives is quite promising matrix for the search of the anti-ulcer agents on its basis. Careful attention to these compounds is primarily due to their high potential as possible pharmaceutical substances.

Aim. The aim of this work was to synthesize new 4-phenyl-5-(4-R-phenoxymethyl)-1,2,4-triazole-3-ylthio-1-(R_1)-acetophenones, to prove their structure and то screen these newly synthesized compounds for anti-ulcer activity.

Material and methods. The synthesis of new 4-phenyl-5-(4-R-phenoxymethyl)-1,2,4-triazole-3-ylthio-1-(R_1)-acetophenone compounds has been carried out. The synthesis of initial 4-phenyl-5- phenoxymethyl -1,2,4-triazole- 3-thiones was carried out from the corresponding phenols. Resulting from the alkylation of ethyl chloroacetate and subsequent hydrazinolysis substituted phenoxyacetic acid hydrazides were involved into interaction with phenylisothiocyanates with vigorous stirring in ethanol. Several key types of the reactions were generally used us that allowed to obtain new started 4-phenyl-5-phenoxymethyl -1,2,4-triazole- 3-thiones. The existence of thiol-thione tautomerism is known for the compounds, and thione forms predominates according to the data of ^{1}H NMR spectroscopy. To further transformations 4-phenyl-5- phenoxymethyl -1,2,4-triazole- 3-thiones synthesized were alkylated by chloroacetophenones in a homogeneous base catalysis conditions, resulting to the compounds 4-phenyl-5-4-

(R)-phenoxymethyl-1,2,4-triazole-3-ylthio-1-(R_1)-acetophenones. Reactions were monitored by thin layer chromatography carried out using pre-coated silica gel plates.

Results and discussions. Target products have been obtained with satisfactory yields. The structures of synthesized compounds were verified on the basis of elemental analysis and ^{1}H NMR-spectroscopy. The NH group protons signal after alkylation disappears in finished compounds. The signals of aromatic protons were observed in the ranges 6.75–8.20 ppm. As shown in Table 2, the signals of both methylene groups associated with sulfur and oxygen atom are common and occur. Due to the absence of protons in their surroundings they look like singlet. The signals of methylene groups have been interpreted by us in accordance with the electronegativity of neighboring atoms so – signals at 5,28-5,29 ppm has been attributed to the presence of a group OCH_2; at 5,15-5,18 ppm – group SCH_2. Methyl groups of the *tert*-butyl residue are shown on the spectra as a single signal intensity in 9 protons at 1,20-1,25 ppm. The purity of the obtained compounds determined by TLC. Prediction of biological activity derived substances was conducted using a computer program PASS. To optimize the pharmacological screening of new compounds «drug-like» parameters have been calculated and simulation of biological properties has been done. It was established that the synthesized compounds comply with Lipinski's Rule of Five and can be recommended for experimental biological tests. Based on data PASS-prediction as priority directions for experimental trials screening for anti-ukcer and anti-helicobacter activity has been chosen. By the computer program PASS *online* we can make the presumption that all compounds of the group may exhibit high anti-ulcer (probable activity (P_a) by inhibition of histamine H_2-receptor from 0.52 to 0.69) and anti-helicobacter activities (P_a from 0.50 to 0.65).

The most perspective substances for experimental biological tests were elected.

A docking study synthesized compounds to antiulcer biotargets were carried out; was established ability to «structure-leader» to inhibit histamine H_2-receptor, enzyme microsomal prostahlandynsyntaze and the growth of the pathogen Helicobacter pylori as probable mechanisms of antiulcer action.

Conclusions The group of new 4-phenyl-5-4-(R)-phenoxymethyl-1,2,4-triazole-3-ylthio-(R_1)-acetophenones have been synthesized by alkylation of initial 4-phenyl-5- phenoxymethyl -1,2,4-triazole- 3-thiones with chloroacetophenones. The structures of the synthesized compounds have been proved by elemental analysis and ^{1}H NMR spectroscopy data. All substances for which the PASS program prognosis was carried out can show themselves as potential anti-ulcer and anti-helicobacter drugs.

SYNTHESIS OF 6-AMINO-1-R-2-THIOXO-2,3-DIHYDROPYRIMIDIN-4(1*H*)-ONES AS PROMISING SYNTHONS FOR CONSTRUCTION OF NEW CONDENSED HETEROCYCLIC SYSTEMS

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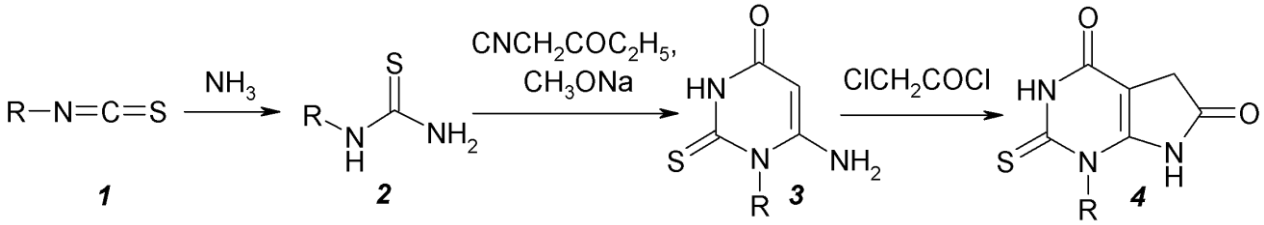
Introduction. Previously, we have demonstrated the possibility of construction of new 1-alkyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-2,4,6-triones which comprise the novel heterocyclic system. These compounds were obtained by the interaction of 6-amino-1-R-uraciles with 2,2-diphenyl-2-chloroacetylchloride. Synthesized derivatives were evaluated to possess valuable biological activities and as a result compounds that have antiexudative and antihypoxic activities were found among the pyrrolo[2,3-*d*]pyrimidine-2,4,6-triones. In continuation of these investigations, we have drawn their attention on the synthesis of 2-thioanalogues of abovementioned fused heterocycles to extend the series of pyrrolo[2,3-*d*]pyrimidines and to determination of "structure-bioactivity" relations. Furthermore, the SciFinder® database showed the poor data about synthesis, bioactivity and chemical properties of such 2-thioxo derivatives.

Aim. Our research was focused on the synthesis of 6-amino-1-R-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones for their further application for new condensed heterocyclic systems construction.

Materials and methods. We used common methods of organic synthesis. Also we used ^{1}H NMR spectroscopy to confirm the structure of synthesized compounds.

Results and discussion. Initial thioureas **2** were obtained by the action of ammonia on the isothiocyanates **1**. The next stage was the interaction of the thioureas **2** with ethyl cyanoacetate in the presence of sodium methylate which led to the 6-amino-1-R-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones **3**. Interaction of dihydropyrimidines **3** with 2-chloroacetylchloride allowed to obtain the target 1-R-2-thioxo-2,3,5,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-diones **4** in good yields.



Conclusion. Thus, we have shown that 6-amino-1-R-2-thioxo-2,3-dihydropyrimidin-4(1*H*)-ones are convenient synthons for construction of new 1-R-2-thioxo-2,3,5,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] pyrimidine-4,6-diones.

SYNTHESIS AND ANTIMICROBIAL ACTIVITY STUDY OF 2,4-DIOXO-*N*-ARYL-3-(ARYLMETHYL)-1,3,7-TRIAZASPIRO[4.4]NONANE-7-CARBOXAMIDES

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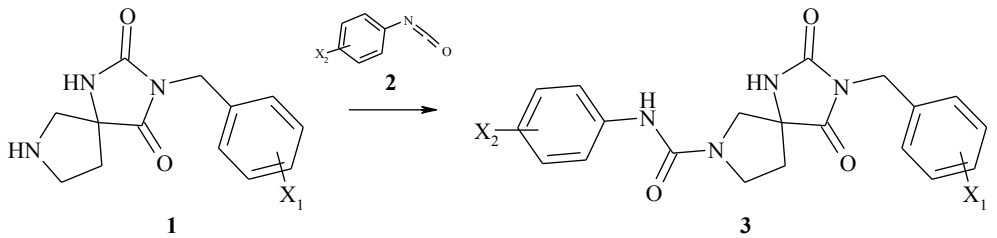
Introduction. The recent studies in the field of imidazoline-2,4-dione, which is also called hydantoin, confirm the high potential for antibacterial activity of the compounds with this fragment. Hydantoins were also reported as the compounds potentiating the antibiotic activity of oxacillin and cloxacillin, that is why the design of the promising antibacterials based on hydantoin moiety modification is a good way for modern antibacterial drugs discovery. It was earlier reported that 3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonan-2,4-diones and the products of their secondary amine group acylation with arene carboxylic acids showed high antibacterial activity against the gram-positive and gram-negative bacteria and some strains of fungi.

Aim. The aim of our research was the development of synthetic method for 2,4-dioxo-*N*-aryl-3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonane-7-carboxamide preparation and antimicrobial activity study thereof.

Materials and methods. All the reagents were obtained from the commercial sources. Synthesis was performed using the standard equipment for parallel liquid-phase procedures. The melting points (°C) were measured with a Kofler melting point apparatus and were not corrected. The structures of the obtained compounds were assigned using the ^{1}H, ^{13}C NMR and liquid-chromatography-MS methods. The antimicrobial activity study against the strains of gram-positive and gram-negative bacteria was performed using the agar "well" diffusion method.

Results and discussion. For the preparation of the target 2,4-dioxo-*N*-aryl-3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonane-7-carboxamides **3** the reaction of the starting 3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonan-2,4-diones with aromatic isocyanates was used according to the scheme 1.

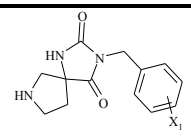
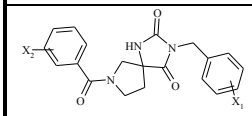
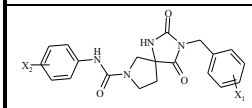
The series of the 2,4-dioxo-*N*-aryl-3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonane-7-carboxamides **3** were tested for antimicrobial activity against the standard strains of bacteria and the strain of *Candida albicans* fungi. It was found that introduction of the aromatic urea fragment increases the antibacterial activity of the compounds **3**.



Scheme 1 *– Syntehsis of 2,4-dioxo-N-aryl-3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonane-7-carboxamides*

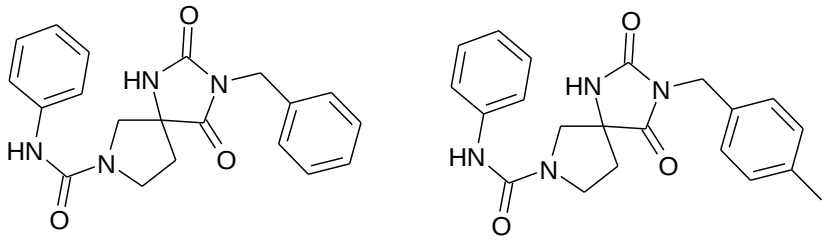
The obtained 2,4-dioxo-*N*-aryl-3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonane-7-carboxamides **3** were found to be more active than the 3-(arylmethyl)-1,3,7-triazaspiro[4.4]nonan-2,4-diones **1** and also than the compounds modified with aroyl radicals (table 1).

Table 1

№	The average diameter of growth inhibition zones, mm					
	Gram-positive bacteria			**Gram-negative bacteria**		**Fungi**
	S. a.	***B. c.***	***E. c.***	***P. v.***	***P. a.***	***C. a.****
	16	16	15	14	14	14
	16	16	15	13	13	13
	17	17	17	16	16	20

**S. a.*– *Staphylococcus aureus* (ATCC 25923); *B. s.*– *Bacillus subtilis* (ATCC 6633); *E. c.*– *Escherichia coli* (ATCC 25922); *P. v.*– *Proteus vulgaris* (ATCC 4636); *P. a.*– *Pseudomonas aeruginosa* (ATCC 27853); *C. a.*– *Candida albicans* (ATCC 885/653).

Conclusions. The highest antifungal activity was determined for the compounds with unsubstituted phenyl radical in the urea fragment and the benzyl or 4-methylbenzyl radicals as the substituents at hydantoin cycle.



*The most active compounds **3** structures*

The similar compounds **3** with 3-methylbenzyl and 2,5-dimethylbenzyl substituents at hydantoin cycle effectively inhibited the growth of *Staphylococcus aureus* and *Bacillus subtilis.*

QUINOLINE DERIVATIVES: CANDIDATE MEDICINES FOR RESPIRATORY SYNCYTIAL VIRUS TREATMENT

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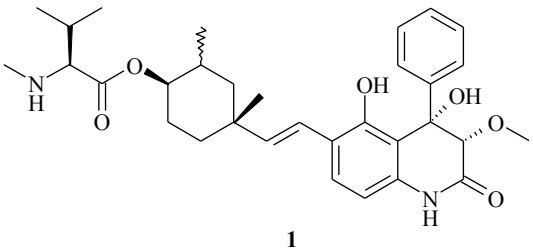
Introduction. Respiratory viruses are responsible for significant global morbidity and mortality. Nearly half of pediatric community acquired pneumonia and a quarter of adult cases have evidence of viral infection. The World Health Organization predicted that lower respiratory tract infections will be the third leading cause of death in 2016. Respiratory syncytial virus (RSV) accounts for 17.19% of viral disease outbreaks in neonatal units (2013), being one of the five most frequent viral agents. RSV conferred higher fatality than influenza, and was the second killer among hospitalized elderly.

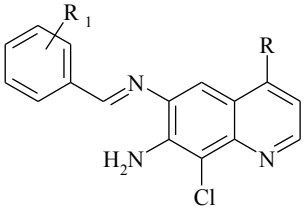
Aim. The study is dedicated to analysis of resent progress in anti-RSV small molecule fusion inhibitors development, and design of quinolone derivatives as perspective new agents against RSV.

Materials and methods. Scientific data analysis, drug design strategy, methods of organic synthesis.

Results and discussion. Small molecule inhibitors for RSV identified to date belong to benzimidazoles, benzodiazepines, and some other nitrogen containing heterocycles. In 2014-2015, their bioisosteres, e.g. quinazoline, quinoline and isoquinoline derivatives, were studied for the same activity, and some active compounds (for example, structures **1** and **2**) were revealed.



1



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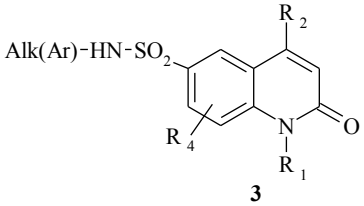

3

Being involved in quinoline medicinal drug development, we have suggested structures **3** that include quinolone-2 cycle and sulfonamide moiety as main pharmacophore fragments for antiviral study. It has been already shown that sulfonamide group presence in anti-RSV substances has proved its efficacy and negligible toxicity.

Conclusions. Despite the fact that modern medicine still has no treatment for RSV infection, some recent progress has been made in the development of RSV fusion inhibitors and its results have been reviewed. The new molecular scaffold based upon quinolin-2-one heterocycle has been proposed for further investigation.

IN SILICO STUDIES IN DIRECTED SYNTHESIS OF PERSPECTIVE ANTICONVULSANTS

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Introduction. The treatment of epilepsy is always a challenge for researchers and clinical practitioners. Over the last decades, several new drugs for the treatment of epilepsy have been introduced. Despite this progress, about 30% of patients with epilepsy are resistant to current pharmacotherapy and many of the available antiepileptic drugs. Based on this reason, there has been a continuous attempt to find new antiepileptic drugs, which increases the demand to conduct more studies in this area.

Thus, the reviewed literature data about 2-amino-5-mercapto-1,3,4-thiadiazole derivatives as anticonvulsant agents as well as results of our previous studies allow us to anticipate their anticonvulsant properties that are tested at the moment.

Current approaches to the rational design of drugs definitely include the use *in silico* methods. Synthetic strategy of this study is the structure modification of 1,3,4-thiadiazoles ring scaffolds in the positions 2 and 5 with the aim of obtaining more potent pharmacologically active compounds. That is why we have used a series of promising anticonvulsant, namely 2,5 substituted 1,3,4-thiadiazoles, to identify the main descriptors that have an impact on the activity.

Aim. The aim of this work was to identify correlations and to make on their basis some recommendations for rational design of anticonvulsant agents among of substituted 1,3,4-thiadiazoles.

Materials and Methods. Software packages Hyper-Chem 7.5 and BuildQSAR have been used to calculate the 3D molecular descriptors and to build QSAR models.

The protective activity of 2,5 substituted 1,3,4-thiadiazoles against the pentylentetrazole-induced seizures (at the doses of 50 mg/kg; 100 mg/kg) was evaluated after administering orally 30 min. Distilled water or depakine 5 mg/kg were administered orally 30 min or 60 min before injecting pentylentetrazole, as control and positive control group, respectively. Mice were observed for 60 min after receiving water or testing chemicals. The latency of convulsive onset, severity of seizures and mortality rate was measured.

Results and discussions. The 3D molecular descriptors, namely (Total Energy, Binding Energy, Isolated Atomic Energy, Electronic Energy, Core-Core Interaction, Heat of Formation, $E_{HOMO,}$ $E_{LUMO,}$ D, logP, Refractivity , Polarizability, Aprox, Grid) were calculate. Regression analysis was carried out for identification of the important

3D molecular descriptors that most adequately reflect the features of the molecules that are responsible for anticonvulsant activity. Experimental parameters of seizures severity, duration of seizures, latent period and the percentage of animals surviving as dependent variables and calculated 3D molecular descriptors of the compounds as independent variables were used for this calculation. The two-parameter linear QSAR-models were built. A statistically significant number of QSAR-models intended for the pre-experimental prediction of the effective anticonvulsants with prescribed set of properties of 1,3,4-thiadiazole derivatives. The accuracy, reliability, and prognostic value these models were confirmed by statistical criteria. (Fig.1)

Severity of seizures = +0,00002(±0,00001) IAE +0,25730(±0,17725) D +4,78311(±0,681948)

(n=014; r=0,763; s=0,461; F=7,641; Q2=0,225; S_{PRESS}=0,627)

QSAR-model *1*

Severity of seizures = +0,30473(±0,17946) P -0,01577(±0,00860) V +7,49729(±1,671281)

(n=014; r=0,795; s=0,432; F=9,462; Q2=0,187; S_{PRESS}=0,642)

QSAR-model *2*

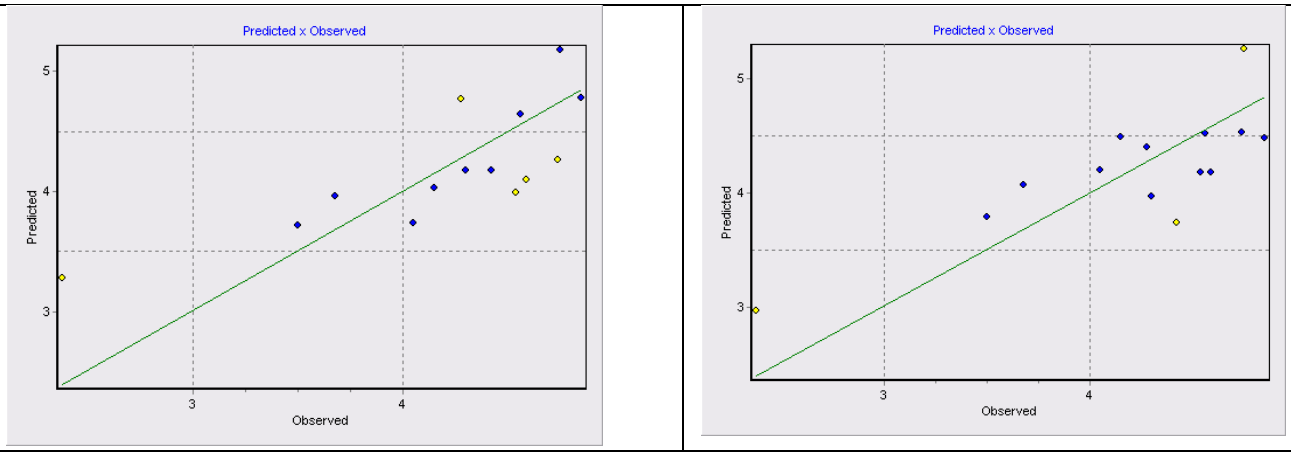

Fig.1. *A graphical comparison of predicted values and experimental activity for A)QSAR-model 1 and B) QSAR-model 2*

As a result, it was found that the anticonvulsant activity of the compounds depends on the value of isolated energy atoms, dipole moment, polarizability and volume of the molecule.

Conclusions. Based on structure activity relationship, the number of statistically probable two-parameter QSAR models was built. It has been shown, that anticonvulsant activity of the analyzed substances depends on the isolated energy atoms, dipole moment, polarizability and volume of the molecule.

PERSPECTIVES OF SEARCH OF BIOLOGICALLY ACTIVE COMPOUNDS AMONG THE DERIVATIVES OF 6-HYDROXY-4-OXO-1,2-DIHYDRO-4*H*-PYRROLO[3,2,1-*ij*]QUINOLINE-5-CARBOXYLIC ACID ARYLALKYLAMIDES

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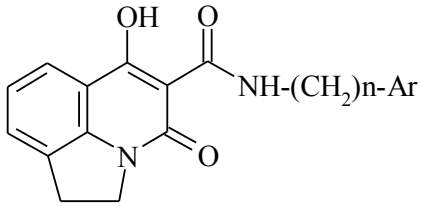
Introduction. The problem of creation of new anti-inflammatory drugs does not lose its relevance during several decades.

Aim. Taking this into consideration, we have developed a preparative method of synthesis and anti-inflammatory activity was studied of arylalkylamides series of 6-hydroxy-4-oxo-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-5-carboxylic acid.

Materials and Methods. So we thought it is appropriate to carry out arylization reactions of ethyl ester 6-hydroxy-4-oxo-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-5-carboxylic acid and study the biological activity of the obtained compounds.



***Ar** = 2-F-Bn; 4-Cl-Bn; 4-Me-Bn; 2-OMe-Bn; 3,4-(OMe)$_2$-Bn; piperonyl; 2-(4-Cl-Ph)-Et; 2-(4-OMe-Ph)-Et; 2-[3,4-(OMe)$_2$-Ph]-Et; pycolil-3.*

Results and discussions. To prove chemical composition of all synthesized compounds an elemental analysis and ^{1}H NMR spectrum were applied.

Their capacity to keep inflammatory process actively down has studied by a standard method on white rats within oral supplementation comparing to Voltaren.

Analyzing the data of conducted pharmacological trials and results of our previous research, it must be admitted that transferring from alkyl- till arylamides is accompanying with significant increase of anti-inflammatory activity, however this indicator is low than the one of a reference-preparation, and, thus, in sense of search of potential anti-inflammatory agents is of little promise.

Conclusions. The elemental analysis and ^{1}H NMR spectroscopy we used in the study of the structure of the obtained derivatives 6-hydroxy-4-oxo-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-5-carboxylic acid. The studied arylalkylamides show a moderate anti- inflammatory activity, but do not exceed reference drugs.

THE SYNTHESIS PROCESS AND THE STUDY OF COMPLEX MATTER OF NICKEL WITH PYRIDOXINE AND AMID OF NICOTINIC ACID

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Introduction. All cells and tissues of the human body contain the chemical elements in the free state and as a set of chemical compounds. Medical properties of elements and their compounds, usually close or identical. These compounds include complexes and components characteristic to a living organism. With the development of the chemistry, scientists began to note that the action of, for example, metals may be enhanced with the formation of compounds with medicinal substances that are specific to one or another disease. This is because in the body the chemical elements are mainly in the form of coordination compounds that usually have a high biological activity, therapeutic efficacy and safety.

Aim. The main goal of the research is to synthesize the complex matter of nickel with pyridoxine and amid of nicotinic acid, as well as studying its properties.

Materials and methods. The synthesis process of the complex is divided into two stages. Pyridoxine is usually manufactured in the form hydrochloric salt. The first stage is receiving the base of pyridoxine from its hydrochloric salt. 20.00 g of pyridoxine hydrochloride and 8.12 g of sodium bicarbonate are ground in a mortar to the fine powder. Pyridoxine hydrochloride is dissolved with 250 ml of ethanol. Consequently, the sodium bicarbonate is added partly into the previous solution and continuously stirred by heating (70-75 °C) until the carbon dioxide removed completely. After that, the solution of pyridoxine is separated from the precipitate of sodium chloride. The precipitate is washed with small amount of ethanol and added to the pyridoxine solution. Solution of pyridoxine is evaporated 1/5 of the original volume and precipitated with 200 ml of ether. The precipitate is filtered, then washed with ether and dried. The next stage is related to the synthesis of complex of nickel with pyridoxine and the amide of nicotinic acid. 0.06 mole of pyridoxine and 0.02 mole of amide of nicotinic acid were resolved in 200 ml of ethanol. 0.02 mole of ethanolic solution of $NiCl_2 \cdot 6H_2O$ is combined with a solution of bioactive ligands and stirred on a magnetic stirrer during the 5 hours. The precipitated mass is filtered, then washed with ethanol and ether. The obtained complex is provisionally called by the name of “Pyrnicam”. The structure of complex was studied by the method of IR-spectroscopy, while the thermal property was determined with TGDSC analysis.

Results and discussion. The synthesized powder of complex is green colored, tasteless and with characteristic odor. In the IR-spectrum of the complex was obtained by the IR-spectroscope of Shimadzu (Japan) in the Republican drug

standardization centre (1 chart). It was ascertained that bands characteristic bidentate ion coordinated in pyridoxine at 1306-1308 and 1014, 1017 cm^{-1}. The presence in the spectra of intense bands at 1525-1530 cm^{-1} and a broad absorption in the region 2600-3400 cm^{-1} are assigned to $\delta(NH^+)$ and $\nu(NH^+)$ respectively, indicates the coordination of pyridoxine in molecular form. The hydrogen of the phenolic hydroxyl is split off and migrates to the nitrogen heteroatom. Moreover, the ligand monodentately coordinated through the pyridine nitrogen atom. In the complex the anion of Cl^- is located on the outer sphere, this shows that in the spectrum of the complex bonds of ν (Me – Cl) is missed.

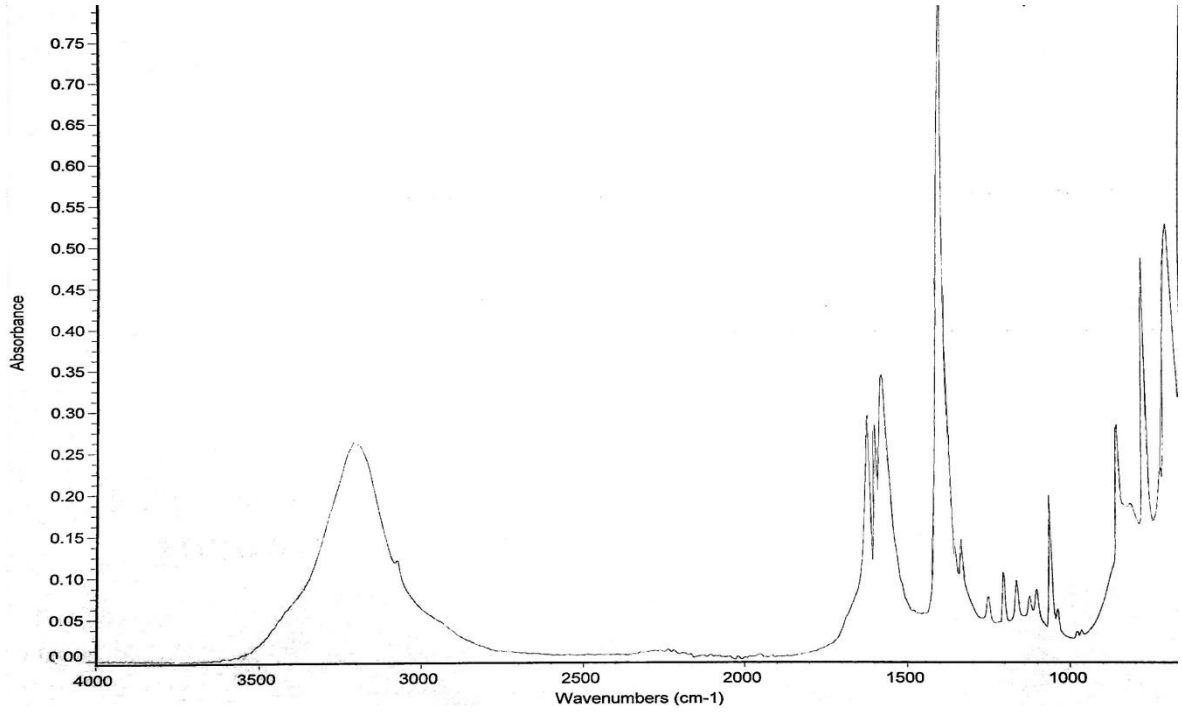

Chart1. Designed by Shamshiddinova M.

In the connection of the polyhedron coordination was not completed till octahedron through the coordination of the one water molecule. This was confirmed by derivatographic analysis. On the derivatograph were observed the endoeffects at 80, 160 °C that corresponds to the removal of outer-sphere coordinated water molecules. The mass decrease is respectively 6% and 3%. At the temperature of 228.7°C and above the ligands begin to decompose.

The UV-spectrum of complex was studied in the UV-spectroscope of Agilent Technologies (Germany). According to the UV-spectrum complex gives a pick at 289 nm.

Conclusions. New complex matter of nickel with bioactive substances is synthesizes in the central scientific laboratory of Tashkent pharmaceutical institute. The IR-spectrum, UV-spectrum of this complex is identified, as well as the decomposition temperature of matter is studied by the method of TGDSC.

SYNTHESIS, STRUCTURE AND PROPERTIES OF MAGNESIUM CHELATE COMPLEXES OF PROTEINOGENIC S-AMINO ACIDS AND THEIR MIXTURES WITH R-ENANTIOMERS

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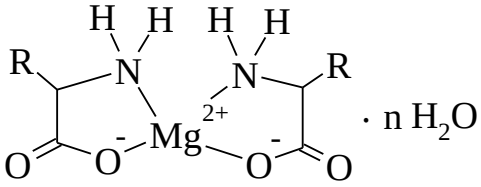
Introduction. Magnesium kation (Mg^{2+}) is one of the most important essential nutrient (not synthesised in the organism macronutrients), which entered in organs and tissues in the form of magnesium salts acids (MSA). According to the cell content he ranks second place after potassium and take part more than in 325 biochemical processes of metabolism fats, proteins and carbohydrates as coenzyme. We have found and systematized 57 MSA which are permitted for medical and food use in the farmaceutical and food world markets.

Aim. The aim of our work was to synthesise, identify and examine some properties of magnesiumdiaminoacids (MgDAA) chelate complexes of proteinogenic S-amino acids and their mixtures with R-enantiomers which have general formula:



n=0-6, R=amino acid

Materials and methods. Identification, analysis, determination of the structure and properties were conducted by known methods: per melting temperature, pH-metrically, gravimetric, complexometric; n was determined by comparing the found and calculated values of the percent of water in the homologous series of hydrates.

Results and discussion. For synthesis target compounds was used the typical neutralization reaction of magnesium oxide with corresponding amino acid. It was carried out in aqueous medium with heating to establish a certain value of the pH. As a result white or slightly yellowish-white crystalline substances, odorless, soluble or sparingly soluble in water were obtained. Their composition was: $Mg(Gly)_2$; $Mg(R,S\text{-}Asp)_2 \cdot 4H_2O$; $Mg(S\text{-}Asp)_2 \cdot 2H_2O$; $Mg(R,S\text{-}Glu)_2 \cdot 6H_2O$; $Mg(S\text{-}Glu)_2 \cdot 3H_2O$;$Mg(S\text{-}Arg \cdot HCl)_2 \cdot H_2O$;$Mg(R,S\text{-}Phe)_2 \cdot 2H_2O$;$Mg(R,S\text{-}Tyr)_2 \cdot H_2O$; $Mg(R,S\text{-}Trp)_2 \cdot H_2O$. The yields of the synthesized compounds were 44.0-96.9% of the calculated theoretically, the content of the basic substance (for Mg) was equal to 85.4-101.6% .

Conclusions. Thus, we have developed a general method for the synthesis of 9 MgDAA chelates proteinogenic amino acids, proved their structure and studied the basic properties.

«KRASUSKY'S RULE» AND ITS APPLYING IN MODERN ORGANIC SINTHESIS

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Introduction. Professor Konstantin Adamovich Krasusky (1867-1937) is a famous Soviet scientist in the field of organic chemistry, associate-member of the USSR Academy of Sciences (1926), academician of the National Academy of Sciences of Ukraine (1933). He made a significant contribution to the organic synthetic chemistry in Ukraine. K.A. Krasusky led the Organic chemistry course (1922-1924) in Kharkiv Pharmaceutical Institute (now National University of Pharmacy) in cooperation with work in Kharkiv University. He engaged in aminoalkohols synthesis from α-oxides. Moreover, he investigated the mechanism of the interaction of ammonia (amines, hydrogen chloride) with α-monoxide. Found patterns are known in organic chemistry as "Krasusky's rule".

Aim. We aimed to investigate the Krasusky's biography, his role in the study of α-oxides reactivity (ethylene oxide, epoxides) and applying of "Krasusky's rule" in current studies.

Materials and methods. Data comprising the applying of Krasusky's scientific achievements in the study of ethylene oxide reactions with nucleophilic reagents.

Results and discussion. According to the "Krasusky's rule", epoxide cycle is opened by the action of H_2O, NH_3, HCN, H_2S, ROH, RSH, RCOOH, RHal etc. in neutral or basic medium. The disclosure proceeds with cleavage of C–O bond with participation of carbon atom which is less substituted (or has less bulk substituent) in the presence of base. Reaction proceeds through a bimolecular nucleophilic substitution (S_N2) mechanism.

Conclusions. There are many current synthetic investigations in which the "Krasusky's rule" is used, for example, synthesis of nitrophenylsubstituted 1,3-thiazolin-2-thiones based on the ring disclosure reaction of ethylene oxide by the action of dithiocarbamates (И.В. Кулаков и др., ХГС, 2010, №4); synthesis of acyclic derivatives based on N-ethyl-N-(oxiran-2-ylmethyl)aniline (Э.Г. Месропян, ЖОрХ, 2010, Т. 46, вып. 9); transformation of N-R-N-(oxyran-2-ylmethyl)bicyclo[2.2.1]hept-5-ene-exo-2-yl methylamines (Л.И. Касьян, ЖОрХ, 2011, Т. 47, вып. 7). Interaction of alkyl (oxyran-2-ylmethyl)malonic esters with aromatic dithiols follows Krasusky's rule and results in new sulfur-containing butyrolactones (Э.Г. Месропян и др., ЖОрХ, 2012, Т. 48, вып. 3).

ASPECTS OF FUMARIC ACID USING IN PHARMACY AND OTHER AREAS

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Introduction. Fumaric (*trans*-ethylenedicarboxylic) acid (FA) derivatives have been traditionally attracted researchers attention as building blocks for medicines creating. They are presented in every living organism, human skin produces them under the sunlight. They also take part in the Krebs cycle as intermediate metabolites. Fumaric acid was first extracted from the mushroom *Boletus pseudoignarius*, it was also found in lichens and Iceland moss. It was named after the plant *Fumaria officinalis*, from which it was isolated in 1832.

Aim. To analyze the current state of the FA derivatives using in various areas, particularly in pharmacy.

Materials and methods. FA, fumarates, alkyl esters, amide derivatives. The study of biological activity and application.

Results and discussion. Nowadays FA is produced by chemical industry. It is used for succinic and malic acid, polyester resins, synthetic drying oil and plasticizers production. It is also used as acidifying agent in food industry for preparation of beverages and bakery since 1946 (food conservant *E297*). Based on FA food additive *Libekrin* is used for poultry. It is also used in hygiene products manufacturing. There are many different pharmacological groups of drugs based on FA at the pharmaceutical market. *Konfumin, Mafusol, Sodium fumarate complex* are infusion drugs for rehydration and detoxification. *Polioxyfumarin is a* multifunctional blood substitute. *Iron fumarate, Heferol, Ferronat* have hematopoietic, erythropoietic, antianemic properties and replenish iron deficiency. *Tenofovir disoproxil fumarate, Viread* are antivirals, *Zaditen* is antihistamine drug for systemic use. *Fumaderm* is used in psoriasis therapy, *Fumaramidmicin* is a broad-spectrum antibiotic. *Tekfidera dimethyl fumarate* is used for treatment of adult patients with relapsing-remitting multiple sclerosis. *Bisoprolol fumarate* is used in coronary heart disease and hypertension treatment. The scientific school led by Academician of NAS of Ukraine, prof. Chernykh V.P. (Organic Chemistry Department, NUPh) carried out the research of biologically active substances synthesis based on FA heterylamides, 2-carboxyphenylamide, arensulfonohydrazides. New amides, esters, hydrazides, salts with anti-inflammatory, analgesic, hemostatic, diuretic, glucose-lowering and antihypoxic activities were synthesized.

Conclusions. FA is a perspective substance for various industries, especially for new drugs creation.

APATITE – BIOPOLYMER NANOCOMPOSITES FOR BIOMEDICINE

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Introduction. Currently, synthetic biomaterials are widely used as a substitution bone material in medical practice (craniofacial surgery, trauma surgery, dentistry, orthopedics and traumatology). Different approaches have been developed for synthetic materials to produce biomaterials like calcium phosphate, biodegradable polymers and porous metals. It must be emphasized that synthetic materials have several advantages as compared with transplants from human donors: they available in enough amounts and do not pose any risk for an immune reaction or possible infections.

It is the **aim** of this work to present the results concerning the synthesis and investigations of physical, chemical, mechanical, structural properties, porosity, swelling, and biocompatibility of the nanocomposite materials based on chitosan, alginate biopolymers and hydroxyapatite with different ratios of an organic and an inorganic phases.

Materials and methods. In synthesize were used calcium nitrate tetrahydrate, ammonium hydrogen phosphate, ammonium hydroxide, sodium alginate (E401) with molecular weight 15 kDa, chitosan with degree of deacetylation 85%.

In the synthesis we used aqueous solutions of 0.167 M calcium nitrate tetrahydrate (A) and 0.1 M ammonium hydrogen (B). Sodium alginate was dissolved in (NH4) 2HPO4 in the oven at a temperature 37^{o}C within 1 day (C). For the formation of the composite solution A was added drop by drop to a mixture of C synthesis reaction was carried out at a temperature 80^{o}C, mixture's pH = 12 reached by adding 25% aqueous NH_4ON. The mixture was kept at ambient temperature (27 °C) for 24 hours, after which the precipitate repeatedly washed with distilled water to pH ~ 7.4 and separated using a centrifuge. As a result, the obtained gel-like substance had a humidity of 90%. To further research the product was dried at 37°C and calcinated at 900°C for 1 hour to achieve the degree of crystallinity sufficient for X-ray studies, followed by grinding. 5 specimens were prepared with subsequent weight ratio of sodium alginate to HA: 4: 1 (sample №1), 3: 2 (sample №2), 1: 1 (sample №3), 2: 3 (sample №4), 4: 1 (sample №5). The interaction between the agents is according the reaction:

$$10Ca(NO_3)_2 + 6(NH_4)_2HPO_4 + 8NH_4OH = Ca_{10}(PO_4)_6(OH)_2 + 20NH_4NO_3 + 6H_2O.$$

The study of mechanical properties was held at the Ukrainian Medical Dental Academy (Poltava) on the strain machine MRK-1. To investigate the *in vitro* bioactivity of the obtained composite materials SBF solution was used. Structure of samples was determined by X-ray diffraction on automated diffractometer DRON-3

("Burevestnyk", Russia). Electron microscopic study of structure and phase composition of samples were carried out by using transmission electron microscope TEM-125K (JSC «Selmi», Ukraine). Spectra HA / Alg composites were obtained by using infrared spectroscopy on FTIR (Agilent Technologies, USA).

Results and discussion. The results of X-ray analysis showed that the main phase of nanocomposites is HA. Bioactivity of composites sharp change in pH during the study period indicates a composite material interaction with the environment. In contrast, there is virtually no change in the control sample. It was shown, that swelling of the samples is carried out by fluid absorption and porosity of the polymer material, mostly due a polymer component. The biggest degree of swelling was shown for HA/Alg samples due to the polymer portion and the porosity of the material. Among all of the samples a highest degree of swelling was shown by HA / Alg with ratio of fractions 2: 3, by the largest polymer content. While comparing the mechanical properties by testing in compression, it can be said that the best modulus which equals 220.6 correspond to compounds that consist of alginate and hydroxyapatite. The TEM photos show needle structure consisting of particles of hydroxyapatite composite material in samples № 1-4. Increasing the number of polymer in the synthesis leads to changes in the shape of crystallites, HA formation of nanoparticles surrounded by a polymer shell. From the TEM images it was shown that with increasing content of sodium alginate in the reaction mixture during the synthesis of composite material particle's size decreases from 120 nm (№1) to 50 nm (№4). The TEM of sample №5 with the highest content of alginate shows change shape and reduce the size of crystallites HA.

Conclusions. Bionanocomposites with different ratios of polymer and inorganic phases were synthesized. Physical, chemical, mechanical, structural properties, such as porosity, swelling, and biocompatibility of the nanocomposite materials based on biopolymers chitosan, alginate and hydroxyapatite have been studied. It was determined that all obtained materials inherent biocompatibility. The synthesized apatite-biopolymer nanostructured composites for medical use with different ratios of organic (sodium alginate) and inorganic (hydroxyapatite) phases were investigated by using X-rays, which spectra confirm the formation of hydroxyapatite crystallites in the presence of sodium alginate, the amount of which decreases with increasing number of alginate introduced the reaction system for synthesis. The study of the morphology of synthesized nanocomposites shown the formation of crystallites HA needle shapes with different size. Research porosity and degree of swelling shows that with increasing of content of polymer component composite porosity decreases and the degree of swelling increases.

SYNTHESIS AND DEHYDRATION OF N'-AROYLHYDRAZIDES OF (±)-CAMPHORIC ACID

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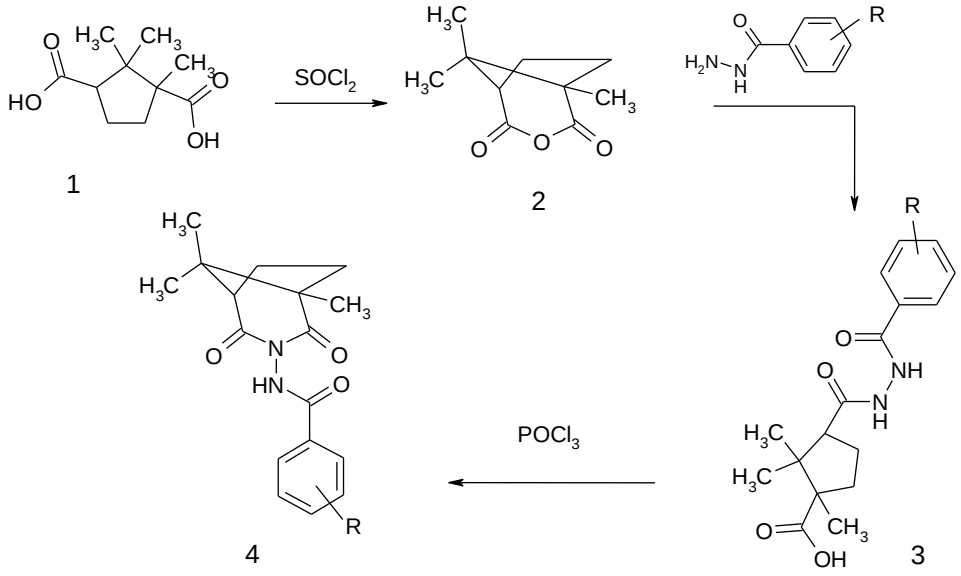
Introduction. Camphoric acid is the known compound which introduction in molecules of new substances reduces their toxicity and improves bioavailability. In previous studies derivatives of camphoric acid containing heterocyclic moiety such as quinazolone, thiophene and furan have been obtained. The results of pharmacological studies showed that they had diuretic, anticonvulsant and hypoglycemic activity.

Aim. With the purpose of further diversificasion of range heterocyclic derivatives of (±)-camphoric acid N'-aroylhydrazides 3 (scheme) have been synthesized as potential intermediate compounds in synthesis of 1,3,4-oxadiazoles.

Result and discussion. At the first stage (±)-camphoric anhydride 2 was obtained from (±)-camphoric acid 1. N'-aroylhydrazides 3 have been synthesized by interaction of (±)-camphoric anhydride 2 with hydrazides of aromatic acids. Dehydration of the obtained hydrazides 3 by $POCl_3$ ended up with closure of imide cycle and formation of N-[(1S,5R),(1R,5S)-1,8,8-trimethyl-2,4-dioxo-3-azabicyclo[3.2.1]oct-3-yl]benzamides 4. N'-aroylhydrazides 3 and benzamides 4 are colourless crystalline substances with the precise melting points. The purity of synthesized compounds was proved by TLC, and their structure was confirmed by methods ^{1}NMR spectroscopy and elemental analysis.

Scheme



Conclusions. The series of N'-aroylhydrazides 3 have been synthesized. Dehydration of hydrazides 3 by $POCl_3$ does not lead to formation of the 1,3,4-oxadiazoles but end up with formation of benzamides 4.

MEDICINE FOR RESPIRATORY SYNCYTIAL VIRUS: GREAT CHALLENGE IN MEDICINAL CHEMISTRY

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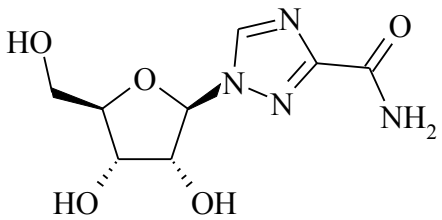
Introduction. Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory-tract infections and admissions to hospital worldwide, especially in infants, the elderly and immunocompromised, with high mortality rates due to RSV-related complications. Around 66 million people are infected worldwide, and it cause 199 000 deaths each year. It is the only agent of the three major organisms that causes death from respiratory tract infections—RSV, Streptococcus pneumoniae, and Haemophilus influenzae—for which no vaccine is available.

Aim. This work is aimed to analysis of the current state of research and development of medicines for treatment of infection caused by RSV.

Materials and methods. Scientific data (journal articles, patents, reports so on) reviewing and analysis.

Results and discussion. Despite the burden on the healthcare system in the developed world and the high mortality rates in certain high-risk groups, there is no treatment for RSV infection. Ribavirin (**1**), broad-spectrum antiviral agent, was approved by the US Food and Drug Administration but is rarely used (high cost, lack of demonstrated benefit in decreasing hospitalization or mortality) and only for the children with severe RSV disease. Immunoprophylaxis against RSV infections with palivizumab (Synaggis), a monoclonal antibody, is only moderately effective and reserved for the highest risk preterm infants and those with conditions such as chronic lung disease and congenital heart disease due to the high cost of treatment.



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Some recent progress in the development of anti-RSV agents has been made, and small molecule fusion inhibitors have been found among different azaheterocycles (e.g., benzimidazoles, benzodiazepines, pyrimidines, quinolines, thiazoles etc.).

RSV has already been prioritised for control and vaccine development by global and national health organizations for more than 20 years. Successful immunisation against RSV was predicted, in 1994, to be achieved within 10 years. But, unfortunately, it has still not been done.

Conclusions. Thus, significant unmet medical need exists for the development of a convenient, safe and effective antiviral therapy for RSV infection.

PROTECTIVE GROUPS IN DRUG DISCOVERY

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Introduction. Synthesis of the complex organic compounds is a multi-step process, where the different fictional groups of a molecule in the same conditions may react at the same time, which is mostly not desired. Therefore, the temporary blocking of some fictional groups, which may undergo the reactions performed for the other fictional groups of a compound is commonly used.

Aim. Systematization of the collected information about the functional groups used for synthesis of modern drugs, the methods of their protection methods; the methods of introduction together with the stability and methods for protective groups removal by chemical reactions were also analyzed.

Material and methods. The search engines of Google and the data of the specialized text-books and periodicals, the methods for the analysis the most valuable information selection and scientific induction method were applied for this study.

Results and discussion. Acetal protective group is used for protection of aldehydes and ketones from nucleophiles and bases, the acid catalyzed reaction of ethyle glycol with more electrophilic carbonyl group is the way for its introduction; deprotection is performed by acid catalyzed hydrolysis. TBDMS protects alcohols from nucleophiles; it is introduced in the presence of imidazole and removed by action of water solutions of fluorides. THP protects alcohols from strong bases, it is introduced by dihydropyran reaction with alcohols, and removed by acidic hydrolysis. ArOMe protects phenols form strong bases; for its introduction sodium hydride is used, deprotection is performed by action of HBr. Cbz-group protects amines form the action of electrophiles, it is introduced by action of benzyl chloroformate and removed by action of HBr or by hydrogenation. t-Boc is a group for protection of amines form nucleophiles, which is derived form Boc_2O anhydride; for the cleavage of this group water solution of HCl is applicable. The Fmoc is similar to Cbz but protects amines from nucleophiles; it is introduced fluorenylmethoxycarbonyl chloride and removed by the action of a base.

Conclusions. The protective groups are of the great importance for synthesis and developments of novel drugs. Application of the protective groups helps to block any unsuitable functional group, which presence complicates the synthetic steps. Protective groups enlarges the number of methods for effective drug discovery in laboratory and also in industrial conditions.

TESTING OF 2-PHENYLIMINOTHIAZOLE DERIVATIVES FOR COMPLIANCE WITH "DRUG LIKENESS" CONCEPT

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Introduction. Pre-experimental research methods in silico successfully used at various stages of the search and optimization of the structures of biologically active compounds. «The rule of five» Lipinski is one of such methods. This method is based on the calculation of physical and chemical parameters that determine bioavailability of investigated molecules and prediction of their drug-like properties.

Aim. The aim is testing of eleven synthesized 2-[4-aryl(alkyl)-5-aryl(alkyl)-2-phenyliminothiazole-3-yl]-1-morpholylethane (Figure I) and 3-[4-aryl(alkyl)-5-aryl(alkyl)-2-phenyliminothiazole-3-yl]-1-morpholylpropane derivatives (Figure II) for compliance with «The rule of five» Lipinski. The molecules that do not comply specified parameters will not be subjected for the further pharmacological screening.

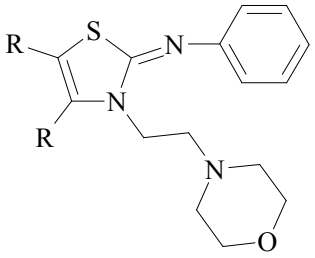

Figure I

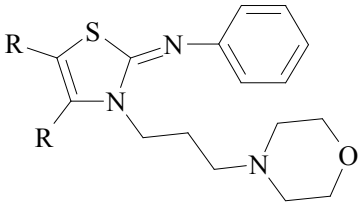

Figure II

Materials and methods. Such drug-like parameters as molecular weight, partition-coefficient, number of hydrogen bond donors and acceptors have been calculated by using online version of Molinspiration software, and molar refraction - by using ACD/Labs software.

Results and discussion. According to the the results of calculation of drug-like properties, tested substances have the following average values of physical and chemical parameters: molecular weight – 371.14, partition-coefficient – 5.34, molar refraction – 116.82, number of hydrogen bond donors and acceptors - 0 and 5, respectively.

Analysis of the results showed that determined drug-like properties are in the range of permissible values for six of the eleven test compounds. Two test compounds have one deviation and three compounds have two deviations from «The rule of five» Lipinski.

Conclusions. Eight from eleven synthesized compounds comply with requirements Lipinski and can be recommended for experimental biological tests.

ANTIFUNGAL AND ANTIOXIDANT ACTIVITY OF (Z)-3-(3,5-DI-TERT-BUTYL-4-HYDROXYPHENYL)-1-(2,4-DICHLOROPHENYL)-2-(1*H*-1,2,4-TRIAZOL-1-YL)PROP-2-EN-1-ONE

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Introduction. The treatment of fungal infectious diseases remains a challenging problem because of the increasing number of microbial pathogens. 1,2,4-Triazole derivatives templates is a privileged structure fragments in modern medicinal chemistry considering its broad pharmacological spectrum and affinity for various bio targets of these class heterocyclic compounds. The current interest in the development of new agents can be partially ascribed both to the increasing emergence of fungal resistance to antibiotic therapy and to newly emerging pathogens, reinforces the need for the development of new and potent chemical entities or an improvement in the activity of well-known 1,2,4-triazole derivatives. Considering this statement, the synthesis of analogues can be seen as an efficient approach to optimize an active chemical structure and design new drugs, since simple structural changes can lead to better biological activities through modifications of physicochemical properties.

Aim. The aim of this investigation dedicated to the development of selective synthesis of 3-(3,5-di-tert-butyl-4-hydroxyphenyl)-1-(2,4-dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-one and the study of antifungal as well as antioxidant properties.

Materials and methods. The target compound was synthesized starting from 1-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl)ethanone and 3,5-di-tert-butyl-4-hydroxybenzaldehyde. Final compound was evaluated for antioxidant generation ability on of DPPH▪, and screened for antifungal activity against fungi. In order to determine the reaction stoichiometry, different molar ratios, expressed as moles of antioxidant per mole of DPPH▪, were tested, ranging from 0.1 to 10. For each molar ratio, the remaining concentration of DPPH▪ at the plateau was determined and graphed, and EC50 was read on the graph as the molar ratio which reduces half of the initial DPPH▪ concentration, was determined from the graph. A lower EC50 value is associated with a stronger DPPH radical scavenging capacity under the same testing conditions. These results for clarity were also expressed in terms of antiradical power

(ARP) calculated as ARP=1/EC50 in which larger ARP values represented a larger scavenging capacity. The number of reduced DPPH▪ molecules per one molecule of antioxidant was defined as σ = 1/(2 x EC50). The results obtained for EC50, σ and ARP of the studied compounds were compared to those of ionol (control).

Antifungal activity has been tested on *Aspergillus ochraceus* (ATCC 12066), *Aspergillus flavus* (ATCC 9643), *Aspergillus fumigatus* (plant isolate), *Aspergillus niger* (ATCC 6275), *Aspergillus versicolor* (ATCC 11730), *Penicillium funiculosum* (ATCC 36839), *Penicillium ochrochloron* (ATCC 95 9112), *Trichoderma viride* (IAM 5061) and *Candida albicans* (ATCC 10231) by the diffusion plate method. The test compound was dissolved in dimethylsulfoxide (1 mL), mixed with potato dextrose agar PDA at concentrations of 50, 100, 150 and 200 μg/mL and poured onto sterile Petri dishes (with diameter of 9 cm). A 6 mm disc containing mycelia was transferred to the center of PDA plate. Tree replications were maintained for each concentration and DMSO was used as a control solvent then the inoculated plates were incubated at 37 °C for 4 days and the zone of inhibition was observed and measured.

Results and discussion. The target compound was synthesized under a Knoevenagel condensation by nucleophilic addition of 1-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl)ethanone to 3,5-di-tert-butyl-4-hydroxybenzaldehyde followed by a dehydration reaction. The compound was characterized by mp, elemental analyses and spectroscopic data and the Z- configuration at C=C double bond could be established unambiguously by ^{1}H NMR as well as ^{13}C NMR spectroscopy.

Antifungal activity of 3-(3,5-di-tert-butyl-4-hydroxyphenyl)-1-(2,4-dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)prop-2-en-1-one was tested against eight fungal strains. Minimal inhibitory and minimal fungicidal concentration was determined using microdilution method. The tested compound showed antifungal activities in the MIC range of 0.3-38.6 μmol x 10^{-2}/ml and MFC range of 0.6-77.2 μmol x 10^{-2}/ml. It was observed that 1-{(1R,3S,4S,6S)-4-hydroxy-4,7,7-trimethylbicyclo[4.1.0]heptan-3-yl}-3-methyl-1*H*-imidazol-3-ium (S)-2-[(S)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate **2** shows a similar radical scavenging capacity to that of ionol.

Conclusions. Heterocyclic compound based on 1-(2,4-dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanone and 3,5-di-tert-butyl-4-hydroxybenzaldehyde, possessing strong antifungal activity with concomitant very good antioxidant are potential leads for developing efficacious double action therapeutics.

SECTION № 2

STUDY OF MEDICINAL PLANTS AND CREATION OF HERBAL MEDICINAL PRODUCTS

THE BIRCH OF BARK IS PERSPECTIVE SOURCE OF BIOLOGICAL ACTIVE SUBSTANCES

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Introduction. A considerable sector of modern medical preparations market is occupied by non-steroidal anti-inflammatory drugs (NSAIDs). They are widely used for treating inflammation of soft tissues, locomotor system, rheumatic, cardio-vascular, nervous deceases, injuries, during postoperative period, for symptomatic treatment of pain syndrome of different genesis. However, despite the fact that NSAIDs are clinically effective, there are many contraindications and limitations for their use. Therefore search of new drugs on the basis of phytogenous substances with anti-inflammatory action is an important direction of modern medicine. The information as for the birch tree use in folk medicine confirms that the birch bark features healing, anti-inflammatory and anti-tumor activities. Pharmacological activity of thick extract of Betula verrucosa was studied based on the data of experimental and clinical studies present in the literature, which confirm the ability of some bioactive substances (steroids, flavonoids, tannin agents) to influence the process of healing and regenerations of tissues.

Aim. The expressive of major groups of biologically active substances (compounds of steroid nature) from the bark and birch sprouts, separating them into individual components.

Materials and methods. The objects of study were middle part of the bark of the trunk (collected at 1-2 meters) bark, shoots 1, 2, 3, 5-6 years of birch verrucosa. The qualitative composition of the compound nature of the steroid was determined by Lieberman-Burchard reaction, the reaction of Salkovskij, the reaction of Lafon, the reaction of Sanyo.

Results and discussion. When stratification of concentrated sulfuric acid dissolved in acetic anhydride in extracts of bark and birch sprouts on the border of two layers of liquid appeared red color, which passed in emerald green. Into a solution of lipophilic fractions adding 5-6 drops of concentrated sulfuric acid. Into 2 ml of lipophilic fractions was added 1 drop of 10% solution of copper (II) sulphate and gently heated. The colour of solutions in test tubes with extracts from the bark and shoots on blue-green. Into 2 ml of lipophilic fractions were added to 1 ml of 0.5% etanol solution of vanillin, 3-4 drops of concentrated sulfuric acid and heated in a boiling water bath, the color of reaction was yellow.

Conclusions. Various chemical composition and widely used birch verrucosa further detailed study of birch bark.

PHARMACOGNOSTIC STUDY OF RAW MATERIALS FROM THE ARACEAE FAMILY

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Introduction. Demand for phytopreparations has been constantly growing lately. It is connected with the wide spectrum of pharmacological effect, insignificant side effects as compared with the synthetic analognes. The search of new available sources of medicinal vegetable raw materials is one of the top priority tasks of modern pharmacy. Our attentions is attracted by the plants of the Araceae family, species Dieffenbachia, which are widely cultivated in Ukraine and are used in traditional medicine.

Growing wild plants of the Araceae family are spread in the tropics and subtropics and run to 2000 species. These are perennial herbs, usually with large leaves close to the roots, though lianas and trees are also found. The raw materials of the majority of this family's specimen contain saponins, glycosides, alkaloids and are poisonous. But they mostly lose these properties when boiled or dried. Some plants of the Araceae family are cultivated in Ukraine. They, grow monstera, some kinds of kala, dieffenbachia and anthurium, philodendron and some others as decorative and hot-house plants.

Inverstigation Aim. So summarize printed information as to spreading, chemical composition, aspects of usage of Dieffenbachia representatives from the Araceae family, to determine morphological and anatomical peculiarities of the raw materials texture.

Materials and Methods. The objects of the study were overhead organs of different kinds of dieffenbachia. The raw materials were stored up in spring 2015.

Results. It is found out that in morpholohical aspect diagnostically important for leaves are: the size and the form of a leaf's lamina, upper and lower surfaces' colour, the type of nervation, the number of bunches of the midrib;for a stalk: the length, surface's nature and colour, the presence of fissures and pubescence.

Anatomical investigation showed that important diagnostic features to indentify leaves as raw materials are: the nature of epidermis' cuticle, the type and frequency of occurrence of the respiratory apparatus, the presence and type of hairs, the texture of the stalk and the main nerve (the number of bunches), the presence of rounded elongate crystals, of calcium oxalate.

Conclusions. Analysis of the investigation results has become the first step in pharmacognostic study of raw materials of the specimen from the Araceae family – prospective sources of medicinal vegetable raw materials.

PHYTOCHEMICAL RESEARCH OF SALIX VIMINALIS L.

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Introduction. Willows (genus Salix, family Salicaceae) are popular plants since more than 400 species occur in Nature (including Salix viminalis). Particularly, Northern Hemisphere is a natural region for different willow species bearing sometimes traditional and very unique names like Sageleaf Willow, Goat Willow, Pussy Willow, Coastal Plain Willow, Kimura, Grey Willow, Sand Dune Willow. The variety of willow species partly results from ease of hybrid formation by cross-fertile of particular Salix genotypes in a natural process and/or by planned cultivation.

Salix viminalis L. is a species of willow (Salix) native to Europe and western Asia. Common names: Osier willow, Common Osier, Basket Willow, Energetic Willow. It is commonly found by streams and other wet places. The exact native range is uncertain due to extensive historical cultivation; it is certainly native from central Europe east to western Asia. It is one of the least variable willows, but it will hybridise with several other species. Their bark, buds and the leaves of Salix L. which contain phenolic glycosides, flavonoids, tannin, organic acids, vitamins, terpenoids. However the Salix genus plants aren't studied enough.

Our goal is the research of qualitative composition and quantitative composition of flavonoids in the branch of Salix viminalis L.

Materials and methods. These branch were gathered for the research in Kharkov regions in 2015. Chromatographic method (TLC , paper "Filtrak"(FN № 1,4,12)). Spectrometric method (410 nm on the spectrophotometr SPh-46).

Results and discussion. There were pointed the presence of phenolic compounds (phenolic glycosides , flavonoids, tannin) when the primary studying of the Salix viminalis L. leaves was. The presence of fl avonoids was defined in the ethanol extracts with cyanidin test, ferric(III) chloride. In results of reaction show the presence of fl avonoid aglycones and glycosides. Besides the substances of flavonoids were discovered due to chromatographic method. For this method the and silica gel TLC plats were used. In accordance with the reference pattern rutin, quercetin, ferulic, chlorogenic, salicylic asides were identified. The method of spectrophotometrywas applied for the analysis of flavonoids. The contain of flavonoids is turned out not less 2.3%.

Conclusions.The Salix viminalis L. has the practical interest as a source for getting plant drugs of many-sided pharmacological action due to considerable quantity of phenolic compounds.

STUDY THE GENERAL ANATOMIC FEATURES OF LEAVES OF *CRATAEGUS FLAVA* AIT.

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Introduction. In the territory of Ukraine is successfully cultivated the big-fruits species of hawthorns are representative of North American flora.

Crataegus flava Ait. – as tall as 6 meters; branches form an asymmetrical crown; spines are thin, straight, brown; leaves are broadly ovate, with acute apex and cuneate base, slightly lobed, thin, glabrous above, pubescent below; petioles are glandular, wing; stipules falcate; inflorescence 3-7-flowered; petals white; the fruits are large, dark orange; seeds 4-5, on the back ribbed.

As a result of our studies in the leaves of Crataegus flava Ait. identified different classes of biologically active substances (BAS): phenolic compounds, terpenoids, lipophilic substances, microelements. Considering the above, the most relevant is a detailed pharmacognostic study of leaves of *Crataegus flava* Ait.

The **aim of our study** was to investigate the morphologyc and anatomic features of *Crataegus flava* Ait. leaves.

Materials and methods. The object of the study was the dried leaves of *Crataegus flava* Ait., collected in May, 2015 year.

Raw materials is collected in Botanical Garden of V.N. Karazin Kharkiv National University. For microscopical study the leaves are boiling in 3% aqueous solution of sodium hydroxide.

The microslides were examined in the solution of chloral hydrate. The diagnostic features were determined using a МБР-1 and МБР-2 microscope with an increase of 100 and 600.

Results and discussion. As result of the study was determined the main anatomic features of *Crataegus flava* Ait. leaves: the presence of simple hairs and single multicellular glands in the leaf blade; anomocytic type of stomata; wavy wall epidermal cells; simple hairs in petiole; veins with crystals of calcium oxalate; epidermal cells with dark contents.

The histochemical reaction with ferric alum was carried out, resulting in the leaves of *Crataegus flava* Ait. were found phenolic compounds (flabophens).

Conclusions. For the first time anatomical study of leaves Crataegus flava Ait. was carried out. The obtained information can be used in conducting further standardization of raw materials.

STUDY THE PHENOLIC COMPOUNDS OF *CRATAEGUS FLAVA* AIT. LEAVES

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Introduction. Phenolic compounds are the most widespread class of biologically active substances (BAS), encountered in plant raw material. In plants phenolic compounds are involved in the process of breathing, it natural coloring agents, play the role of filters and protects the plants from UV radiation, perform antioxidant affect, influence in plants growth process. Phenolic compounds have a broad spectrum of pharmacological activity: hypotensive, cardiotonic, diuretic, astringent, anti-inflammatory, hemostatic, choleretic, antimicrobial.

Well known that basic BAS of representatives of genus Hawthorn (Crataegus) is phenolic compounds (flavonoids and hydroxycinnamic acids). The most studied of hawthorn raw materials are fruits and flowers, leaves insufficiently studied. Therefore we think that a promising the depth study of the chemical composition of the leaves of unpharmacopoeia species of hawthorn. One of these species is *Crataegus flava* Ait.

The **aim of our study** was to investigate the phenolic compounds of *Crataegus flava* Ait. leaves.

Materials and methods. The object of the study was the dried leaves of *Crataegus flava* Ait., collected in May, 2015 year. Raw materials is collected in Botanical Garden of V.N. Karazin Kharkiv National University.

For the study of phenolic compounds obtained alcohol extract in the proportion raw material-extractant (1:10). Extraction was conducted of 70° ethanol. For identification of phenolic compounds used qualitative chemical reactions and chromatographic methods. Chromatographic research were carried out using one-dimensional and two-dimensional paper chromatography in solvent system: I direction - ethyl acetate-formic acid-water (10:2:3); II direction – 2% acetic acid.

Chromatograms were analyzed in daylight and UV-light after processing of ammonia pairs. The identification of compounds was carried out by R_f values and color of spots after processing of alcoholic solution of alkali. Also used chromatography in compared whis a reference samples: quercetin, rutin, hyperoside, kemppherol, chlorogenic acid. For identification of flavonoids used cyanidine reaction by Briant, the reaction with 10% alcohol-water solution of alkali, reaction with lead acetate, reaction with $FeCl_3$.

Results and discussion. In leaves of *C.flava* Ait. were identified 8 compounds of phenolic nature. The results of chromatographic research are shown in Fig. 1. and Table 1.

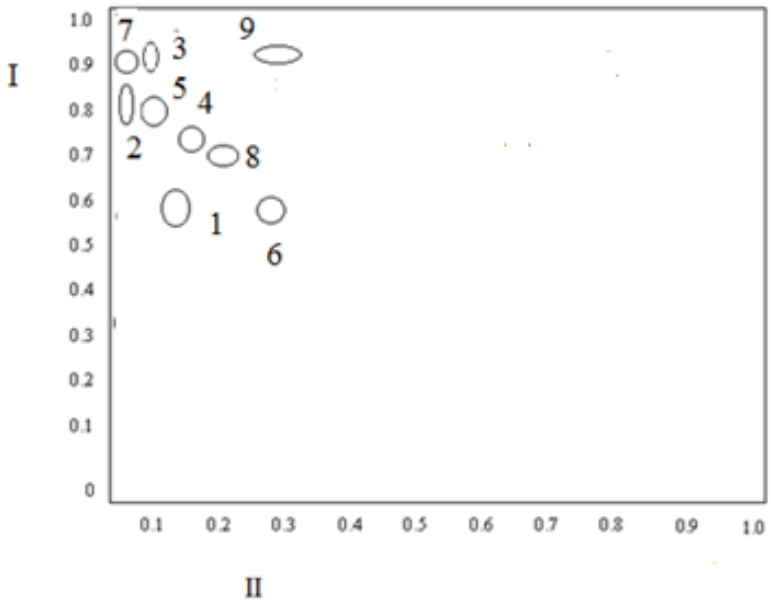

Fig. 1. Chromatogram of phenolic compounds from C. flava Ait. leaves

Table 1

Chromatographic characteristic of phenolic compounds from *C. flava* Ait. leaves

№ of compound	Rf·100		Fluorescence in UV-light	
	I direction	II direction	before processing the reagent	after processing of ammonia pairs
1	62	15	Dark	Orange
2	85	5	Dark	Dark
3	93	13	Dark	Dark
4	70	20	Dark	Dark
5	80	10	Yellow	Yellow
6	62	31	Dark	Green
7	90	7	Yellow	Yellow –green
8	70	17	Yellow	Yellow
9	93	30	Light blue	Light blue

Conclusions. For the first time in *C. flava* Ait. leaves were identified phenolic compounds. According to the results of qualitative reactions, chromatographic research in compared with standard substances was established: 1 – hyperoside, 5 – quercetin, 7- kemppherol, 9 - chlorogenic acid.

THE IMPORTANCE OF HEMOSYSTEMATICS IN SEARCHING OF NEW DRUGS

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Introduction. The significance of the data of biochemistry for systematics was first expressed by the German scientist F. Rohleder in 1854. He found out that there was a pattern between systematic position of plants and the presence of chemicals in them. Later it was discovered that related species often contain similar chemicals. Thus, many species of tobacco contain alkaloid nicotine, nightshade species contain solanine, coffee species caffeine, and so on.

The purpose of the work. To analyze the latest achievements of leading scientists in the field of hemosystematics of plants. The aim of hemosystematics is to clarify the systematics of certain species or groups of species (taxons); search of the promising for medicine or economics species; identification of correlative links between morphological structure, ecological conditions of existence and chemical composition of plants.

Materials and methods. Comparative and descriptive, search, logical.

Results. In hemosystematics of plants data on the composition and biosynthesis of major classes of natural compounds (proteins, nucleic acids, carbohydrates, fats, etc.) are used, although products of secondary metabolism (alkaloids, terpenoids, flavonoids, etc) are of strong prognostic value. The composition and content of terpene hydrocarbons is studied most frequently in hemosystematic of ligneous plants, especially conifers. This is because their consistency (resin ducts in wood) does not change with age, environmental factors exert a weak effect on their biosynthesis, synthesis of some components under the control of individual genes. Flavonoids, which are easily distinguished, well preserved in fossils (it was discovered that the flavonoid composition of flowers has been unchanged during 22 million years), and their content is often correlated with certain morphological changes, are important in hemosystematics of flowers. The study of chemical composition of plants can extend the set of knowledge about the contents of various biologically active substances that may be used to manufacture new drugs. Plants of the *Genisteae L.* tribe are used as essential oil, soil-protecting, decorative, industrial cultures, and in traditional medicine. Morphological features of many representatives of this family are not enough for accurate attribution of plants to the same species. That is why the interest in

hemosystematical studies using certain groups of chemical compounds as characteristic features of taxons is clear. Analysis of the data of the literature shows that plants of the *Genisteae* tribe were studied in terms of the content of alkaloids, flavonoids and pirokateholamins concerning hemosystematics. French researchers selecting as hemosystematical signs alkaloid content, concluded that plants *Spartium L.* families and *Genisteae* have the chemical composition and there is no reason to distinguish between them and chemical point of view to allocate to individual families. Harborn D.B divides *Genisteae* group into three by the prevalence of flavonoids: actual *Genisteae*, *Crotalarieae L.* type and *Lupineae L.* type. The first group is characterized by the presence of glikoflavons, fizetin and isoflavones, including 5-metilgenistein are often found. In the second group there are glikosidymyrytsetin, quercetin, kaempferol, but there are no isoflavones. In the third group all studied species contain isoflavones, leykoantotsianidins, often glikoflavons. Unique approach to biochemical systematics of plants was made by the group of Brazilian researchers. Having based on the chemical structure of flavonoids they identified the similarity indexes of the biogenetic groups, indicators of the relative probability of finding and used the developed method as a supplement to conventional morphological classification. The Russian scientists Bandyukova V. A. and Avanesov E. T., having summarized the data on the distribution of flavonoids in a number of families of plants, suggested using the probability of location of different groups of these compounds for hemosystematical forecasting. Thus, in the legume family the presence of the isoflavonoids and flavonols is more likely, the presence of flavones is less likely, and the likelihood of finding flavanones is the least. It is important to add that the families of the *Lotoideae L.* tribe often contain a 3.7-diglikosids, but the *Spartioides L.* section of the *Genisteae* tribe contains 5 flavonoid glycosides.

Conclusion. The data on the chemical composition of plants are increasingly being used in the modern classical works on systematics. The assumption that the morphological similarity of species divisibility always determines their chemical composition, can not replace specific hemosystematic research, and vice versa, the lack of a direct relationship between the chemical characteristics and morphology of plants doesn’t deny the existence of certain correlations and their usage to search for a promising plant is a source of holding certain biologically active substances.

A STUDY OF THE PHENOLIC COMPOUNDS IN THE FLOWERS OF COMMON LILAC OF BUFFON VARIETY

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Introduction. Flavonoids and hydroxycinnamic acids are the most numerous classes of phenolic compounds that feature structural diversity, versatile and high biological activity and low enough toxicity. Over 4000 different flavonoids isolated from the plant material are known worldwide and their structure has been determined. The variety of biological properties of flavonoids and hydroxycinnamic acids is wide enough and not only limited to the antioxidant activity. In the in vivo and ex vivo studies they have shown to possess antitumor, antianginal, antiallergic, anti-inflammatory and radioprotective activity. Thus the search of new plant sources of phenolic compounds is a prospective phytochemical trend.

The object of our research was the flowers of common lilac of Buffon variety. The plant material for the study was collected in the National Botanical Garden nd. a. M. M. Grishko (Kyiv).

Aim. The aim of our research was the phenolic composition study of the flowers of common lilac of Buffon variety.

Materials and methods. The extraction of the sum of biologically active compounds (BAC) from the plant material was carried out with purified water. 50.0 of the crashed flowers were placed to a conical flask with ground glass joint where 150 ml of water was added. The extraction was carried out 5 times on a water bath, 30 min each. The solutions were combined and then evaporated to 200-250 ml, then cooled and filtered through a paper filter to a measuring flask with capacity of 250 ml where purified water was added till the mark (solution A).

Paper, thin-layer chromatography and quality reactions were used for the phenolic compounds identification. Compounds were identified by the R_f value and colouring before and after ammonia vapor treatment. Quantitative analysis was carried out by the means of spectrophotometric method using the Mecasys Optizen POP (Korea) spectrophotometer.

The sum of flavonoids content was determined spectrophotometrically calculated on rutin. 2.0 ml of the solution A were placed into a measuring flask with the capacity of 25 ml where 2.0 ml of 3% aluminum chloride in 96 % ethanol was added and then the mixture was stirred. 70% ethanol was added till the mark. The absorbance of the solution obtained was measured in 30 min on the spectrophotometer in a 10 mm thick cuvette at the wavelength 420 nm.

The solution containing 2.0 ml of the solution A in the 25 ml measuring flask with 70% ethanol added till the mark was used as a reference solution. The absorbance of Pharmacopoeial Standard Solution (PhSS) of rutin was measured in parallel under the same conditions. 0.01 g of rutin was placed into a measuring flask with 25 ml capacity, where 96% ethanol was added till the mark and the solution was shaken. 2.0 ml of aluminum chloride solution in 96% ethanol were added to 1.0 ml of the solution obtained and 70% solution was added to 25 ml. the solution containing 1 ml of rutin PhSS solution in the 25 ml measuring flask with 70% ethanol added till the mark was used as a reference solution. The content of flavonoids (X, %) calculated on rutin and absolutely dry plant material was calculated using the formula: $X = A \cdot m_0 \cdot 250 \cdot 1 \cdot 25 \cdot 100 \cdot 100 / A_0 \cdot m \cdot 2 \cdot 25 \cdot 25 \cdot (100 - W)$, where A – absorbance of the solution studied; A_0 – absorbance of the rutin PhSS with aluminum chloride complex; m_0 – weight of the rutin PhSS, g; m – weight of the plant material, g; W – weight loss on the plant material drying, %.

The hydroxycinnamic acids content was determined spectrophotometrically calculated on chlorogenic acid. 1.0 ml of the solution A was placed into a measuring flask eith 2000 ml capacity where 20% ethanol was added till the mark. The absorbance was measured at the wavelength 327 nm. The experiment with chlorogenic acid was carried out in parallel under the same conditions. 0.05 g of chlorogenic acid were placed into a measuring flask with 100 ml capacity and diluted with 20% ethanol, adding the same solvent till the mark. 1.0 ml of the solution obtained was placed into a measuring flask with 50 ml capacity, where 20% ethanol was added till the mark and the mixture was shaken. Then the absorbance was measured. 20% ethanol was used as a reference solution. The content of hydroxycinnamic acids (X, %) calculated on chlorogenic acid and absolutely dry plant material was calculated using the formula: $X = A \cdot 200 \cdot 50 \cdot 100 / A^{1\%}_{1\ см} \cdot m \cdot 1 \cdot (100 - W)$; where A – absorbance of the solution studied; m – weight of the plant material, g; W – weight loss on the plant material drying, %; $A^{1\%}_{1см}$ – specific absorption rate of chlorogenic acid which equals 531.

Results and discussion. The results of the chromatographic study have allowed to identify such flavonoids as rutin and quercetin and hydroxycinnamic acids such as chlorogenic and caffeic acids.

As a result of quantitative analysis of the phenolic compounds in the flowers of common lilac of Buffon variety it was determined that the content of flavonoids was 1.5±0.8%, and hydroxycinnamic acids – 5.5±1.5%.

Conclusions. The results of the studies carried out prove the prospects of further research on the flowers of common lilac of Buffon variety with the aim of the new effective phytoremedies working out.

QUALITATIVE AND QUANTITIVE COMPOSITION OF STEVIA (STEVIA REBAUDIANA BERTONI) VOLATILE COMPOUNDS

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Introduction. The search for sweeteners that is actively conducted in many countries nowadays is caused by the necessity for optimization of diet of healthy people, and also by the urgent need to resolve the question of balanced diet for people who suffer from a number of diseases that are associated with overconsumption of sugar or with inability to consume it, e.g. diabetes mellitus. The advantage in this search is given to the compounds of plant origin.

Among the plants that contain sweet compounds, stevia (*Stevia rebaudiana Bertoni*) from the Asteraceae family, commonly known as "candyleaf", arouses considerable interest. More than 100 chemical compounds were identified in stevia. It contains considerable quantities of terpenes and flavonoids. In 1931 a glycoside stevioside was discovered and described. It is contained in stevia leaves in quantities of 6-18% and is 300 times sweeter than sugar. But the chemical composition of stevia leaves is not entirely clear to this day, in particular the content of its volatile components.

Aim of the study. To determine the qualitative and quantitative content of volatile compounds in stevia leaves (Steviae folia).

Materials and methods. The investigations were conducted with the help of the *Agilent 6890N/5973 inert (Agilent technologies, USA)* gas chromatograph with mass-spectrometer detector, using the *NIST 02.* mass-spectral library.

Results of the study. Based on the stevia essential oil chromatogram 51 peaks were detected, from which 29 compounds were identified that constitute 85.86% from the general quantity. The main components of the stevia essential oil were identified: epoxy caryophyllene (20.82%), phytol (8.95%), spatulenol (6.03%), humulene (4.51%). 21 methyl ester of the stevia leaves volatile fraction were identified with the total content of 88.5%. The presence of saturated and unsaturated fatty acids, low-polymeric organic acids, di- and triterpenoids, and high-molecular acyclic alkanes was also detected. A specific diterpenoid – isosteviol was identified in the quantity of 6.23%, which is a marker for the identification of the stevia leaves volatile fraction.

Conclusions. The established parameters indicate a high phytochemical potential of the "candyleaf" and explain the wide range of its indications, which include not only its use as a sweetener but also as an effective antiinflammatory, antibacterial, and antioxidant agent.

STUDY OF INULIN COMPLEX FROM DAHLIA TUBERS KEN'S FLAME CULTIVAR

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Introduction. In medical practice together with medicines commonly used plants that contain reserve polysaccharide – inulin. It affects the regulation of metabolism in diseases of diabetes, obesity, and atherosclerosis. Plants of the genus Dahlia are promising sources of inulin. According to the literature Dahlia tubers can contain up to 50% inulin. Plants of the genus Dahlia widely cultivated throughout the world and are a good source of raw materials. The pharmacological effects of fructans depend mainly on the degree of polymerization. Low molecular inulins (or oligofructose) are used in the food industry and as prebiotics. High molecular weight inulins have a pharmacological effect in the distal parts of the colon, fermented more slowly, have a prolonged effect.

Aim. The aim of this work was to study was to study of inulin complex from Dahlia tubers Ken's Flame cultivar.

Materials and methods. For the experiment we used tubers of Dahlia Ken's Flame cultivar, collected in September 2014 (Kharkiv, Ukraine) and were cut to a particle size of about 1x1 cm were dried to air-dry state at ambient temperature. Water-soluble polysaccharides obtained by the usual method. Inulin complex was purified by calcium carbonate (to remove water-soluble pectins, proteins and organic acids) and aluminum oxide (to remove phenolic compounds). Chains of degree of polymerization was determined high-performance anion exchange chromatography coupled with pulsed amperometric detection (HPAEC-PAD) using Dionex DX 500 system, equipped with the electrochemical detector ED40 and a CarboPac PA1 (9 x 250 mm) analytical column. The evaluation of inulins with different chain polymerization was carried out using a simple normalization.

Result and discussion. Yield was 15.4% of air-dried raw materials. After purification the complex does not contain pectic substances, organic acids, amino acids and phenolics. Using HPAEC-PAD in the inulin complex short, medium and long chain inulins content was determined. The results of the experiment showed that the complex contained 39.36% of inulins with a low degree of polymerization, 35.88% with a medium degree of polymerization and 13.00% with high degree of polymerization.

Conclusions. Purified inulin complex from Dahlia tubers Ken's Flame cultivar more contained inulins with a low degree of polymerization. The obtained data will be used in the development of drugs with specific pharmacological effects.

THE STUDY OF THE CHEMICAL COMPOSITION AND HYPOGLYCEMIC ACTIVITY OF THE DRY EXTRACT FROM *VACCINIUM VITIS-IDAEA* LEAVES

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Introduction. WHO projects diabetes deaths will be the seventh in 2030. At present, 9% of the adult population suffers from this disease, so the search for new drugs is relevant in our time. Currently on the Ukrainian market antidiabetic drugs from origin plants is only one tea "Arphasetinum", which is quite inconvenient to use. The composition of the tea "Arphasetinum" includes *Vaccinium myrtillus* branches, which in scientific and folk medicine attributed hypoglycemic effect. Among plants from *Ericaceae* family in Ukraine *Vaccinium vitis-idaea* is widespread, which leaves has a chemical composition similar to *Vaccinium myrtillus*. Therefore, it would be advisable to develop a new standardized drug with hypoglycemic action based on new-galenical and galenical extracts from *Vaccinium vitis-idaea* leaves.

Aim. The purpose is to study the qualitative composition and quantitative content of biologically active substances of the dry extract from *Vaccinium vitis-idaea* leaves and study its hypoglycemic activity.

Materials and methods. An alcohol extract from *Vaccinium vitis-idaea* leaves were got by fractional maceration with using 50% ethanol. The resulting extracts were combined, allowed to stand for a day, filtered, and sterilized. The filtrate was evaporated with a rotary vacuum-evaporating device to dry the extract. The output of the dry extract is 11%. Previous chemical analysis of the obtained extract was performed by conventional methods of paper chromatography and thin layer chromatography sorbent. It was identified such substances as arbutin; 2 phenol carbonic acid: gallic and elagic acids; 3 hydroxycinnamic acids: chlorogenic, coumaric and ferulic acids; 4 coumarins; 3 flavonoid aglycone: luteolin, kaempferol and quercetin; gallotannin and ellagitannin.

Quantitative determination of hydroxycinnamic acid derivatives, flavonoids and polyphenolic compounds were performed by spectrophotometry. Total quantitative content of hydroxycinnamic acid derivatives – 2.17±0.02%; flavonoid compounds – 3.36±0.01%; polyphenolic compounds – 20.48±0.01%.

Results and discussion. The hypoglycemic activity of the dry extract from the *Vaccinium vitis-idaea* leaves was studied in 18-month-old male rats at the Department of Biological Chemistry under the supervision of prof. Zagayko A. L. Insulin resistance was modeled on the content of animals at fructose diet. The animals treated with the extract of dry *Vaccinium vitis-idaea* leaves observed a significant decrease of glucose level by 43% in comparison with a group of animals that had fructose, indicating that the hypoglycemic activity of the extract.

Conclusions. Thus, confirmed the prospect of a drug hypoglycemic action of *Vaccinium vitis-idaea* leaves.

PHARMACOGNOSTIC STUDY OF RAW MATERIALS FROM THE FRAXINUS EXCELSIOR

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Introduction. European ash (Fraxinus excelsior) – it is a tall tree, a representative of the family Oleaceae, with openwork oval crown and straight subramose branches. Bark gray, cracked, black kidney, large leaves, imparipinnate. Flowers of Ash are small, purple or brown, without perianth, gathered in panicles. Fruit-lionfish linear form. Flowering ash in April and May, and the flowers he appear before the leaves. He is originally from Europe and the Caucasus, from where it spread in Asia Minor. Now it is customary to plant deciduous and mixed forests of the European part of Russia, it is growing in the Crimea, Moldova and the North Caucasus. Spring juice ash, because of the high content of mannitol is used as a substitute for sucrose for diabetic patients.

Medicinal raw materials in the tree are the leaves, fruits and bark. In European ash contains carbohydrates in large quantities, salts of organic acids, essential oils, saponins, vitamin C, carotenoids, resin and bitter. In fruits, fats and proteins, in addition, can be found vitamins C and P.

The bark ash contains sugars, mannitol, phenolics, including coumarins, alkaloids. Established antibacterial activity of infusion ash leaves against the tubercle bacillus. The essential oils of the plant detrimental effect on fungi and protozoa. Ash bark extract is part of the food additive "Revmavit", which is used in the treatment of arthritis. Ash Drugs used in official medicine in Germany and Switzerland as antirheumatic and diuretic.

Aim. To conduct a pharmacognostic studies of the semina of Fraxinus excelsior.

Materials and methods. The object of the study were the semina of Fraxinus excelsior, harvested in May – July 2015.

Results and discussion. In the light of a comprehensive study of the plants studied European ash seed.

We conducted obtain polysaccharide fractions from leaves, bark and flowers of European ash and studied their qualitative structure. Obtained fatty oil, determined the amounts, studied the fatty acid composition of fat oil.

Conclusions. These results confirm the prospect of studying European ash as a source of various kinds of medicinal raw materials.

PHARMACOGNOSTIC STUDY OF ARTICHOKE HEADS

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Introduction. Remedies of plant origin, unlike the synthetic ones, have much less side effects on the human body. The plant material for their production can also be edible plants, e.g., artichokes (*Cynara*) from the *Asteraceae* family. These are perennial herbs up to 1.5 m highwhich are distributed in the wild in the Mediterranean countries, Asia, Central and Northern America.

There are mainly two species which are cultivated – globe artichoke (*Cynara scolymus*) and artichoke thistle, or cardoon (*Cynara cardunculus*). The globe artichoke leaves are included into the State Pharmacopoeia of Ukraine. Flower heads are used as edible parts of the former one, and leaf petioles – of the latter. The globe artichoke leaves and herb (*Cynarae folium*, *Cynarae herba*) are the raw material for foreign and domestically produced remedies which are used in the hepatobiliary system function disorders, gastric and duodenal ulcers, and as a cholagogue. «Cynarix» (Austria), «Chophytol» (France), «Bilicure» (Germany), «Artibel» (Belgium), «Artichoke extract» (Ukraine) can be examples of such drugs.

The **aim** of our research was the pharmacognostic study of globe artichoke (*Cynara scolymus*) flower heads.

Materials and Methods. The plant material samples were collected in the summer of 2014 in Kharkiv region. Quality reactions and paper chromatography were used for the biologically active compounds' identification. The quantitative analysis of hydroxycinnamic acids was carried out spectrophotometrically using the Mecasys Optizen POP spectrophotometer at the wavelength 315 nm in a cuvette with 10 mm thick layer. Some technological parameters and numerical indices of the plant material were also determined. The methods described in the State Pharmacopoeia of Ukraine and USSR Pharmacopoeia XI ed. were used.

Results. Polysaccharides (reaction with ethanol), flavonoids (cyanidin test, reaction with sodium hydroxide, aluminum chloride, ferric chloride solutions etc.), hydroxycinnamic acids (paper chromatography), and tannins (tests with gelatin, ferric-ammonia sulphate, alkaloids etc.) were identified in the plant material. The quantitative content of polysaccharides was hydroxycinnamic acids – 1.16%, total ash content – 0.1424%, the plant material grinding degree – 1.5-2.00 mm; extragent absorbance coefficients: 96% ethanol – 4.1950, 70% ethanol – 4.1987, 40% ethanol – 4.9819, 30% – 5.4898; water – 5.3786.

Conclusion. The results obtained can be used for the plant material grown in Ukraine standardization.

PHARMACOGNOSTIC STUDY OF ALOE LEAVES

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Introduction. *Aloe vera* (L.) Burm. f. (syn. *A. barbadensis* Mill.) is a plant from *Liliaceae* family which grows naturally in Africa, Asia, China and many other parts of the world. The earliest documented use of *Aloe vera* comes from the ancient Egyptians, but it was also grown and used by King Solomon, who was said to have valued it highly. The plant, because of its medicinal value, it has been used for thousands of years as a herbal plant. Popular topical uses of the inner aloe leaf include treatment of abrasions, burns, cancers (as a poultice), inflammation, psoriasis, skin irritations and fungal infections, UV-radiation damage; as an emollient; and as a common cosmetic ingredient. Indications for internal use include diabetes, coughs and sore throat, kidney pains, digestive problems, stomach ulcers, and jaundice. The juice is also used as a mild laxative and for relief of difficult childbirth. Mixed in rum, the juice of aloe leaf is used as a carminative; with sugar, to relieve asthma and other bronchial afflictions, and with milk for dysentery in children.

Aim of the research. The aim of our research was to carry out pharmacognostic study of Aloe leaves collected in summer 2015 in Zambia.

Materials and methods. The identification of the leaf was carried out macro- and microscopically. Identification of biologically active compounds was carried out using quality reactions, paper and thin-layer chromatography.

Results and discussion. The leaf of aloe vera can be described as consisting of two major parts: the outer green rind and the colorless inner leaf. The inner leaf, alternatively referred to as “gel,” “pulp,” “mucilage layer,” “aquiferous tissue,” or “mesophyll,” is a clear, transparent, colorless mass. As the microscopic identification showed, the aloe leaf consists of the following tissues: epidermis covered with a waxy thick cuticle, chlorenchyma with needle-shaped oxalate crystals (styloids), a single row of vascular bundles between chlorenchyma and the inner parenchyma, which it encircles, and colorless inner parenchyma occupying the center of the leaf.

The reaction with 96 % ethanol allowed to identify polysaccharides in the plant material studied. Reactions with gelatin, ferric (III) chloride, quinine hydrochloride confirmed the presence of tannins in the aloe leaves. *p*-Coumaric and cinnamic acids, as well as such amino acids as arginine, lysine, leucine, phenylalanine, glutamine, alanine, aspartic and glutamic acids, were identified by paper chromatography, quercetin – by TLC. Thus, further study of the quantitative content of the main groups of biologically active compounds will be carried out in order to determine the quality of the plant material studied.

COMPARATIVE STUDY OF BIDENS TRIPARTITA AND BIDENS CERNUA HERBS

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Introduction. There are only four species of Bidens generation in Ukraine.

These are Bidens tripartita, Bidens cernua, Bidens connata, Bidens frondosa. Bidens tripartita is the most widespread species in Ukraine. The herb of Bidens tripartita is included into Pharmacopeia of Soviet Union of XI edition and widely used in folk medicine. The morphological characters of Bidens tripartita and Bidens cernua are very similar (the difference lies in number of phyllaries of anthodium, the position of anthodium in the air and cypsela), that is why Bidens cernua herb is often an impurity to Bidens tripartita herb. Therefore, comparative studying of Bidens tripartita and Bidens cernua herb for determination of distinguishing characters was actual.

The **aim** of the work is comparative studying of Bidens tripartita and Bidens cernua herb.

Research techniques. The Bidens herbs were prepared in the area of Kyiv and Vinnitsa in 2013-2015. The anatomical structure was studied on the surface and cross section view. We used test-tube reactions for preliminary research of qualitative composition of the raw material. The quantitative content of hydroxycinnamic acids and phlavonoids was studied by spectrophotometry.

Results. The anatomical structure of Bidens tripartita and Bidens cernua herb was similar. The diagnostic features of Bidens tripartita herb were middle pubescence of the leaf, which was presented by two types of hairs and less quantity of schizogenous conceptacles in cortex part of stem. The diagnostic features of Bidens cernua herb were more anfractuous cell walls of epidermis cells, sparse pubescence of leaf, which was presented by the only type of hairs, the cortex part of stem is formed by aerenchyma and many schizogenous conceptacles in cortex part of stem.

The herbs of Bidens tripartita and Bidens cernua contained free sugars and amino acids, polysaccharides and phlavonoids. The quantitative content of hydroxycinnamic acids and phlavonoids in Bidens tripartita herb was two and tree time higher, respectively, than in Bidens cernua herb.

Conclusions. As the result of studying of Bidens tripartita and Bidens cernua herb the difference features ~~of~~ in anatomical structure and quantitative content of hydroxycinnamic acids and phlavonoids were determined. Besides, free sugars and amino acids, polysaccharides and phlavonoids were detected. The obtained data will be used in further researches.

SEARCH PLANTS FLORA OF UKRAINE USED FOR NORMALIZATION OF METABOLISM

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Introduction. Under metabolism understand the totality of the changes taking place with agents from the moment they arrive in the organism from the environment until the formation of the final decay products, and output them from the body. Metabolism - those processes that are the foundation of a living organism. One of the first causes of metabolic disorders can be identified the hereditary factor. Also disorders can be caused by organic disease. However, most of these disorders are due to malnutrition. For the treatment of these disorders using tinctures, decoctions and drugs which include raw materials of medicinal plants.

Today there are many different plants in the Ukraine, which affect the metabolism of the human body. Basically, it is the representatives of the Asteraceae family Asteraceae.

Purpose of the study. Search plant that is used for normalization of metabolism, especially the flora of Ukraine.

Materials and methods. The objects of our research were representatives of family Asteraceae, Lamiaceae, Ranunculaceae, Fabaceae.

Results. In preliminary studies of the chemical composition of plants, it has been found that the pharmacological action due to the presence of phenolic compounds such as flavonoids, and an essential oil in the feed. In addition to the normalization of metabolism, burdock root and grass succession exhibit diuretic, diaphoretic, bactericidal effect, and improve digestion. Infusion of chamomile flowers is used for rinsing during inflammation oral mucosa, for washing the festering wounds, ulcers, hemorrhoids, douching with coleitis, Endocervicitis. Therefore, medicinal plants, have long been used in folk and scientific medicine, such as a real Burdock (Arctium lappa), A series of tripartite (Bidens tripartita) and chamomile (Chamomilla recutita), widely used in a number of diseases.

Conclusions. The findings suggest that the prospects of in-depth study of the burdock, chamomile, and a succession of tripartite representatives of both influence on metabolism.

OBTAINING AND RESEARCH OF EXTRACTS CALLUS MASS OF *GLADIOLUS IMBRICATUS*

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Introduction. Many imported drugs are in pharmacies of Ukraine in the moment, although we have drugs with similar effect. They are much cheaper than imported drugs. One reason for absence of domestic medicines - absence enough and assortment of of medicinal plants for their production. Modern biotechnology methods proposed to address of obtaining medicinal plants. Using the method of growing plants in conditions in vitro, can be obtained biomass in unlimited quantities. Callus biomass can use as a medicinal raw stuff, because it is clean, not contaminated and contains all biologically active substances that are in the original plant.

The **aim** is to develop a method for producing biomass from the tissue *Gladiolus imbricatus,* extracts research content of biologically active substances. Introduced into the culture *in vitro Gladiolus imbricatus*, as this is a rare plant Carpathians, is endangered and is listed in the Red Book of Ukraine with the status of "vulnerable". The plant contains many biologically active substances, such as flavonoids, glycosides, polysaccharides, vitamins, essential oils.

Materials and methods. In this paper, method cell cultures and tissues used for the cultivation of *Gladiolus imbricatus*. This method is based on growing undifferentiated callus mass in sterile conditions on agar nutrient medium. One of the important features of cell culture and tissue is preserving the capacity for synthesis of secondary substances, specific to original plant.

Results and discussion. Selected conditions obtaining callus biomass (2000 lux illumination, 16-hour photopriod, temperature 24-28 °C), growth regulators in the medium (NAA (0.5 mg/l), IAA (3.0 mg/l), kinetyn (0.5 mg/l). Extracts callus biomass of *Gladiolus imbricatus* were obtained and they were researched of qualitative and quantitative methods. Extracts were studied on the content of extractives and on the presence of phenolic compounds: simple phenols, polyphenols, flavonoids.

PHYTOCHEMICAL RESEARCH OF *TUSSILAGO FARFARA* L. LEAVES

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Introduction.

Coltsfoot (*Tussilago farfara L.*, *Asteraceae*) – a perennial herb with the outgoing rhizome into to one meter a depth of earth and giving the from seventeen to nineteen thousand seeds per year. Although, that *Tussilago farfara* L. was official plants, scientific interest of phytochemists and pharmacologists from different countries continues unabated to it.

The official herbal drugs was leaf of *Tussilago farfara* L. (*Tussilaginis farfarae folium*). In Chinese medicine, buds of *Tussilago farfara* L. flowers were herbal drug, which have used as anti-inflammatory and expectorant remedy. In ancient times, in England and America leaves of *Tussilago farfara* L. replaced tobacco with an analgesic effect; chronic cough was treated through the smoking of flowers.

Biologically active substances (BAS) of leaves *Tussilago farfara* L. have been studied completely and contains polysaccharides (mucus up to 10%), inulin; bitter glycosides; tannins (around 6%); sitosterol; saponins; organic acids; carotenoids; traces of essential oil; flavonoids (rutin, hyperoside); some of pyrrolizidine alkaloids senkirkine and tussilagine; vitamin C (to 80 mg%).

The aim of study – chromatographic study of biologically active substances of *Tussilago farfara* L. leaves, flowers, and reduced leaves.

Materials and methods.

The objects were flowers, reduced leaves and leaves of *Tussilago farfara* L., that have been harvested in different periods of plants ontogeny in Kharkiv region, Ukraine, in 2015.

For thin-layer chromatography (TLC) study 90% ethanol extracts of studied part have used, sorbent – wax «Sorbfil», the solvent system: ethylacetate – formic acid – water (10:2:3) and butanol – acetic acid – water (4:1:2); chromatographed at the temperature 20-22 °C.

The resulting chromatograms were studied in daylight after reaction with dimethyl sulfonic acid and solution of potassium hydroxide, 2% solution of aluminum chloride, Dragendorff reagent (solution of bismuth iodide in potassium iodide) and Zonnensteins reagent (solution of phosphomolybdic acid), fluorescence – in filtrated UV-light (354 nm) before and after reactions with chromogenic reagents.

The compounds have identified used by features fluorescence in UV-light and staining with chromogenic reagents, as well as the value of R_f.

The results and discussion.

In study objects of *Tussilago farfara* L. phenol carbonic acids, hydroxycinnamic acids, flavonoids and triterpenoids have been identified.

In leaves 2 alkaloids and 2 alkaloids in reduced leaves of *Tussilago farfara* L. have been found.

According to values of R_f and features fluorescence in UV-light, color of spots of BAS before and after reactions with chromogenic reagents 11 phenolic compounds have been identified in leaves, including 5 flavonoids; in reduced leaves – 6 phenolic substances, including 4 flavonoids; in flowers – 10 phenolic substances, including 6 flavonoids. In the result of acid hydrolysis of studied sum extracts of samples of raw material flavonol aglycones (kaempferol and quercetin); flavone (luteolin and diosmetin) chromatography identified; sapogenin had been present that R_f coincide to R_f uronic acid.

In the quantitative determination of hydroxycinnamic acid content in leaves and reduced leaves was carried out, and were 4.02% and 2.64% respectively.

Conclusions.

In leaves, flowers and reduced leaves of *Tussilago farfara* L. phenolic compounds, alkaloids and saponins were studied by chromatography.

For the first time BAS of reduced leaves of *Tussilago farfara* L. was studied.

PHARMACOGNOSTIC STUDY OF RAW MATERIALS OF MEMBERS OF THE FAMILY GERANIACEAE

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Introduction. The development and use of preparations based on plant raw materials is promising due to its wide spectrum of pharmacological activities and minimal side effects. Plants of the Geran family (Geraniaceae) are combined into more than 750 species of plants, mainly distributed in areas with temperate and subtropical climates. Distributed in South Africa, Australia and New Zealand. In Ukraine 3 known genera and 32 species. Plants of the genus Pelargonium are widespread, often cultivated in the open ground, are grown as houseplants. It is a perennial plants or herbal anist shruble. Has long been known beneficial properties of the plants of this genus. Our attention was drawn to the zonal Geranium (Pelargonium zonale), the popular name "cuddles". Favorable way It affects the human nervous system. Essential oil from the flowers improves the work of gastrointestinal tract, liver, pancreas, improves metabolism. In diseases of the cardiovascular system using a tincture of the roots of geranium.

Aim. To conduct a preliminary pharmacognostic studies of the raw materials members of the family Geraniaceae.

Materials and methods. The ground part Pelargonium zonale was harvested in the flowering period may-July 2015, underground organs – November 2015, late February-early March 2016.

Results and discussion. On leaves visible concentric circles of dark green or brown colors that share puberulent leaves the zone. Hence the name – zonal geranium. Distinctive morphological feature of this species is the pattern on the petals, it has the shape of a drop. As the fruit ripens the upper part of the ovary elongates, resembling the beak of a crane. Fruit – capsule, which is revealed from the bottom up. In the preliminary study of the chemical composition of geranium zonal revealed that the roots of the plant contain carbohydrates, triterpene saponins, tannins, phenolic compounds. Aboveground part of the plant contains carbohydrates, minerals, phenolics and alkaloids, in the leaves contains essential oil.

Conclusions. Preliminary morphological and chemical analysis of raw materials. The zonal geranium is a promising source of medicinal plant raw material.

AS FOR THE PROSPECTS OF GROWTH IN UKRAINE HERBS THAT CONTAIN SAPONINS

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Introduction. Medicines that contain saponins is often used in medicine. They are found in 900 species of plants belonging to 90 families. Saponins have mucolytic properties, so they are used in a dry and prolonged cough. Some saponins are diuretics, other tone up central nervous system or detect antihypertensive, anti-inflammatory and antimicrobial effects. In Ukraine, the largest demand is with species that contain saponins: : *Astragalus dasyanthus* Pall., *Eryngium campestre* L., *Helianthus annuus* L., *Inula helenium* L., *Nepeta cataria* L., *Oplopanax elatus* (Nakai) Hara, *Paeonia anomala* L., *Phlomis tuberose* L., *Potentilla alba* L., *Pulmonaria officinalis* L., *Thalictrum foetidum* L., some of which are as autochthonous as adventitious species.

The **aim** of our work was to study the environmental conditions for the growth of species that contain saponins and analysis of the prospects for their growth in different regions of Ukraine.

Results and discussion. A large number of native species is drought-resistant and photophilous that leads to their growth in the plains of the Ukraine. *Astragalus dasyanthus* is species listed in the Red Book of Ukraine, it is heliofit and xerophyt. It occurs in forest-steppe and steppe regions in the north among the remnants of steppe vegetation. In Ukraine it is widespread mainly in the Middle Dnieper. *Phlomis tuberosa* grows in all regions of Europe in the stripes of black soil, it is heliofit, xerophyt. In Ukraine in natural coenoses it is amplified in the forest-steppe and steppe regions. *Eryngium campestre* is widespread in steppe and forest-steppe zones of Ukraine; it rarely happens in the south Woodlands. The plant is heliofit and xerophyt. It is growing in the steppe grasslands, fields, roadsides and dwellings as a part of ruderal vegetation. *Potentilla alba* grows on various soils from dry to wet, nutrient-poor, sandy and clay. It is an oligotroph, mesophyt and optional heliofit. It prefers light, particularly oak and pine forests, forest edges and meadows. In Ukraine it grows in Polissya and Forest-steppe. *Pulmonaria officinalis* mainly grows in forests, among shrubs. In Ukraine the area covers Western regions. *Nepeta cataria* grows on forest edges, slopes, ruderal places. This species is optional heliofit and

mesophyt. The area covers the whole Ukraine. *Thalictrum foetidum* grows in light forests, forest edges, in the steppes, on open rocky cliffs and rocks on limestone, chalk, granite. It is heliofit and xerophyt. In Ukraine the plant grows in the western regions, especially in the Carpathian Mountains. *Inula helenium* grows along the banks of lakes and ponds, in the river valleys, wet meadows, forest edges, among the bushes. This medical plant is heliofit and mezohihrofit. It grows in territory of all Ukraine. In the southern part of our country it is rare, in the steppe regions Inula helenium is listed to the regional Red Lists.

Analysis of the adventive flora shows that *Paeonia anomala* is typical mesophyt, optional heliofit, which is widespread in Eastern and Western Siberia, which grows in forests, meadows and forest edges. *Helianthus annuus* is plant that originates from North America, mezotrof, mesophyt and heliofit. In the Central and Southern regions of Ukraine is widespread agricultural crop. *Oplopanax elatus* is an endemic of the southern Primorye and the Korean Peninsula. It is stsyofit, mesophyt, kind which is demanding to humidity. It grows in alpine spruce, fir and birch forests.

Analysis of the of natural distribution and ecological requirements of medicinal plants to growing conditions allows to determine most appropriate areas for cultivation, because phytochemistry methods proved that the most biologically content in raw materials will be at growing in the natural habitat types of the investigated medical plants. So, *Astragalus dasyanthus, Phlomis tuberosa, Eryngium campestre* is advisable to grow in the plains regions of Ukraine. *Inula helenium, Nepeta cataria, Potentilla alba* is better to grow in Forest-steppe region or in the Polissia. *Thalictrum foetidum* and *Pulmonaria officinalis* is the most productive if they are grew in the West of Ukraine. To determine the best regions for growing of the Siberian species *Paeonia anomala* we need more research. And in general the cultivation of endemic species *Oplopanax elatus* in open ground in Ukraine is problematic. Growing technology and regionalization of certain varieties only of *Helianthus annuus* among the studied introduced species of medical plants is developed in detail in Ukraine.

RESEARCH OF QUANTITATIVE VALUE AMOUNT OF γ – PIRON OF IRIS HUNGARICA AND IRIS SIBIRICA LEAVES

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Introduction. Plants of genus *Iris* are poorly understood and known only by decorative importance. In folk medicine iris was used as an analgesic, enveloping, expectorant, as well as a flavoring in the confectionery industry.

In the world there are more than 250 types of irises, about 13 species – in the territory of Ukraine.

According to the literature it is known that in the leaves of *iris* contain phenol carbonic acid: coffee, sinapic, *n* - coumaric, ferulic; flavonoids – quercetin; Ascorbic acid, also have xanthones, flavonoids, and isoflavones.

The biological activity of plants of genus *Iris* caused the presence of various groups of biological active substances, so they exhibit anti-inflammatory, analgesic, astringent, hemostatic, cardiotonic, anti-viral activity. Of particular importance has xanthones, namely mangiferin, which has immunostimulatory and antiviral effect.

Aim. Research of quantative value amount of γ-piron of plants of genus *Iris*.

Materials and methods. The objects of the study were the *Iris hungarica* leaves, harvested on May, 2014, and *Iris sibirica*, harvested on September, 2014 in N. N. Gryshko National Botanical Garden of the National Academy of Sciences of Ukraine, Kiev (Ukraine).

Previously we conducted a qualitative analysis of the studied objects by paper chromatography. On chromatography paper «Filtrak FN- 4» was applied 70% alcohol – aqueous extracts of irises leaves and then placed in a system of solvent: I – direction – *n*-butanol – acetic acid – water (4: 1: 2); II direction – 15% acetic acid.

After passage, the chromatogram was dried and viewed in visible and UV-light. Spots, that are characteristic for xanthones, had a yellow color, after tilling by ammonia vapors became yellow-orange, and after tilling by solution of 3% $FeCl_3$ – green color.

Quantitative determination of the content of xanthones in the feed conducted by spectrophotometry at 369 nm in the re-calculation of mangiferin.

About 2.5 g the crushed material was placed in a flask capacity of 250 ml and extracted with 80% ethanol. After obtaining the extract was treated with chloroform three times by 10 ml. The purified extract was transferred into a volumetric flask of 50 ml and adjusted to the mark by 80% ethanol. After 1 ml of solution was transferred into a flask of 25 ml and volume of solution was adjusted to mark by the same solvent.

The optical density was measured on a spectrophotometer 60 S UV - Visible, Thermo Scientific (USA) at a wavelength of 369 nm in a cuvette with a layer thickness of 10 mm. Calculation of quantitative content of xanthones in the re-calculation of mangiferin conducted by the formula:

$$X = \frac{A \times 50 \times 25 \times 100}{E_{1CV}^{1\%} \times m \times 1 \times (100 - W)},$$ where:

A – the optical density of test solution;

$E_{1CV}^{1\%}$ – specific absorption rate of mangiferin (295) at a wavelength of 369 nm;

m – mass of the sample, g;

W – moisture of feed,%.

Results and discussion. Statistical analysis of the results was conducted in accordance with the requirements of the State Pharmacopeia of Ukraine, the 1st issue, supplement 1, p. 5.3 in Excel XS application.

Iris hungarica

m	n	X_i	X_{cp}	S^2	S_{cp}	P	t(P, n)	confidence interval	ε_, %
1	2		3	4	5	6	7	8	9
5	4	1,65 1,66 1,63 1,60 1,68	1,644	0,000930	0,013638	0,9	2,13	**1,64 ± 0,03**	1,76

Iris sibirica

m	n	X_i	X_{cp}	S^2	S_{cp}	P	t(P, n)	confidence interval	ε_, %
1	2		3	4	5	6	7	8	9
5	4	1,30 1,27 1,31 1,28 1,29	1,29	0,000250	0,007071	0,9	2,13	**1,29 ± 0,02**	1,1675

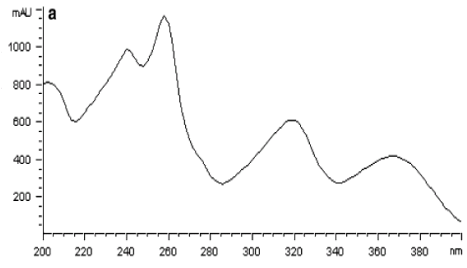

Fig. UV-spectrum of alcohol solution of I. hungarica leaves (96% ethanol)

UV-spectrum has 4 absorption maxima, which is typical of xanthones. As a result of quantitative determination of xanthones found that the leaves of *I. hungarica* content 1.64±0.03%, *I. sibirica* – 1.29±0.02%, in the re-calculation of mangiferin.

Conclusions. According to the results of previous studies, we can conclude that in the leaves of plants of genus *Iris* content xanthones more than in the underground organs.

STUDY OF DYNAMICS OF BIOACTIVE SUBSTANCE EXTRACTION FROM YELLOW BEDSTRAW (Galium verum) HERB MEAL

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Introduction. The yellow bedstraw *Galium verum* L. of the *Rubiaceae* Juss. family belongs to cosmopolitan plants; its areal covers almost all the temperate zones of Eurasia. In the territory of Ukraine, it is found everywhere, excepting the Carpathian Mountains. The plant is not officinal but widely used in the traditional medicine of many countries as a choleretic, diuretic, anti-inflammatory agent. Anteriorly, at the Pharmacognosia Chair of the National Pharmaceutical University of Ukraine, the chemistry of the herb and rhizomes with roots of the yellow bedstraw was studied. In the herb, hydroxycinnamic acids, coumarins, flavonoids, iridoids of asperulosid group, saponins, ethereal oil were fond; it has been established that in the underground organs, antracene-derived alizarin groups accumulate. The lipophilic and phenol fractions obtained in the experiment showed antimicrobial and fungicide activity. The antioxidant and citostatic activity of dry yellow bedstraw herb extracts obtained by aqueous and 70% ethyl alcohol extraction of the starting materials has been studied.

Aim. Continuing the earlier studies, it was a hot topic to determinate the possibility of a complex raw material processing, specifically, obtaining a dry extract from the yellow bedstraw herb meal remaining after subsequent obtaining lipophilic and phenol complexes.

Materials and methods. The objective of this work was to study the dynamics of bioactive substance (BAS) extraction from the yellow bedstraw herb meal. The object of the study was the meal remained after a subsequent and exhaustive extraction of the yellow bedstraw herb by chloroform and ethyl acetate-alcohol mixture (8:2). The obtained dry meal (m=23.61 g) was covered with water (V=235.0 ml) and heated in the boiling-water bath for 30 min, after which it was filtrated. The procedure was repeated 6 times. Six overflows were obtained: 100 ml, 230 ml, 207 ml, 222 ml, 203 ml, 239 ml, respectively. In the obtained overflows, dry residue was determined as the parameter of the extractive substance.

Results and discussion. As a result of the study, it was established that the water saturation factor of the meal was 7.7 ml/u. The dry residues in the overflows are 1 – 2.30%, 2 – 2.35%, 3 – 2.36%, 4 – 1.86%, 5 – 1.95%, 6 – 0.97%, respectively.

Conclusions. The obtained findings provide a background for subsequent study of the dynamics of BAS extraction from the yellow bedstraw herb meal, specifically, the determination of the main BAS group content in the relevant dry extracts.

PHARMACOGNOSTIC STUDY MATERIALS PLANTS FAMILIES ROSACEAE AND FABACEAE

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Introduction. Many plants family Rosaceae have a huge economic value as fruit plants. In addition to eating their fruits are used in perfumery and medicine.

Representatives of the family Fabaceae long been cultivated as food plants that have become public in agriculture; in medicine and pharmacy used by many different pharmaceutical effects.

The aim of the study. Identify which pharmacological effects have plants families Rosaceae and Fabaceae.

Materials and methods. Representatives of the family Rosaceae: Sorbus aucuparia (rowan) (Sorbus aucuparia), European raspberry (Rubus idaeus), Rosa Canina(dog-rose)(Rosa canina); and Fabaceae: Yellow melilot(Melilotus officinalis), Common bean(Phaseolus vulgaris), Liquorice(Glycyrrhiza glabra) and Soybean (Glicine hispida).

The obtained results. The fruits of rowan, raspberry and dog-rose are multivitamin material. Fruits contain, phenolic compounds, organic acids, sugars, pectin and tannins, flavonoids, it causes the following pharmacological effects: a multivitamin, immune-stimulating, antioxidant, anticoagulant.

Grass yellow melilot contains: coumarone, protein, essential oils, mucus, nitrogen compounds, flavonoids, purine derivatives, sugars, so has the pharmacological effects expectorant, anticoagulant, emollient. Grass and/or oplodni common bean contain: flavonoids, coumarone, nitrogenous compounds, protein, amino acids, which cause hypoglycemic and diuretic action. Root of are Liquorice composed of: flavonoids, triterpene glycosides, pectin, carbohydrates, resins, lipids, bitter compounds, sugars, so have expectorant, laxative, antiulcer and antisecretory action. Seeds of soybean contains: fatty oil, proteins, vitamins, isoflavone glycosides; soybean phospholipids with flakuminom complex vitamins and is a component of the drug lipofen that take diseases used to treat gastro-intestinal tract.

Conclusions. That plants families Rosaceae and Fabaceae may be eligible for further in-depth study to parsing entire spectrum of pharmacological effects.

PHARMACOGNOSTIC ANALYSIS OF HERBAL MIXTURES USE IN OPHTHALMOLOGY

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Introduction. Nowadays different medications which have antioxidant, anti-inflammatory and immunomodulating effects are used to treat diseases of eye. Therefore, the development of the herbal mixtures, that affects various components of the disease, may be used in the long-term treatment and prevention, as well as the herbal mixtures standardization are relevant trends of research in pharmacy.

We have developed a herbal mixtures that includes red clover blossoms, blueberry fruits and ginseng roots. The choice of these types of raw herbal materials is caused by various groups of biologically active substances (BAS): anthocyanins, isoflavones, triterpenoids, which have antioxidant, immunomodulating and adaptogenic effect.

The aim of our research is to develop methods of establishing the authenticity of the herbal mixtures components.

Materials and methods. Red clover blossoms, blueberry fruits and ginseng roots have become the object of studying (producing plant - cultured Panax ginseng). A macroscopic analysis of the herbal mixtures component was carried out visually and by magnifying glass. A microscopic examination was performed using pharmacopoeial methods described in articles of 1.vol of SPU 1.4 add. (2.8 - "Methods of Pharmacognosy", "Medical raw herbal material") and private articles on the corresponding raw material. A microscopic analysis revealed the presence of diagnostically significant signs that are characteristic to the herbal mixtures components.

Herbal mixtures humidity indicators, common ash of herbal mixtures, based on absolutely dry raw herbal materials, in percent; the fineness and the content of impurities in the herbal mixtures have been determined. Types of materials included in the herbal mixtures contain different groups of biologically active substances (BAS): phenolic compounds: anthocyanins, flavonols, flavones, isoflavones, coumarin, tannins; triterpenoids. Quality, quantity and

composition of BAS identification was carried out using modern methods of chemical, physical and physical-chemical analysis.

A chromatographic investigation of flavonoids and phenol carbonic acids amount was carried out by ascending chromatography in a thin layer of sorbent (TLC) on Silufol, Sorbfil PTLC-P-A-UV, Sorbfil PTLC-AF-A-UV, Sorbfil PTLC-AF-B UV plates. By TLC method alcoholic extraction with ethyl alcohol (50%, 70%, 90%) in a ratio of extractant and raw herbal material 1:10 and the amount of aglycones obtained from acid hydrolysis were analyzed. In order to separate amounts of BAS: ethyl acetate - acetic acid (8:2); benzene - ethyl acetate - acetic acid (50:50:1); ethyl acetate - formic acid - water (8:1:1).

Chromatograms were studied by UV-light at 354 nm wavelength. The plates were developed by 5% ethanolic solution of aluminum chloride and the change in fluorescence stain substances were observed. To identify natural substances in the chromatograms the authentic samples of substances were used: quercetin, kaempferol, hyperoside, rutin, formononetin, daidzein, caffeic acid, chlorogenic acid and also were compared with such drugs – tincture of ginseng and "Blueberry-F", the manufacturer PLC ITF "Pharmacom", Kharkiv.

Results. The basic diagnostic signs of significant anatomical signs of herbal mixtures were established. As a result flavonols – quercetin, kaempferol, hyperoside, rutin; hydroxycinnamic acid – caffeic, chlorogenic; saponins were found, R_f values of which correspond to some saponins of ginseng tincture.

Conclusions. Pharmacognostic analysis of herbal mixtures which includes red clover blossoms, blueberry fruits and ginseng roots and is used in ophthalmology was carried out.

THE STUDY OF RAW MATERIALS COMMON REPRESENTATIVES OF THE GENUS *TRIFOLIUM*

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Entry. An important aspect of the development of modern pharmacy is to develop high quality, effective and low-toxic medicines. From this side of attracts the attention of medicinal plant material, especially plants, which have long been used in folk medicine. Our attention was drawn by the representatives of the genus *Trifolium,* of the subfamily *Faboideae* family *Fabaceae*. The genus has 230 species which are distributed in temperate and subtropical areas of the globe, except Australia. Plants of the genus *Trifólium* – one-, two - or perennial herbaceous plant, reaching a height of 15-55 cm, with a stalk that rises. The people you can meet such names as: white clover, clover, Krasnogorovka, meadow trefoil, bee bread.

It is known that the flowers and leaves have expectorant, antiseptic and diuretic properties and is used in cystitis, as an astringent in diseases of the gastrointestinal tract. From leaves receive vitamin concentrates. The infusion and decoction of flowers is used in tuberculosis, whooping cough, uterine bleeding and as a tool that increases appetite. Has found its application in homeopathy and is a member of therapeutic teas. Agriculture serves as a forage grass for animals.

The purpose of the study. To conduct a preliminary pharmacognostic studies of the raw material of the genus *Trifolium*. To determine the morphological features of raw materials.

Materials and methods. The leaves are harvested April-Jun, flowers in July – August 2015

The results. Leaves – palatised, tricast, the components of the simple leaves are short with shirokoryadny leaf blades with finely toothed margin. The stipules are joined to the main petiole , leaf-like or scarious. The inflorescence is a rounded or oval head are usually in pairs and spike-like and umbrella-shaped, flowers – red, white, purple, yellow, at the end of flowering light brown, 4-6 mm, fruit – simple Bob.

The leaves contain essential oil, fatty oil, vitamins, organic acids and flavonoids, including MacIan, tannins. In the flowers contain phenolic compounds and amino acids.

Conclusions. Analysis of the results showed that members of the genus *Trifolium* is a promising plant for further studies and creation of drug substances on their basis.

A NEW UKRAINIAN VARIETY “PERSEI” OF DESMODIUM CANADENSE - PROSPECTIVE HERBAL RAW MATERIALS

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Introduction. The interest in medicinal plants has always been high, as they have helped mankind for centuries to treat a variety of ailments. They were used, and used in all continents of the world today, so the creation of drugs from medicinal plants has not lost its relevance. In the wild harvested raw materials for the industrial production of drugs has become difficult due to the plowing of land, the construction of various infrastructures, the high financial cost of transportation of raw materials, storage. Reduced plant area. Many species are listed in the "Red Book", such as Adonis vernalis. All this complicates harvesting of medicinal raw materials in nature. In connection with this, it was efficiently to cultivate plants in the plantation zone stations, making it easy to monitor the development of plants, cleaning, preparation of raw materials for storage, to keep seed fund.

Aim. Introduction into the culture, a new variety desmodium canadian – Persei. In connection with the gradual transition of Ukraine to work with the pharmaceutical raw material according to reguirements of GACP (order №118 of the Ministry of Health 2013), there is a need for the reproduction of cultivated raw materials, especially of foreign origin.

Materials and methods. Desmodium canadian – North American plant, so the new variety of desmodium candian was established on the basis of these requirements - Persei with stable indicators. In 2014, included in the State Register of plant varieties suitable for dissemination in Ukraine. The variety provides a distinction, uniformity, and stability of indications under cultivation.

Result and discussion. The variety cultivated in Ukraine in conditions of the forest-steppe zone on the station for many years (Poltava region, Berezotocha) for use as herbal raw materials. The plant is a perennial, not demanding to the culture is subjected to mechanical harvesting; the yield is quite high, and it can reach up to 60 centners for 1 hectares, seeds to 15.5 centners for 1 hectares. In the season of mowing is carried out 2-3, which ensures demand for raw materials. Ability to bookmark a plantation area of 5-7 hectares.

Conclusions. Raw materials from desmodium Canadian varieties Persei can provide the need not only for the production of ointments "Fladeks" on Pharmaceutical company "Zdorovye", but also are used for the making other dosage forms for the treatment and prevention of viral dermatitis, as well as for a more complete study of the chemical composition plants. Persei variety may be used as a fodder crop, as well as other types of herbaceous desmodium, replacing Medicago sativa and Trifolium pratense when sowing in combination with other plants for crop rotation.

THE POSSIBILITIES OF IMPORT SUBSTITUTION OF MEDICINES ON UKRAINIAN PHARMACEUTICAL MARKET

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Introduction. Economic difficulties in the country put the currently retrofit-ting the problem and improve production to all sectors of the economy to meet the needs of the population. To solve the difficult economic situation is necessary and the pharmaceutical industry. On the market today, there are more than 9 thousand registered medicine of foreign and domestic production, of which only 30% -. medicines produced domestically. The development of the pharmaceutical market puts high demands on the specialists, who should be informed of the most significant medical and social problems of modern medicine, the presence of the range of certain drugs, their effectiveness, the use of features, cost, etc., across all groups of drugs and in particular anti-herpes drugs group.

Aim. Given the need for import substitution should be based on the capacity of the pharmaceutical industry to develop the creation of new dosage forms, availability of raw materials, substances, production, analysis and quality control.

Materials and methods. Pharmaceutical company "Zdorovye" based on fladeskan substance, representing the amount of flavonoid anti-herpetic action, produced ointment "Fladeks". The raw material for its production is a Desmodium canadense , family Fabaceae, which provides the raw material base. Depending on the application fladeskan-substance can be used to develop the technology to other dosage forms. Currently, there are more than 100 types of herpesvirus, carriers which, according to WHO, is 75-95% of the adult population. Despite all the advances in the treatment of herpes virus infection, the problem of treatment of herpes simplex virus remains valid.

Results and discussion. Analyzing the amount of drugs used to treat viral diseases, we can conclude that the number is insufficient for practical use in medicine. The range of domestic products today has a narrow range of products, taking into account the problem diseases. Reducing dependence on imported drugs has some economic sense since local products are much more accessible of import in the context of pricing but it is not inferior to the efficacy and safety of other imported goods.

Conclusions. Considering the above, we have developed other dosage forms of the substance-fladeskan: eyedrops, aerosols, liquid dosage form, the tablets. Ongoing product development will ensure efficient health queries, exclude the purchase of imported drugs of similar action and become competitive in the pharmaceutical market in Ukraine.

PHARMACEUTICAL STUDY OF RAW MATERIAL OF LILIACEAE FAMILY REPRESENTATIVES

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Introduction. Medical plants are widely used in conventional medicine through availability, wide spectrum of biological action and small toxicity. One of modern pharmacology primary concerns is a search of new sources of medical raw materials. Liliaceae – Lilies class family counts 19 monocotyledonous genus and over 600 types of plants. The representatives of Liliaceae family are wide spread almost on all earth. Mostly meet in the moderate breadths of Eurasia, North America, in Africa. Some representatives are wide spread in the mountain districts of South America, tropical Africa. Family is presented by long-term herbares. Leaves are long linear with arc venation. Above-ground shoot is not ramified. Underground shoot is modified, has the appearance of rhizome, bulb or tuber onion, due to what a plant is kept during a cold or heat. A perianth is simple, consists of 6 flower leaves in two circles. Flower leaves are free or growing, often brightly painted or white.The amount of stamens equals 6, they are located in two circles for 3. Cookery gynoecium, an ovary is overhead. A fruit is a three slot small box or berry. Family of Liliaceae includes medical (lily of the valley) and food (onion, garlic) plants. Many representatives are popular as decorative; first of all it is tulip. About 4000 sorts are shown out for today. Also popularity is used by lilies with astrong aroma and hyacinths. Among room plants aloe and asparagus are popular. Our attention was attracted by the plants of Chlorophytum sort of Liliaceae family.

Aim. To undertake a previous pharmaceutical study of raw material of Chlorophytum genus representatives. To define the morphological features of raw material.

Materials and methods. Leaves were provided from hemerophytes in May-June and in September 2015.

Results and discussion. Chlorophytum is a grassy plant with drooped stems. Leaves are light green, long linear bow-shaped curved, collected in root fascicules. Flowers are small, collected in a panicle. Pointers of flowers are arched form. After flowering form on the ends the fascicules of leaves with air roots. A plant grows quickly, and on spring and summer on thin stems appear white flowers, and then rosettes of leaves. Chlorophytum is considered to be one of most effective air clearance in a room. It takes in formaldehyde and carbon dioxide, and distinguishes oxygen. A plant contains essential oils in the composition, anthraquinone and cascarosides.

Conclusions. The analysis of research results became the first step in the pharmaceutical study of raw material of Liliaceae plants families, which are the perspective sources of medical raw materials.

SELECTION CONDITIONS OF DETERMINE THE EXTRACTIVES IN THE HERB PEONY

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Introduction. Herbal drugs occupy a significant place among range of medicines, due to their efficacy and relative safety. An important trend is the extensive study of previously known plants of Pharmacopoeia and expanding the range of herbal medicines. Paeonia anomala L., commonly known as peony, is used since ancient times in traditional and folk medicine for the treatment of diseases of the nervous system, gastrointestinal tract, urogenital system, etc. However this plant having valuable properties is included in the red books of Republic of Bashkortostan and Komi, Sverdlovsk, Chelyabinsk, Kurgan and Tyumen regions, Khanty-Mansi and the Yamal-Nenets Autonomous district. It was suggested to use of garden varieties peony as raw material for producing drugs with the aim of preserving this species.

The content of extractives is an important measure of the quality of medicinal plant raw materials which is used to obtain the extraction drugs. This indicator characterizes the content of amount of biologically active substances in raw materials.

Aim. The aim of this work was determination of extractives in the herb peony and herb peony garden.

Materials and Methods. Herb peony and herb peony garden were used as objects of investigation. Purified water, ethyl alcohol in concentrations of 40% and 70% were used as extractant.

Result and discussion. The research showed that тhe use of purified water and alcohol in a concentration of 70% does not allow to extract the complex of biologically active substances in full. The highest content of extractives in the herb peony and herb garden peony was observed when using the ethyl alcohol 40% as the extractant. The content of extractives was 59.95±2.51% in the herb peony. Also it was determined the content of extractives in the herb peony garden varieties – 54.21±2.33%. The data show that the peony and the peony garden have close values of parameter "Extractive substances".

Conclusions. Thus, it was found of extractives in the herb peony and herb peony garden, as well as the choice of the optimal extractant for the determination of this parameter which is important for the standardization of medicinal plant raw material and subsequently can be included into the regulatory documents.

COMPARATIVE CHARACTERISTIC OF QUANTITATIVE CONTENT OF ALKALOID BERBERIN IN ROOTS OF COMMON BARBERRY AND HERBS OF GREATER CELANDINE, GROWING IN KAZAKHSTAN

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Introduction. Alkaloids are organic nitrogen-containing compounds of the main character, meeting in vegetable organisms and possessing strong physiological action. One of representatives of alkaloids is berberin with a chemical formula – $C_{20}H_{17}NO_4$ which is contained in various parts of many plants and considered as one of widespread in a vegetable kingdom. Berberin has the following physiological properties – lowers blood pressure, reduces cardiac function, causes contraction of smooth muscles and intestines, strengthens the separation of bile, etc.

Aim. To determine the content of berberine in the roots of common barberry – Radices Berberidis vulgaris and herb greater celandine - Herba Chelidonii majus by spectrophotometric method.

Materials and methods. By accurately weighed, it has taken by 0.5 g of dried roots of common barberry and 0.5 g of herb greater celandine, which then have been crushed by a crushing machine Retsch "SM300". The crushed received mixes have been placed in 2 conic flat-bottomed flasks with a capacity of 100 ml. To each mix 0.5 ml of 25% of solution of sodium of hydroxide have been added and carefully mixed before obtaining the homogeneous humidified mass. Then 50 ml of air have been added to each flask. . After thorough mixing the two flasks were left for the night. By pipette 15 ml of radio extraction of each mix which have placed in flat-bottomed conical with a capacity of 100 ml. Alkaloids were extracted by 2% solution of sulfuric acid in the portions of 20,10 and 10 ml (until negative reaction by silicowolframic acid. The joint acid extraction have been placed in a measured flask with a capacity of 50 ml and brought by solution volume to a tag of 2% sulfuric acid. After careful hashing the optical density has been determined by a spectrophotometer “Spekol 1300”: solution of herb greater celandine at the wavelength of 420 nanometers in layer of 1 cm, and solution with roots of common barberry

ordinary at the wavelength of 345 nanometers.

Results and discussion. The content of berberin bisulfate in percentage in terms of absolutely dry raw materials has been calculated (X) by a formula:

$$X = \frac{50 \cdot 50 \cdot 100 \cdot D}{15 \cdot 128 \cdot (100 - W) \cdot m}$$

50 – volume of ethereal extract in milliliters;

50 – volume of sulfuric acid extraction in milliliters;

15 – volume of ethereal extract taken for analysis in ml;

128 – specific indicator of absorption of a berberin bisulphate E at the wavelength of 420 nanometers;

D – optical density of sulfate extraction;

m – weighed quantity in grams;

W – loss of drying weight in percent.

The content of berberin bisulfate has appeared in a herb greater celandine – 1.7%, and in roots of a common barberry – 0.9%.

Conclusions. The content of alkaloid berberin in a herb greater celandine was 1.9 times more, than in roots of a common barberry. It confirms that alkaloids in a greater celandine are as, a free and connected states. Therefore the preparations of a greater celandine are widely applied for cauterization of warts and a candilomas, and also can detain the growth of malignant tumors, and have the fungistatic and bakteriostatic effect on Mycobacterium tuberculosis. In a common barberry, the content of alkaloid berberin is the main, except it contains other alkaloids - palmitin, yatrorizin, kolumbanin. Therefore, the roots of a common barberry serve as the main raw materials for receiving berberin sulfate which is applied at treatment of diseases of biliary system - chronic hepatitis, cholecystitis, cholelithiasis.

PHARMACOGNOSTICAL COMPARATIVE ANALYSIS OF THE RHIZOMES OF YELLOW IRIS FROM DIFFERENT GROWING PLACES

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Introduction. *Iris pseudacorus* L. is quite common in nature. Its range covers Europe, Asia, North America, parts of Africa. In nature it occurs along waterways, in floodplains. Iris is the ancestor of many varieties and hybrids of Irises. Irises have been bred, hybridized and selected for more than 150 years. There are some 300 species of irises and more than a thousand named hybrids and selections.

There are tannins, essential oil, a glycoside of an isoflavones iridin, organic acids, fatty oils, starch in the rhizomes. Rhizome of *Iris* includes main active ingredient for therapeutic use – unique essential oil, which contains a ketone iron that gives the oil the smell of violets. The Iris roots' has anti-inflammatory, expectorant, enveloping properties. The rhizome was formerly much employed as a medicine, acting as a very powerful cathartic, but from its extremely acrid nature is now seldom used. An infusion of it has been found to be effective in checking diarrhoea, and it is reputed of value in dysmenorrhoea and leucorrhoea.In folk medicine it is used in diseases of the spleen, pneumonia, tonsillitis, women's diseases, treatment of purulent wounds, ulcers, fistulas, and for removing freckles. The decoction of root is used for inflammation of the gums, toothache, and for washing the hair with dandruff.

Medicinal raw materials are rhizomes of Iris, its quality is regulated FS 42-17-72. Rhizomes harvested in the fall or in early spring before growth (April). The raw material consists of whole or cut along the rhizomes, with the tracks cut off roots and leaves.

Aim: to carry out morphological and anatomical studies of 7 series of a raw material rhizomes of *Iris pseudacorus* L. from different regions and years of collection, set similar or distinctive features of the *Iris* series from different places of growing, using modern methods and devices.

Materials and methods. The objects of study were 7 samples of the rhizomes of *Iris pseudacorus* L. in the flora of Ukraine that was prepared in: 1. Kirovohrad region, village Verblyuzhka (2014); 2. Kharkiv region, village October (2015); 3. Kharkiv region, village Borscheva, (2013); 4. Kharkiv, Botanical Garden of the National University of Pharmacy (2015); 5. Kiev, N. N. Gryshko National Botanical Garden of the National Academy of Sciences of Ukraine (2015); 6. Kharkiv, V.N. Karazin National Botanical Garden of the National Academy of Ukraine (2014); 7. Nikolaev region, Nikolaev (2014).

For macro - and microscopic studies used fresh and fixed in a mixture of alcohol-glycerin-water (1:1:1) plant material. A solution of chloral hydrate and 3% alkaline solution is used as a developing liquid. Cuts and drugs made by known techniques with the surface by the blade from the arm.

Anatomical structure was determined by microscope MBI-6, sections were photographed with the camera CANON IXUS 120.

Determination of loss in mass when dried, general ash carried out according to the methods of SPhU; identification; quantitative content of isoflavonoids was held by spectrophotometric method with wavelength 271 nm; transfer content held on onozìd (FS-42 in Grass beans'). Spectrophotometric techniques are used to measure the concentration of solutes in solution by measuring the amount of light that is absorbed by the solution in a cuvette placed in the spectrophotometer.

Morphological investigation. Rhizome of Iris is up to 10 cm in length, up to 3 cm. There is thick, powerful, creeping, branched, the cut has a pink tint. Outside color is earthy-brown, fracture - lilac-pink. Odor is faint and taste is astringent. Comparative analysis of the morphological structure rhizomes' of Iris of 7 samples showed that all the samples of raw iris are identical.

Results and discussion. A rhizome is covered by a monolayer epidermis, stomates and trichomes are absent. A border between a primary bark and central cylinder differentiates on the ring of shallow leading bunches that on periphery meet more often, but have little sizes, to the center their amount diminishes and a size grows. According to the structure beams are centralloan. Among cells of the phloem are parenchyma cells filled with simple starch grains concentric. The vessels of vascular bundles are porous and spiral. Cells of stocking parenchyma are large, with thick shells, containing starch, and in the triangular intercellular spaces are found styled square and elongated shape. Conducted microscopic studies of various series of iris testify about the identity of their diagnostic anatomical features.

Identification of phenolic compounds was performed by conventional reactions: 1% ferum (III) chloride, appears dark blue colour.

Conclusions. As a result of the research, the following numerical indicators: loss in weight on drying not more than 12.0 percent; total ash – not more than 5.0%. In addition, it was determined that impurities not more than 5.0% (residues of stems and leaves, including those separated during analysis), as well as old dead roots; not more than 5.0% of foreign particles, including not more than 3% of impurities of mineral origin. The sum of isoflavonoids in terms of onozid and the dry raw material should be not less than 1.5%.

Thus, studies can be recommended in the development of the monograph "The rhizome of Iris " to enter it into SPhU.

A STUDY OF THE MINERAL COMPOSITION OF THE UNDERGROUND ORGANS OF SYRINGA VULGARIS

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Introduction. Syringa vulgaris is one of the most common and favorite ornamental plants all over the world. There are more than 600 different species of this shrubbery. This diversity of species promoted to use the plant for landscaping parks and public gardens in many countries. However, Syringa vulgaris is known not only for its unique beauty, fragrance and resistance to various natural and climatic conditions, but also valuable medicinal properties.

The chemical composition of lilac is very diverse. The major active ingredients are flavonoids, coumarins, tannins, iridoids, vitamins and a glycoside syringin. Syringa vulgaris has been used for a long time in folk medicine for the treatment and prevention of numerous diseases, such as kidney stones, colds, malaria, nervous disorders, diabetes. It is also used to treat wounds, bruises and other injuries. The plant is an excellent and almost the only remedy in the treatment of the joints (arthritis, rheumatism, gout) due to its strong anti-inflammatory action. The officinal medicine uses the Syringa vulgaris bark as a raw material for syringin (eleutheroside B) obtaining, which is a marker for standardization of drugs derived from the rhizomes and roots of Eleutherococcus senticosus.

Aim. A wide range of biological action of Syringa vulgaris is a promising direction for its phytochemical research. The aim of our study was to investigate the mineral composition, qualitative and quantitative content of macro- and microelements in the underground organs of Syringa vulgaris. Raw materials were harvested in autumn of 2014 and 2015 at Kharkiv region.

Materials and methods. The mineral composition was determined using atomic emission spectrographic method. For obtaining spectra and their registration on photographic plates, a DFS-8 spectrograph with a diffraction grating of 600 lines / mm and a three-lens system lightening of the gap was used. Spectra were registered in the region 230-330 nm. The content of the element at the cinders (a, %) were found using the calibration curve.

Results and discussion. Element content (x, %) in the ash of roots of Syringa vulgaris was calculated by the formula: $x = \frac{a \cdot m}{M}$,

where m – ash weight (g), M – mass of raw material (g), a – the element content in ash (%). Results are reported in Table 1.

Table 1

Results of the analysis of the mineral composition
of Syringa vulgaris roots

№	Element	Content, mg / 100 g
1.	Fe	16.00
2.	Si	70.00
3.	P	80.00
4.	Al	6.90
5.	Mn	1.10
6.	Mg	80.00
7.	Pb	<0.01
8.	Ni	0.34
9.	Mo	<0.03
10.	Ca	230.00
11.	Cu	0.23
12.	Zn	1.10
13.	Na	23.00
14.	K	575.00
15.	Sr	<0.01

As seen in Table 1, 15 elements were found. Seven of these elements (Fe, Si, P, Mg, Ca, Na, K) belong to macronutrients, 8 – to micronutrients (Al, Mn, Ni, Mo, Cu, Zn, Sr). It should be noted that the underground parts of the plant have a high content of potassium (575.00 mg/100 g), calcium (230.00 mg/100 g), magnesium (80.00 mg/100 g), phosphorus (80.00 mg/100 g) and silicon (70.00 mg/100 g). Roots of plant also accumulate sodium (23.00 mg/100 g), iron (16.00 mg/100 g) and aluminum (6.90 mg/100 g), but in smaller quantities. The heavy metal content didn't exceed 0.01 mg/100 g.

Conclusions. The conducted researches prove the existence of a significant number of macro- and microelements in underground organs of Syringa vulgaris. Results of the analysis of the mineral composition will be used for new drugs creation, in developing methods of quality control of plants from the Syringa genus.

PROSPECTS OF A NEW DRUG CREATION FROM *SALVIA OFFICINALIS* LEAVES EXTRACTS

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Introduction. The task of the modern pharmaceutical industry is the development of complex processing methods of medicinal plant raw materials (MPRM), allowing maximum use of its capabilities.

In the market of Ukraine more than 40 medicines were registered, which contain biologically active substances (BAS) of sage leaves. Earlier, the domestic pharmaceutical industry produced drug "Salvin" - 1% alcoholic solution of acetone extract from sage leaves. Since the acetone was later assigned to precursors, the manufacturers declined to produce this product, although the efficiency of its use for the treatment of infectious and inflammatory diseases of the oral cavity. Acetone extracts more agents terpenic nature (mono-, sesqui- and diterpenes), whereas in the meal still remain more polar substances, in particular of phenolic nature. In connection with the above, it was expedient to develop a method for complex processing of this raw material.

Aim. Therefore, the aim of our research was to investigate the chemical composition and the pharmacological activity of the extracts obtained by processing complex *Salvia officinalis* leaves.

Materials and methods. For replacing acetone we have used ethyl acetate for getting the *Salvia officinalis* leaves extract similar to Salvin. From Sage leaves, after receiving ethyl acetate extract, a dry extract was obtained with purified water.

For preliminary identification of biologically active substances we used thin layer (TLC) and paper (BC) chromatography.

Substances of the flavonoid nature were determined by TLC with authentic samples of flavonoids in the solvent system of glacial acetic acid R – water R – ethyl acetate R (20:20:60). Chromatograms were developed by spraying with dimethylaminobenzaldehyde solution; then the plate was heated at a temperature from 100 °C to 105 °C for 10 min up to development of spots and examined in the daylight.

Results and discussion. As a result of the preliminary study of BAS with authentic samples by TLC the presence of such groups as derivatives of hydroxycinnamic acids (caffeic and chlorogenic acids) and flavonoids (rutin, apigenin and hyperoside) were determined.

Further study of the compounds of terpenoid nature was carried out by gas chromatography-mass spectrometry.

35 substances have been detected in the volatile fraction, of which 23 have been identified in the ethyl acetate extract. Their content was 5.48%. The dominating substances are 1,8-cineole, alpha-thujone, .beta.-thujone, camphor, borneol, viridiflorol and epi-manool.

In addition, the study of the qualitative composition and quantitative content of phenolic compounds as the target of research was conducted by the method of high performance liquid chromatography (HPLC) using an Agilent Technologies chromatograph (model 1100) equipped with a flow-through vacuum degasser G1379A, a four-channel pump of the low pressure gradient G13111A, an automatic injector G1313A, a column thermostat G13116A and a diode array detector G1316A. To conduct the analysis a "ZORBAX-SB C-18" chromatographic column with the size of 2.1×150 mm was used, it was filled with the octadecylsilyl sorbent with the granule size of 3.5 μm.

A result of studying phenolic compounds of thick and dry extract of the *Salvia officinalis* leaves by HPLC (Table 2) revealed 15 phenolic substances, including 3 hydroxycinnamic acid - caffeic, chlorogenic and rosemary; 6 flavonoids - apigenin, luteolin, quercetin, 3-metoksilyuteolin, luteolin-7-O-glucoside and quercetin-3-O-arabinoside; 6 failed to identify substances. The content of phenolic compounds in the aqueous dry extract almost five times higher than in the ethyl acetate thick extract, indicating that the predominant raw glycosidic forms of phenolic compounds and reiterates its promise complex processing.

Study of antibacterial activity of the extracts was determined by agar diffusion in the laboratory of biochemistry of microorganisms and nutrient medium in The Institute of Microbiology and Immunology with help of Osolodchenko T.P.

Extracts from *Salvia officinalis* leaves exhibit antimicrobial activity against *S. aureus*, *B. subtilis*, *S. pyogenosa* and *E. coli* and have almost no effect on *Pr. vulgaris*, *P. aeruginosa* and *C. albicans*. The spectrum of antimicrobial activity and the strength of the ethyl acetate extract is comparable with the activity of the drug "Salvin".

Antiinflammatory activity of the dry extract studied in experiments with white mice weighing 18 - 23 g in edema formalin model. Drug of comparison was chosen Voltaren. Received results show a pronounced anti-inflammatory activity of the dry extract obtained by complex processing. Maximum anti-exudative effect of the dry extract 64.54% was observed at 25 mg / kg.

Conclusions. As a result of studying the chemical composition and pharmacological activity of the extracts, which were obtained from the leaves of Salvia officinalis by complex processing shown prospects of new antibacterial and anti-inflammatory drugs development.

CHROMATOGRAPHIC ANALYSIS OF HERBAL MIXTURES BAS FOR THE NORMALIZATION OF THE MUSCULOSKELETAL SYSTEM AT RHEUMATOID ARTHRITIS

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It is known that arthritis of different etiology, a joint deformation is often occurred, the tissues of the musculoskeletal system (MSS) and organs that contain connective tissue are affected. The main causes of rheumatoid arthritis development are heredity, infectious diseases and injuries. The purpose of herbal medicine is to improve the effectiveness of the treatment, reduce the side effects of synthetic drugs, prevent disability and improve the quality of patients' life. Medical raw herbal materials (MRHM) that are typically used for arthritis have anti-inflammatory, antioxidant, anti-allergic, sedative, immunomodulating activity. In herbal medicine of MSS MRHM of such plants are used: birch, willow, alder, marjoram, nettle, lungwort, aspen, bedstraw, meadowsweet, horsetail, hawthorn, motherwort, mistletoe, valerian, peony, *Greek valerian (Polemonium)*, tormentil.

The aim of our research is to develop techniques for standardization of the herbal mixtures, which can be used to treat rheumatoid arthritis. On the basis of the source of information research, we have developed a herbal mixtures that includes white poplar buds, wood avens roots, rootstocks with the roots of cyanosis azure, calendula flowers, hop cones, white willow bark and purple coneflower roots. These raw materials contain groups of biologically active substances (BAS) of diverse chemical nature, exhibit different kinds of pharmacological activity.

Materials and methods. Chromatographic study of BAS was done by means of paper and thin layer chromatography (TLC). The alcoholic and hydroalcoholic extracts of herbal mixtures were used. Such solvent systems were used: ethyl acetate - formic acid - water (10: 2: 3), 15% acetic acid; sorbents - Silufol and Sorbfil plates; chromatography paper Filtrak №12; chromogenic reagents - alcoholic solutions of sodium hydroxide, vanillin, aluminum chloride; acid sulphate solution; DSC; filtered UV-light (540 nm).

Results. As a result of qualitative studies of BAS composition phenolic compounds such as simple phenols, phenol carbonic and hydroxycinnamic acids, flavonoids and tannins have been found. In the course of pharmacognostic studies moisture, common ash content and ash insoluble in a 10% solution of acid chloride, the fineness and the impurity of herbal mixtures have been established. Macroscopic herbal mixtures analysis allowed us to determine the external characteristic signs of herbal mixtures: color, smell, taste of water decoction. On the basis of microscopic herbal mixtures analysis the basic diagnostic features that correspond to each component of the herbal mixtures have been established.

Conclusions. It is proposed to develop such MQC while determining: merchandising herbal mixtures rates; by TLC method - flavonoids and hydroxycinnamic acids; the main morphological and anatomical diagnostic signs of raw materials components of herbal mixtures.

DEVELOPMENT OF CONTENT AND PHARMACOGNOSTIC ANALYSIS OF VENOTONIC HERBAL MIXTURES

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Introduction. According to medical statistics about 70% of adults have different pathologies of the venous system; 25% of these patients have clinical signs of chronic venous insufficiency. The main causes of chronic venous insufficiency are varicose veins and post-thrombotic syndrome that are being developed after deep vein thrombophlebitis. Venotonic effect of drugs is aimed to the elimination of venous stasis, they reduce capillary fragility, increase their elasticity; improve microcirculation and lymph flow.

Materials and methods. According to literature search of biologically active substances (BAS) and the pharmacological properties of medical raw herbal material with predictable venous activity have allowed us to make the herbal mixtures, which includes blueberry fruits, chokeberry fruits, strawberry flowers, echinacea roots, blackberry and mint leaves. While developing the content of our herbal mixtures we took into account the choice of the type of medical raw herbal material (MRHM), which smoothes or eliminates the side effects of synthetic drugs in complex therapy. BAS of herbal mixtures have different types of pharmacological activities: anthocyanins have antioxidant and anti-inflammatory action, flavonoids – antioxidant, membrane stabilizing, spasmolytic action; phenol carbonic and hydroxycinnamic acids – spasmolytic, choleretic, anti-microbial action; polysaccharides – immunostimulating action.

Results. As a result of qualitative reactions and chromatographic studies (TLC and HD), in alcohol and water extractions of herbal mixtures and after acid hydrolysis such BAS have been found: flavonoids glycosides and aglycones, tannins of condensed group, triterpenoids, polysaccharides, coumarins, ascorbic acid. Pharmacognostic analysis was conducted according to the requirements of 1.4 SPU. (Plantae medicinalis) and individual articles to the corresponding MRHM; moisture, common ash content and ash that is insoluble in 10% hydrochloric acid solution and the content of impurities were determinant. Macroscopic analysis of the herbal mixtures allowed us to determine the characteristic of external signs of herbal mixtures: the degree of grinding, the color, the smell, the taste of water decoction. Microscopic analysis of the herbal mixtures allowed establishing of basic diagnostic features, which correspond to each component of the MRHM herbal mixtures.

Conclusions. A multi-component venotonic herbal mixtures includes blueberry fruits, chokeberry fruits, strawberry flowers, purple coneflowers roots, blackberry and mint leaves; the methods of pharmacognostic analysis of herbal mixtures have been established.

CHROMATOGRAPHIC RESEARCH OF *VERONICA SPICATA* L. HERB

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Introduction. Plants of genus *Veronica* (*Plantaginaceae*) have wide area of distribution in territory of Ukraine, up to 70, formal species are not. There are numerous decorative species of *Veronica* L.

The herb of *V. spicata* L. widely using in folk medicine as an sedative, an expectorant, a wound healing, a hemostatic, an anti-bacterial and content of biological active substances is not completely studied.

The aim of the study was chromatographic research of cultural and wild-growing samples of *V. spicata* L. herb.

Materials and methods. The objects of study were cultural and wild-growing samples of *V. spicata* L. herb. The cultural sample have been harvested in Botanical garden of V. N. Karazin Kharkiv National University in the flowering stage (June), in 2015. The wild-growing sample have been harvested in the flowering stage in Ukraine, Kharkiv region, in 2015.

Extracts of cultural and wild-growing samples of *V. spicata* L. herb obtained by ethanol 96% have used for thin-layer chromatography (TLC). The analysis conditions: chromatography wax «Sorbfil», the solvent system: ethylacetate – formic acid – water (10:2:3), single division at the temperature 20-22 ºC.

The identification was carried out in filtrated UV-light (354 nm) by features fluorescence, by the value of R_f and by results to interaction with chromogenic reagents (ammonia vapor, 10% spirituous solution of potassium hydroxide, 5% solution of iron (III) chloride).

The results and discussion. In cultural sample of *V. spicata* L. herb had been present 7 compounds, in wild-growing – 9 compounds.

In cultural sample by means of a value of R_f, features coloration of spots before and after reaction with reagents in daylight, and fluorescence in UV-light 4 compounds belonging to flavonoids, and 3 compounds belonging to hydrocynnamic acids. Chromatographic methods revealed the presence of at wild-growing sample4 flavonoids, 4 hydrocynnamic acids, and 1 an anthocyane (R_f = 0.13).

The chromatographic research has shown that wild-growing sample of *V. spicata* L. herb had more components with high spots magnitude than cultural sample.

Conclusions. Studies indicate, that the further in-depth study of obtained extracts from wild-growing sample *V. spicata* L. can be considered promising.

PHYTOCHEMICAL RESEARCH OF *VERONICA TEUCRIUM* L. HERB

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Introduction. The informal spesies – *Veronica teucrium* L. belongs to family *Plantaginaceae* Juss. and have the significant raw herbal drug base in Ukraine. The chemical composition of *V. teucrium* L. is not completely studied, it is known that herb contains carbohydrates, steroids, iridoids (aukubin, catalpol), steroid saponins, phenolcarboxylic acids, tannins, coumarins, flavonoids (luteolin, apigenin and their glycosides), choline, vitamine C. In folk medicine infusion and tincture from herb used as sedative, expectorant, anti-inflammatory, anti-bacterial, antispasmodic, hemostatic, analgesic, diaphoretic, diuretic and choleretic remedy. The recent herb had used topically for chronic purulent skin diseases and as wound healing remedy. In experiment a cytotoxic, an antibacterial, an immunomodulating and antioxidant, a reducing and prebiotic activities studied of different extracts of this species.

The aim of the study was preliminary phytochemical screening of *V. teucrium* L. herb.

Materials and methods. The object of study was the herb of *V. teucrium* L., that have been harvested in the flowering stage (May – July) in Ukraine, Kharkiv region, in 2015. The recent herb has the bitter taste and a character smell, which are disappeared during drying. The research was conducted by used thin-layer chromatography (TLC), as well as with the use of qualitative reactions. Extract from *V. teucrium* L. obtained by ethanol 70% (exstract A) and 50% (exstract B) have used for TLC on «Sorbfil», the solvent system: ethylacetate – formic acid – water (10:2:3), single division at the temperature 20-22 °C. Detection was performed in filtrated UV-light (354 nm). The compounds were identified by features fluorescence in UV-light and coloration with chromogenic reagents (ammonia vapor, 10% spirituous solution of sodium hydroxide, 5% solution of iron (III) chloride) and by the value of R_f.

The results and discussion. Previous studies (qualitative reactions) revealed the presence of such groups of biologically active substances: flavonoids, saponins, tannins of condensed group, iridoids and coumarins. In the result of the chromatographic study of the *V. teucrium* L. herb extract A had been found 8 compounds, in exstract B – 8 compounds. According to the results a value of R_f and features coloration of spots before and after reaction with chromogenic reagents in daylight, and fluorescence in UV-light in exstract A: 4 compounds belonging to flavonoids, 5 compounds – to hydrocynnamic acids, in exstract B – 4 compounds belonging to flavonoids, 5 compounds – to hydrocynnamic acids.

Conclusions. The results of our study shown, that the further in-depth study of obtained extracts from *V. teucrium* L. can be considered promising.

OBTAINING AND RESEARCH OF BI OMASS EXTRACT OF *CARLINA ACAULIS*

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Introduction. Resources of medicinal plants that once allowed Ukraine to be one of the leading countries in which grown and provide herbs exhausted due to chemical and radioactive contamination, and because of the inability of many medicinal plants growing in culture. Modern methods of biotechnology and cell biology offers solutions to this problem. Using the methods of cultivation of cells, tissues and organs of plants under controlled conditions on artificial nutrient media, can receive biomass in unlimited quantities and clean.

Endemic plants species have the scientific and practical value that are part of the natural flora invaluable gene pool. *Carlina acaulis L* refers to such plants. Seed has high viability it is the basis for its introduction into the culture. Preparations based *Carlina acaulis L.* in medicine used in the hypnotic state, general lethargy functions cortex dysfunction of higher nervous activity; drugs from plants close to the action of bromine. These drugs are not toxic, do not cause side effects and their effect on the nervous system similar to the action of vitamin B_2. Introduction *Carlina acaulis L.* in culture *in vitro* year-round offers the prospect of obtaining plant material as a possible source of biologically active substances.

Results and discussion. Callus biomass *Carlina acaulis L.* obtained at 23 °C and 16-hour photoperiod on nutrient medium of Murasyhe-Scoog. Also we used different concentrations of kinetin, NAA, IAA (3.0 mg/l; 0.5 mg/l; 0.5 mg/L respectively). Raw of plants and callus mass *Carlina acaulis L.* are identical similar sources of biologically active substances. They can replace natural sources medicinal plants in the future. Extracts of callus mass obtained, researched, chosened extragents and conditions of extraction.

Extragents affects not only on the extraction of specific substances, but the total number of extractives. As extractant used purified water, ethanol and other polar extractants in an amount to ensure a comprehensive extraction of active ingredients. Crushed callus mass extracted of 40% alcohol in the flask with reflux on a water heater for 120 min, the optimal balance between raw material and extractant 1:10.

Conclusions. The optimum conditions for the introduction into the culture were selected, and *Carlina acaulis* was cultivated. Extract of callus biomass obtained and qualitative and quantitative reactions to the presence of phenolic compounds: simple phenols, polyphenols, flavonoids, tannins, hydroxycinnamic acids, coumarins, chromone, quinones conducted.

PHYTOCHEMICAL STUDY OF THALLI PARMELIA

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Introduction. The biologically active substances of Parmelia are known to have a broad variety of pharmacological activity. They exhibit antimicrobial (including vs. *Mycobacterium tuberculosis*), antifungal, antiviral, anti-inflammatory, analgesic, antipyretic, anti-proliferative, hypolipidemic, hepatoprotective, antioxidant, hemolytic, and cytotoxic activity. Parmelia species have been used in diarrhoea, dyspepsia, spermatorrhoea, amenorrhoea, dysentery and as wound healer.

S. A. Begalinova proved high clinical effectiveness of Parmelia in the complex treatment of eczema compared with conventional treatment.

According to S. E. Badmaeva, the biologically active substances of this lichen exhibited protective anti-ulcer effect, increasing the resistance of the gastric mucosa to the action of such ulcerogenic factors such as stress and ethanol.

Parmelia is included in the complex herbal preparation «Speman» manufactured by Himalaya Drug Company (India), which is used for the treatment of benign prostatic hyperplasia and prostatitis.

The chemical composition of this lichen has been insufficiently studied. It is believed that Parmelia shows its action due to the presence of such lichen substances, as usnic, stictic, norstictic, protocetraric, fumarprotocetraric, salazinic, consalazinic, alectoronic, caperatic, divaricatic, lobaric, atraric acid and atranorin.

Carbohydrates present in Parmelia constitute the major part of its dry matter. Most of the carbohydrates are presented by homoplysaccharides, similar in composition to the cellulose – lichenin (which is also called lichen starch) and isolichenin. They are a typical constituent of cell membranes of the mycobiont hyphae. Macromolecule of lichenin was established by A. F. Mazurova by Fourier-IR spectroscopy. It consists of glucose residues, connected by glycoside (acetal) bond in β position (1→3) (1→4) in the ratio 1:3. Mono-, disaccharides (glucose, mannose, galactose, fructose, xylose, ribose, sucrose) and polyols (mannitol, sorbitol, arabitol, volamitol, ribitol) are present in small quantities.

Chitin (a characteristic of most fungi), and nitrogen-containing substances – amino acids (alanine, aspartic acid, glutamic acid, valine, lysine, tyrosine, tryptophan) were found in Parmelia hyphaes. Such enzymes as invertase, catalase, urease, zymase, lichenase were found in Thalli Parmelia.

Phycobiont of this lichen produces vitamins, in particular ascorbic acid, biotin, cyanocobalamin, and nicotinic acid.

Parmelia contains phenolic compounds such as flavonoids and compounds, similar by nature to plant tannins, yet with a simpler structure.

As for fatty substances, lichesterol, arabinitol, ergosterol, α-tocopherol, β-sitosterol, nonacosane, oleic, linoleic, linolenic, palmitic and stearic acid were identified in Parmelia.

Lichens have a unique ability to absorb and accumulate various chemical elements in their raw material from the environment that affects their biochemical composition. Thus, ash-like Parmelia substance are presented Si, S, P,Na, Cl, Al, Ba, Ca, Cu, Fe, Cr, K, Mg, Mn, Sn, Ti, Pb, Ag.

Aim. The aim of our study was the phytochemical study Parmelia thalli.

Materials and methods. All experiments were performed according to the methods of the State Pharmacopoeia of Ukraine.

The content of extractive substances was determined by the gravimetric method in the ratio raw material-extragent 1:50. Purified water and 40%, 50%, 60%, 70% ethyl alcohol were used as extragents for the determination of extractives in the investigated raw materials.

Quantitative determination of the sum of free organic acids was carried out by titrimetric method. 0.1 M sodium hydroxide solution was used as the titrant.

The total hydroxycinnamic acids content was determined on the spectrophotometer Optizen POP (Korea) at a wavelength of 327 nanometers.

Quantitative analysis of the amount of water-soluble polysaccharides in Parmelia Thalli was determined by the gravimetric method.

Results and discussion. It is established that the weight loss on drying is 6.87%, total ash – 20.98%.

The content of extractive substances extracted with 40% ethanol, was 16.35%, 50% – 13.90%, 60% – 12.39%, 70% – 13.70% and water is at 25.94%. The results of the experiment showed that the best extragent for this raw material was purified water.

The total content of free organic acids in terms of malic acid in Parmelia Thalli was 2.09%, the total content of hydroxycinnamic acids in terms of chlorogenic acid – 1.36%.

The study determined that the content of water-soluble polysaccharides was 10.95%.

Conclusions. Concerning the importance of the chemical composition of Parmelia, drugs in the form of dry powder, aqueous or alcoholic tinctures etc. based on the raw material of the members of this genus can be worked out.

The obtained experimental data can be used in the development of the relevant sections of quality control methods for the Parmelia Thalli.

SETTING SOME STANDARDIZATION PARAMETERS OF RAW MATERIALS OF PLANT OF CRASSULACEAE

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Introduction. The possibility of safe use for a long time drugs based on medicinal plants, and a small number of contraindications compared with high therapeutic effect, explains the increased popularity of this group of drugs. Considering this aspect, our attention was attracted by plants of Crassula, family Crassulaceae. The Homeland of plants that are popularly known as "money tree" is considered to be Africa, and more specifically its tropical arid southern and western parts as well as Madagascar and South Arabia. This plant −perennial succulents from a few centimeters to 3.4 meters tall, has fleshy stems and leaves, which can accumulate moisture, which helps to survive in arid, desert regions. The structure of the plant genus Crassula is a huge amount of useful trace elements and volatiles that causes a wide spectrum of pharmacological action material. Crassula used for medicinal purposes, but keep in mind it should be noted that the plant contains a tiny fraction of arsenic, a major caveat on it's internal use. The juice of fresh leaves has antibacterial and antiviral properties, used in the treatment of throat diseases, including angina, also to stop itching and pain of insect bites. The infusion is used in kidney diseases. It is also used to treat diseases such as arthritis, gout, herpes, hemorrhoids, varicose veins, ulcers of the stomach and duodenum.

Aim. To conduct studying of morphological structure of raw plant genus Crassula Crassulaceae family in the light of pharmacognostical research. To Establish some parameters for standardization of raw materials.

Materials and methods. The object of the study were the leaves and stems of plants genus Crassula, harvested in May – July 2015.

Results and discussion. Shoots are strong – enough and prostrate. The leaves are shiny, fleshy, juicy and oval, 2-3 cm long, resembling coins which are located opposite crosswise. Crassula leaves color can vary from gray to bright green. The flowers are small, white, whitish, look like tiny stars, usually five-membered. Stamens as many as petals (5) are resistance petals. Anther isovate or oblong. Nectaries the plants are small scales.−carpels are free or fused at the base. Stiles are shorter then ovaries. In terms of cultivation Crassula blooms very rarely.

Conclusions. Plants of the genus Crassula are a promising source of medicinal plants and development of drugsfor the treatment of various diseases.

USE OF MEDICINAL PLANTS WITH CHOLERETIC ACTION IN UKRAINE

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Introduction. Diseases of the digestive system among adults and children are the most common internal diseases. About 35% of all diseases of the gastrointestinal tract refer to the diseases of hepatobiliary system. In many liver diseases, especially inflammatory and dystrophic, disordered its exocrine function - the formation and secretion of bile. This leads to motility of digestive tract and digestion, absorption of food and some drugs, protein metabolism. Very often stagnation of bile in the gallbladder, especially against the backdrop of infection and inhibition of the synthesis of bile acids, can lower stabilizing properties of bile, cholesterol deposition in the sediment, formation of biliary concrements. In the treatment of liver and biliary tract often used herbal medicinal products, due to the chemical composition of raw materials. Flavonoids, essential oils and other natural iridoids compound have bile, antispasmodic and anti-inflammatory effect. Herbal preparations do a comprehensive therapeutic effect. Therefore, the search of medicinal plants with bile action is urgent task.

Aim. To analyze the medicinal plants those have choleretic, antispasmodic and anti-inflammatory action.

Results and discussion. Analysis of herbal preparations on the market of Ukraine with bile effect has shown that they are presented with mono-drugs, complex herbal preparations and medicinal supplements to food. They contain raw herbs of such plants as artichoke seed, turmeric high, helichrysum arenarium, corn usual, chamomile, rose hips, dandelion, celandine, tansy and nettle. Big part herbal drugs with bile effect contains mainly imported, expensive raw materials - artichoke, turmeric or cultivated - chamomile, corn, artichoke. Studies have shown that the use of wild plants, unfortunately, takes a small percentage of raw materials in the production of herbal preparations with this pharmacological activity. In the current economic conditions on the pharmaceutical market of Ukraine, this approach is not rational, so the use of medicinal plants that have large wild raw material base and easily cultivated, significantly can reduce prices for this category of products. Tansy – one of the most promising plants that have a substantial resource base, undemanding to soil, climate and can be studied in terms of cultivation in Ukraine.

Conclusion. All things consider, the actual direction is the study of herbs with choleretic action, which are widespread in Ukraine. For the manufacture of new dosage forms perspective to study are common tansy, nettle and species of wild rose.

CARPOLOGY OF JUICY FRUITS OF SPECIES *ROSACEAE* AND *ERICACEAE* FAMILIES

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Introduction. The carpology includes studying of morphogenesis, ontogenesis, appropriateness of the distribution of fruits and seeds, the improvement of the morphological classification of fruits and the creation of determinants. There is shortage carpologic information on fruits of medicinal plants.

The purpose of the study. To analyze the data of the literature; to conduct a morphological study of the juicy fruits, which are edible or medicinal raw materials for pharmaceutical and other industry sectors; to examine the fruits that can be harvested instead of the medical fruits or become undesirable admixture of medicinal plant raw materials. To create the Atlas-determinant of juicy fruits on the basis of the results of investigations.

Materials and methods. There were studied juicy the fruits of 27 species of Rosaceae and 10 species of Ericaceae by botanic methods using the binocular glass and the camera Samsung PL50.

The results. The descriptions and photographs of the pericarp and seed were made. The Atlas of juicy fruits with illustrations of the appearance and cuts of fruits and seeds was composed.

A brief description of mature fruits and their shape, size, smell, taste, texture and color of ectocarpus, thickness, structure, and consistency of meso – and endocarpia, structure of seeds, application were done as well as the determinant of juicy fruits of species of Rosaceae and Ericaceae.

Conclusions. As a result of the integration of experimental and literature data the Atlas-determinant of juicy fruits was developed which, allow to determinate, identify and describe the fruits of medicinal plants.

DETERMINATION OF BIOLOGICALLY ACTIVE SUBSTANCES IN HERBAL PREPARATIONS

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Introduction. Alliin and allicin in Allii sativa bulbi pulvis (garlic) Allicin (S-allyl-2- propenthiosulphinate) is one of the most active principles in garlic. It is produced from two molecules of alliin by alliin-lyase or by heart treatment. Allicin posseses a typical odour and it acts as an antibacterial agent, it lowers thrombocytes aggregation and lipid level.

Aim. Determination of biologically active substance presented in herbal preparations.

Method and materials. 1 g of powdered garlic is mixed with 10 ml of methanol in a separator funnel for 1 minute. Methanolic extract is poured out through the upper part of separator funnel and filtered with a filter paper in a round- bottomed flask and concentrated up to 0.5 ml volume. This sample contains alliin (together with other compounds extracted with methanol) and it is used for TLC analysis (sample A).

2 g of powdered garlic are mixed with 10 ml of water in a porcelain evaporating dish and heated with occasional stirring on a water bath for 30 minutes. The cool mixture is poured in a separator funnel and extracted with 25 ml of diethylether. Then, 20 ml of fresh diethyl ether is added, and the upper layer is collected (through the upper part of separatory funnel) in an evaporating dish. The volume is concentrated up to 0.5 ml volume on the water bath. This sample contains allicin (among the other compounds- Sample B).

TLC analysis :Two identic chromatogram plates are prepared: each contains one Sample A and one Sample B. Sample are repeatly spotted (about 20 times) on a silica gel plate and then developed. The first plate is developed in a solvent system n-butanol- acetic acid- water (40:15:10). The air dried chromatogram is sprayed with ninhydrine solution. This plate is heated in an oven until red spots are developed (allicin).The second plate is developed in a system chloroform- benzene(3:1). This air dried plate is once more again developed in the same system and air dried. After spraying with ninhydrine the plate is dried in an oven violet spot of allicin is formed.

Pharmacopoeial purity of this cardioglycoside preparation should be 95% minimally. Admixture presence (gitoxine, digitonine) can be determined by TLC.

2 tablets are crushed and dissolved in 18 ml of chloroform and 12 ml of isopropanol in a 100 ml Erlenmayer flask. The flask is covered by a glass and is heated on the water bath for 10 minutes. The cool solution is filtered through a cotton wool in a 50 ml round-bottomed flask. This solution is evaporated in vacuo to dryness. The rest is dissolved in 0.5 ml of chloroform and 0.5 ml of methanol. This solution is used for TLC analysis:

Sample and standard solutions are repeatly spotted (15 times) on a silica gel plate and then developed in a system ethylacetate – methanol-water (75:10:00.5). The air dried plate is developed once more in this solvent system. The oven-dried plate is sprayed with a 1:1 mixture of 3% solution of 3,5- dinitrobenzoic acid and 2N sodium hydroxide. The blue spots are visible. ¼ of Regulax lump is crushed with 20 ml of sulphuric acid (5 mol/l) in 50 ml Erlenmayer flask. Then, 2 ml of concentrated hydrogen peroxide is dropped and whole mixture is boiled on the heating plate for 1 min. After cooling, 15 ml of diethylether is added, carefully shaked and filtered through a cotton wool into the testing tube.

From the upper (organic) layer is repeatedly applied sample to the Silufol UV 366 plate and developed in the benzene: ethylacetate: formic acid (60:20:4) system. Oven dried plate (about100ºC) is detected after cooling with ethanolic solution of kalium hydrxide (2 mol/l) and then heated in an oven again until the red spots of anthraquinones are developed (Rf= 0.5-0.7). Some other spots (mostly yellowish) could also be visible.

Results and discussion. Two identic chromatogram plates are prepared: each contains one Sample A and one Sample B. Sample are repeatly spotted (about 20 times) on a silica gel plate and then developed. The first plate is developed in a solvent system n-butanol- acetic acid- water (40:15:10). The air dried chromatogram is sprayed with ninhydrine solution. This plate is heated in an oven until red spots are developed (allicin).The second plate is developed in a system chloroform-benzene(3:1). This air dried plate is once more again developed in the same system and air dried. After spraying with ninhydrine the plate is dried in an oven violet spot of allicin is formed.

Conclusion. Except important source of inulin type fructans the determined metabolic profile of its roots revealed their potential application as radical sca`vengers due to the presence of polyphenols. Therefore, this complex of biologically active substance in their roots offers many future applications in field of herbal medicine and nutrition for production of healthy food with well-pronounced healthy effect.

POSSIBILITIES OF SMALL PASQUE-FLOWER HERB USING AS PERSPECTIVE PLANT

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Introduction. Small Pasque-flower (Blackish Pasque, Bohemian Pasque) Pulsatilla pratensis (L.) Mill. s.l. (incl. P. bohemica (Skalický) Tzvelev = P. pratensis (L.) Mill. subsp. bohemica Skalický; P. nigricans auct. non Stöerck, nom. illeg.; P. ucranica (Ugr.) Wissjul.) – a herbaceous perennial poisonous plant of the Ranunculaceae family.

Aim. Investigation of possibilities of small pasque-flower herb using as perspective plant.

Materials and methods. Analysis of scientific literature sources on aspects of the application of Small Pasque-flower.

Results and discussion. Pulsatilla pratensis contains anemonin, ranunkulin, protoanemonin, essential oil, tannin, vitamin C, organic acids, flavonoids, small traces of alkaloids, tannins (approximately 4.5%).

The herb has hypotensive, sedative, soporific, antispasmodic, antimicrobial, antifungal, and anesthetic effect, slows heart rate down and stimulates breathing. Scientific medicine uses Small Pasque-flower herb for treatment of hypertension of 1-2 degrees, glaucoma, at heart palpitation, as a sedative and soporific remedy at menthal diseases.

In traditional medicine, Pulsatilla pratensis is known as pasque-flower. It is used effectively as a sedative remedy at nervous excitement, as well as related headache, dizziness, insomnia, hysteria, convulsions, and dysmenorrhea. Pulsatilla pratensis herb is used as an antispasmodic agent at pertussis, asthma, bronchitis, and migraine. Small Pasque-flower herb has a stimulating effect on the digestive tract, that’s why it’s using is not recommended at gastritis and nephritis. It was determined, that herbal remedies with Pulsatilla pratensis have strong antimicrobial and antifungal effects.

This herb is widely used in homeopathy. Gathered during flowering period fresh herb is used for manufacture of homeopathic remedies named Pulsatilla, with different directions of therapeutic action. It is included in the homeopathic drugs, used as antipyretic and anti-inflammatory agents for treatment of respiratory diseases in children, as well as for elimination of clinical manifestations of primary teeth eruption; for symptomatic treatment of ENT-organs: pharyngitis, rhinitis, and laryngitis; at acute and chronic inflammatory or degenerative diseases of the musculoskeletal system and soft tissues, accompanied by pain: arthritis, osteoarthritis, polyarthritis, arthrosis, osteochondrosis, trauma, and wounds.

Conclusions. Therefore, the use of Pulsatilla pratensis to treat nervousness helps to strengthen the nervous system, and to eliminate of etiologic disease factors (neurotransmitters metabolism disorders).

THE STUDY OF BIOLOGICAL ACTIVE SUBSTANCES OF *LEDUM PALUSTER L.* AND SOME SPECIES OF THE *RHODODENDRON* GENUS

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Introduction. Searching new sources biological active substances for creating new drugs with different actives is actual task contemporary pharmacy in Ukraine.

Only 4 species from family *Ericaceae* is official medicinal plants – *Ledum palustre L., Arctostaphylos uva ursi (L.) Spreng., Vaccinium vitis-idaea, Vaccinium myrtillus,* which find application in traditional medicine, homeopathy and production biological active substances. List of indications for clinical applying extracts from these plants is limited. Some species of genus *Rhododendron* using in traditional medicine for treating colds and gastrointestinal illness, like antiseptic and diuretic cure.

Aim. The aim of this work is comparative study chemical composition biological active substances *Ledum palustre L.* and some kinds of *Rhododendron* family *Ericaceae* for identifying potential sources new kinds of vegetable materials for creating new effective drugs.

Materail and methods. The objects of study were family *Ericaceae*. As the material for studying used aerial part *Ledum palustre L.,* foliage *Rhododendron luteum Sweet., Rhododendron ponticum L.,* flora of Ukraine and the Caucasus. For extraction polyphenolic compounds were used water-alcoholic solutions. Separation of substances carried with using adsorbtion and partition chromatography with different sorbents.

Results and discussion. In plants which study was found 30 substances in the individual state 11. The main compounds are the flavonoids quercetin, kaempferol, myricetin and their glycosides. Hydroxycinnamic acid represented coffee, ferulic, chlorogenic, neochlorogenic, coumarin derivatives - umbelliferone, skolopoletine, eksuletine and eksuline and found arbutin.

Conclusion. The most promising for creation new drugs is *Ledum palustre L., Rhododendron luteum Sweet., Rhododendron ponticum L.,* which characterized diversity biological active substances and combination wide spectrum of pharmacological activity.

RESEARCH OF FLAVONOIDS OF DRY EXTRACT OF GRASS ASPERULA OCTONARIA KLOKOV

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Introduction. Ukraine is represented family Rubiaceae Juss. in the flora species and more than 50 of them to the eastern regions is typical Asperula octonaria Klokov. Earlier in the grass of Asperula octanaria been identified phenolic compounds (hydroxycinnamic acids, kumarins, flavonoids, tannic matters), iridoids, saponins, terpenoidss, in composition essential oil.

Aim. The aim of this work was to investigate the flavonoid extract of dried herbs Asperula octonaria, obtained by complex processing of raw materials.

Materials and methods. For this purpose an air-dry grass of Asperula octanaria was exhaustively extracted at first a chloroform, and then mixture, ethyl-acetate-96% ethanol (8:2). The dried meal was treated three times with hot water for 30 minutes in a boiling water bath. The resulting aqueous extracts were combined, filtered and evaporated to 1/3 original volume. The concentrate was treated with 96% ethanol at a ratio of 1: 3The precipitate is filtered polysaccharides. The filtrate was evaporated in a vacuum evaporator to dryness.

Research conducted flavonoids HPLC chromatograph on firm Agilent Technologies (model 1100), equipped with a flow vacuum degasser G1379A, 4-channel pump low pressure gradient G13111A, G1313A automatic injector, column thermostat G13116A, diodnomatrychnym detector G1316A. For the analysis using chromatographic column size 2,1 × 150 mm filled with sorbent oktadetsylsylilnym, grain size of 3.5 microns, «ZORBAX-SB C-18." The identification of compounds was performed by standard retention time and spectral characteristics.

Results and discussion. The study found dry extract 10 compounds, including not fully identified quercetin glycosides, diosmetynu 4 C-glycosides apigenin, apigenin-7-O-rutynozyd, diosmetyn-7-O-glucoside, rutin, quercetin. The dominant is apigenin derivatives (1.87%). Total flavonoid content in dry extract is 2.76%.

Conclusions. Identified compounds may explain the use of phytotherapeutic Asperula octonaria.

MACRO- AND MICROSCOPICAL STUDY OF CANNA RHIZOMES

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Introduction. *Canna indica* L. (syn. *Canna edulis* Ker Gawl.) is a tropical herb belonging to the family *Cannaceae* – a monogeneric family comprising about 25 species. *Canna indica* was the first species of this genus introduced to Europe, which was imported from the East Indies, though the species originated from the America. The plant is now widely cultivated for its starchy, edible rhizomes, and many hybrids are cultivated in tropical and more temperate regions as ornamentals.

Canna rhizomes are proven to have antimicrobial and antioxidant activity. The plant material is widely used worldwide. Decoction of fresh rhizome is used as jaunditic symptoms: fevers, dropsy and dyspepsia. In the Philippines, decoction of rhizome used as diuretic, antipyretic. Macerated rhizomes are used to alleviate nose bleeds. In Thailand, rhizome has been used with other herbs for cancer treatment. In Costa-rica infusion of rhizomes is used as emollient. In Gabon the rhizome is used in enemas against dysentery and intestinal worms.

Aim of the research. The aim of our research was to carry out macro- and microscopical study of Canna lily rhizomes.

Materials and methods. The plant material was collected in October 2015 in Kharkiv region.

Results and discussion. Rhizomes are sympodial with Y-shaped axes and abundant roots growing both adaxially and abaxially from the nodes. Monopodial or stoloniferous rhizomes are less common. The plagiotropic axis after producing 5-6 nodes, curves its direction upwards to form the aerial plant. From the base of the last node an axillary bud restarts propagation by repeating the pattern. These “active” nodes can also produce up to three aerial branches, so three new plants grow very close to each other.

The transverse section of *Canna* rhizome has the following organization: epidermis, hypodermis, cortex, endodermis, pericycle, vascular plexus and central cylinder.

The epidermis cell walls are scarcely cutinized. Beneath the epidermis there is a three layered hypodermis, which exhibits cells with sub polygonal outline and thickened walls. The cortex is a relatively thin zone placed between the hypodermis and the endodermis. It is mainly composed by a parenchymatous tissue. It also reveals an outer ring of fibrous strands, many internally spread fibrovascular strands as well as foliar and root traces. Thus, the further studies on macro- and microscopical features of other Canna plant material will be carried out.

ANTIAMNESTIC ACTION OF GINKGO BILOBA AND RED CLOVER EXTRACTS IN RATS WITH TRITON WR-1339-INDUCED HYPERLIPIDEMIA

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Introduction. It is well known that hyperlipidemia is one of the main factors which leads to development of atherosclerosis. Cerebrovascular disease in particular cerebral atherosclerosis impairs cognitive-mnestic processes therefore treatment of this disease is an important issue.

Aim. Investigate indicators of cognitive and memory processes in rats with hyperlipidemia with using phytoextracts of Ginkgo biloba and Red clover.

Materials and methods. The effect of administration of Ginkgo biloba and red clover extracts on cognitive-mnestic processes was analyzed in the T-maze task in 48 male albino rats (190±15 g) receiving orally for 14 days the phytoextracts of both plants at doses 50:50 mg/kg b.w./day. Hyperlipidemia was modeled by intraperitoneal administration of TritonWR-1339 at doses 500, 750 mg/kg. The following parameters of behavior were studied: time of reaction – the time, which rat spends to achieve food in T-maze; the number of rats that had made the right choice of maze compartment.

Results and discussion. The data of research show that 14 days administration of Ginkgo biloba and Red clover extracts improves indicators of cognitive-mnestic processes in rats with hyperlipidemia. About it shows statistically decrease the time of reaction in rats which was prepared the phytoextracts, that was 55,5[34,5;67,0] s compared indicators of negative control: 83,5[67,0;115,5] s (triton wr-1339 at dose 500 mg/kg) and 105,5[76,5;128,0] s (triton wr-1339 at dose 750 mg/kg). The number of rats that had made the right choice of maze compartment also statistically increased and was 10 of 10 in group with administration of Ginkgo biloba and red clover extracts. In groups of negative control this index was 4 of 12 (triton wr-1339 at dose 500 mg/kg) and 3of 12 (triton wr-1339 at dose 750 mg/kg).

Conclusions. Administration of extracts of Ginkgo biloba and Red clover as combination improves indicators of cognitive-mnestic processes in rats with triton wr-1339- induce hyperlipidemia.

COMPERATIVE PHARMACOGNOSTICAL ANALYSIS OF THE RAW MATERIALS OF "MAMA" AND "UDAICHANKA" PEPPERMINT VARIETIES

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Introduction. From year to year the demand for remedies of the vegetable origin is constantly growing due to their pronounced therapeutic effect and low toxic effect on the human organism. Some plants which have sufficient raw material base and the possibilities of their cultivation cause our attention. Raw materials of peppermint Mentha piperita L. of Lamiaceae group are widely used in Ukraine. The family representatives grow throughout the territory of Ukraine. Wild species of mint can be found alongside the banks of water reservoirs. Swamps, canals, in the fields and dampy meadows. Field mint should be cultivated. Peppermint is a hybrid of M. aquatic and M. spicata. Many peppermint varieties are known not to be comparatively studied. From peppermint raw materials the tincture, the extract are made which are the organic components of the complex medicine remedies like "Sedasen", "Sedavit", "Persen". Such widely cultivated Ukrainian varieties as "Mama" and "Udaichanka" took our attention.

The Aim of Survey. To conduct comparative pharmacognostical analysis of the peppermint raw materials of "Mama" and "Udaichanka" varieties.

Materials and Methods. The objects of study were the peppermint vegetation of "Mama" and "Udaichanka" varieties. The provisions was made in June – August 2015.

The Results Obtained. The first step of our research was the comparative study of the morphological features of the vegetation of the varieties. It was found that the stems are straight, quadrangular, with thick leaves, many branches. The leaves are opposite, plain, whole, hairy, elongate ovoid with length up to 8 cm and width up to 2.5 cm, with heartlike base, pointed at the top, with well marked venation, dark green top and with a noticeably lighter bottoms, with short cuttings. The distinctive feature are the stem colour, the degree of pubescence. Inflorescence is situated at the top of shoots, the distinctive features are the size of inflorescence and the number of flowers in it.

Conclusions. The findings will be used in further study of the peppermint raw materials of of "Mama" and "Udaichanka" varieties.

RESEARCH TECHNOLOGICAL PARAMETERS OF THE BORAGE (BORAGO OFFICINALIS L.) ROSETTE LEAVES

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Introduction. Borage (*Borago officinalis L.*) of *Boraginaceae Juss.* family has long been used in folk and official medicine. The infusion of herbs has a strong diuretic effect for swelling of cardiac and renal origin, ascites, inflammation of the urinary tract. Polysaccharides of the borage's underground part provide emollient and expectorant effect in catarrh of the upper respiratory tract. The infusion of herbs stimulates the appetite, have a choleretic and anti-inflammatory action. Borage oil from the fruit contains a large amount of unsaturated fatty acids, it's an important component of cosmetic products for dry and sensitive skin: improves water-retaining capacity of the skin, increases its elasticity and protective properties. Flowers of the plant are used as a sedative for treatment of increased jitters, irritability. Rosette leaves, which appear in early spring, are recommended fresh in diets. Succulent leaves with a pleasant smell of fresh cucumber and salty flavor are used as a vitamin, tonic, anti-inflammatory. There are published dataevidence that confirm the similarity of chemical composition and biological effect of herbs and rosette leaves, which can be an additional type of raw material for substance.

Aim. Research the range of technological parameters of the borage's (*Borago officinalis L.*) rosette leaves raw materials for obtaining substance.

Materials and methods. Raw materials are harvested during the stage of the full deployment leaf blade in the Kharkiv region (village Peremoga), then it is dried under canopy outdoors. Exit of the rosette leaves air-dry raw material is 19-21% for fresh. The leaves are crushed at the mill LZM-1, used a fraction which passed through a sieve number 8000. The following technological parameters are studied: the loss in weight on drying, the average particle size, volume weight, bulk weight, specific weight, poroznist of the layer, porosity, free volume of the layer, specific surface area of particles, fluctuation, the absorption coefficient of the extractant by techniques that are described in the literature.

Results and discussion. The loss in weight on drying of the borage's rosette leaves is 12.83±0.19%, the average particle size – 1.14±0.05mm, volume weight 0.34±0.01 g/sm^3, bulk weight – 0.18±0.01 g/sm^3, specific weight – 1.62±0.06 g/sm^3, poroznist of the layer – 0.48±0,01, porosity – 0.79±0.01, free volume of the layer – 0.89±0.01, specific surface area of particles – 187.08+4.86 sm^2/g, fluctuation – ∞, the absorption coefficient of the extractant 50^o ethanol – 4.23+0.14.

Conclusions. The results will be used for development of the technology of raw materials substance.

THE ORGANIC ACIDS OF LEAVES OF *CRATAEGUS FLAVA* AIT.

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Introduction. Organic acids are formed in the plants and used for various synthetic processes in the cell. These compounds in plants content in the free form and in the form of salts or esters.

In plants organic acids are perform several functions: involved in photosynthesis and biosynthesis of terpenoids; breathing and metabolism of carbohydrates and lipids; are sources of amino acids; connect carbohydrate metabolism with proteins and lipids metabolism; promote excretion of ammonia and plant protection.

The most common in the plant world are formic, malonic, fumaric, succinic, benzoic, malic, citric, lilac, salicylic, *p*- coumaric and chlorogenic acids.

These compounds possess pharmacological activities such as: derivatives of benzoic acid (salicylic and benzoic) – bactericidal, anti-inflammatory, a whitening, astringent effect; mono, di - carboxylic acids reduce the formation of carcinogenic nitrosamines in the body, improve digestion, stimulate intestinal peristalsis, improve the skin condition; for hydroxycinnamic acids derivatives most character anti-inflammatory, choleretic, diuretic, antivirus effects.

In cosmetology very Citric, malic, lactic acids - in cosmetology to treat acne, antiwrinkles.

For continue the phytochemical research the *Crataegus flava* Ait. leaves from Hawthorn genus and expand the information about the chemical composition the species of genus, a scientific interest is the study of organic acids in this raw material.

The **aim of our study** was to investigate the organic acids of *Crataegus flava* Ait. leaves.

Materials and methods. The object of the study was the dried leaves of *Crataegus flava* Ait., collected in May, 2015 year. Raw materials is collected in Botanical Garden of V.N. Karazin Kharkiv National University.

Qualitative and quantitative composition of the organic acid content conducted by used chromatography-mass spectrometry method in chromatograph Agilent Technology 6890N with mass spectrometric detector 5973N.

For the extraction used hexane. Analysis conditions: chromatographic column DB-5 capillary (length 30 m, internal diameter 0.25 mm); the carrier gas - helium; thermostat temperature 50°C programming 4°/ min.

To identify the components used data library of mass spectra and NIST05 WILEY 2007 with a total of more than 470,000 spectra in conjunction with programs

to identify AMDIS and NIST.

The content of substances calculated relative to internal standard (tridecane solution in hexane).

Results and discussion. In leaves of *C.flava* Ait. were identified 15 compounds – aromatic and aliphatic acids. The results of research are shown in Table 1.

Table 1

Aromatic and aliphatic acids of leaves *of Crataegus flava* Ait.

The retention time, min.	The name of acid	Content	
		mg/kg	%
5.780	Capronic	15.55	0.21
10.606	Formic	1538.38	21.61
13.552	Malonic	240.30	3.37
14.693	Fumaric	75.83	1.06
15.507	Succinic	729.83	10.25
15.996	Benzoic	133.73	1.87
19.079	Phenylacetic	10.19	0.14
19.515	Salicylic	35.54	0.49
23.777	Malic	3329.67	46.77
31.087	Citric	765.17	10.74
34.390	Vanillic	18.36	0.25
38.115	*p*- Coumaric	115.59	1.62
39.300	*p*-Hydroxybenzoic	115.26	1.61
39.736	Lilac	9.45	0.13
42.470	Ferulic	100.85	1.41
Total amount**:**		7118.11	100

Among aliphatic acids in most high concentration (mg/kg) are presented malic (3329.67), formic (1538.38), citric (765.17) and succinic (729.83) acids.

Conclusions. For the first time in *C. flava* Ait. leaves were identified 15 organic acids: 1 monobasic carboxylic acid – capronic (0.21%); 5 dicarboxylic acid – formic (21.61%), malonic (3.37%), fumaric (1.06%), succinic (10.25%), malic (46.77%); 1 tricarboxylic acid – citric (10.74%); 6 phenolcarbonic acids – salicylic (0.49%), vanillic (0.25%), benzoic (1.87%), lilac (0.13%), *p*-hydroxybenzoic (1.61%), phenylacetic (0.14%); 2 hydroxycinnamic acids - ferulic (1.41%) and *p*-coumaric (1.62%).

RESEARCH THE ANTIMICROBICAL ACTIVITY OF *CRATAEGUS SUBMOLLIS* SARG. FRUITS LIPOPHYLIC EXTRACT

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Introduction. *Crataegus submollis* Sarg. is a representative of the North American flora, is successfully cultivated on the territory of Ukraine as a landscape gardening culture and has a sufficient resource base.

It is a tree with long spines, large leaves and fleshy, large, edible fruits. The plant belongs to the botanical section *Molles* Sarg. From fruits of *Crataegus submollis* Sarg. have been obtained the chloroform, ethyl acetate fraction and phenolic complex (70^{o} ethanol extraction).

In obtained fractions were identified phenol compounds (flavonoids, coumarins, hydroxycinnamic acid), fatty acids, carotenoids. The lipophilic substances of hawthorn practically not been studied, but it is known that these substances possess a wide spectrum of pharmacological activity, including antimicrobial.

So the first thing we decided to explore the antimicrobial activity of the chloroform extract. The output of lipophilic fraction in the chloroform extract was 12%. The most higher concentration in this fraction was for fatty acids and carotenoids.

Scientific interest is the study of antimicrobial activity of lipophilic fraction of fruits *Crataegus submollis* Sarg.

The **aim of our study** was to investigate the antimicrobial activity of lipophilic extract of *Crataegus submollis* Sarg. fruits against the most important in the epidemiological significance bacterial cultures.

Materials and methods. The object of the study was the lipophilic extract of fruits of *Crataegus submollis* Sarg. The raw materials harvested in August 2015 in Kharkiv region. We are used air dry raw material. Extract was obtained with chloroform (method of circulating extraction). Antimicrobial activity of lipophilic fraction was studied on base of «Mechnikov institute of microbiology and immunology» under the leadership of Senior research scientist of immunoreabilitology laboratory Kashpur N. V.

For determining the activity of the lipothilic complex we used the standard bacterial cultures*: Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Proteus vulgaris* ATCC 4636, *Bacillus subtilis* ATCC 6633, *Candida albicans* 885-663. To determine the antimicrobial activity, the bacterial cultures were cultivated on meat pepton agar at

37 °C for 24 hours. Antimicrobial activity was measured as a radius in mm to give a zone of inhibition.

Determination of sensitivity of microorganisms was performed by successive twofold serial dilutions in liquid nutrient medium.

The method is based on titration in liquid nutrient medium investigational antibacterial preparation by successive dilutions certain volume of liquid in the first test tube using these controls - nutrient medium, which does not receive the drug. In all the test tubes were added daily allowance agar suspension of bacterial cultures.

The results were determined after 48 – 72 hours to assess growth delay of micro-organisms in the test tubes containing the appropriate dilution of the drug. The last tube with growth retardation (clear broth) corresponded to minimum inhibitory concentration of antibiotic tested against the strain. For evaluation the bactericidal properties the drug from 2 – 3 tubes the last lack of growth been doing application to dense nutrient media.

After 24 – 48 hours incubation in thermostat that determined the lowest concentration of antibiotic drug in vitro, crop, of which has not given of growth and taking the minimum bactericidal concentration. For most microorganisms as nutrient media used peptonnyy meat broth, for mushrooms - nutrient media Saburo.

Determination of the sensitivity of bacteria was performed by diffusion in agar. In the Petri dish poured 10 ml of molten nutrient uncontaminated environment. After solidification of this layer placed on it sterile stainless steel cylinders (height – 10 mm inner diameter – 6 mm) and filled them "infected" agar of 15 ml.

For this purpose, melted and cooled agar agar added daily washings cultures of microorganisms. For the second layer of agar solidification cylinders were removed in the the wells formed, made investigational antimicrobial agents in volume (0,3±0,05) ml.

Crops were incubated at 37 °C for 24 – 48 hours, then take into account the results of measuring the area of growth delay test microbe. In an experiment used a 2% solution extracts.

Results and discussion. As a result of the study it was found that the lipophilic extract of *C. submollis* Sarg. shows a moderate activity against *S.aureus* and *B.subtilis.*

Conclusions. For the first time established antimicrobial activity of lipophilic substances of fruits *C. submollis* Sarg. The results will allow for expand the information about the spectrum of pharmacological activity of biologically active substances (BAS) of species of the genus Hawthorn (Crataegus L.). The study showed that for the purpose of complex processing of raw materials perspective is the further study of the antimicrobial activity of the ethyl acetate and ethanol complexes obtained from fruits of *C. submollis* Sarg.

DETERMINATION OF FLAVONOIDS

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Introduction. Flavonoids are able to create fluorescent or colored complexes with some ions, e.g. B (III), Al (III), Zr (IV). These complexes can be used for TLC presence proof or colorimetric determination.

Aim. Use of flavonoid complexes for TLC proof or colorimetric determination of some ions.

Methods and materials: About 0.600 g of the powdered drug (Crataegi folium cum flore, Betulae folium, Equiseti herba) is refluxed in a flask with 1 ml of methenamine, 20 ml of acetone and 1 ml of conc. Hydrochloric acid for 30 minutes. The cool mixture is filtered through a cotton wool in a 100 ml volumetric flask. The cotton wool is returned into the flask with drug. 20 ml of acetone is added and the mixture is refluxed for 10 minutes. This cool solution is filtered to the previous solution into a volumetric flask. The cotton wool is returned again into the flask and 20 ml of acetone is added. The same procedure is repeated as before. The solution in the volumetric flask is completed up to the mark with acetone – solution A. 20 ml of solution A is mixed with 20 ml of water and then shaken with 15 ml of ethylacetate in a separatory funnel. The upper organic layer is collected in a flask. The lower layer is shaken 3 times with each 10 ml of ethylacetate. The upper layer is always collected, and then the whole volume of organic solution is shaken 2 times with each 50 ml of water in a separatory funnel. The upper organic layer is filtered into a 50 ml volumetric flask and ethylacetate is added up to the mark – solution B. To the 10 ml of solution B is 1 ml of aluminium (III) chloride solution added in a 25 ml volumetric flask, and the mixture of methanol – acetic acid (95 : 5) is added up to the mark. The absorbance of this solution is measured at 425 nm after 30 minutes. The blank solution contains 10 ml of solution B and 15 ml of a mixture methanol – acetic acid (95: 5). The flavonoid content (in %) is calculated from a calibration curve.

Results and discussion: About 0.3 g of powdered drug (Verbasci flos, Tiliae flos, Rutae herba) is heated in a tube with 5 ml of methanol on the water bath for 5 minutes. The cool solution is filtered through a cotton wool and then evaporated on the water bath to the minimal volume. This volume is used for

TLC analysis. The TLC is carried on the silica gel plate Silufol UV 254 in an eluent system ethylacetate – formic acid – water (8 : 1 : 1) together with standards of quercetin, rutin and hyperoside. The oven dried plate is sprayed with a prepared mixture of 1 part of 5% trihydrogenboric acid solution and 2 parts of oxalic acid solution. The flavonoid sports are recognized (after a plate heating in the oven for 10 minutes) in UV at 366 nm. Retention factors of the flavonoid sports are calculated.

Part C: Identity tests of flavonoid drugs

SAMBUCI FLOS: 0.2 g of powdered drug is boiled shortly with 5 ml of methanol in a beaker. The cool solution is filtered through a cotton wool. The filtrate is evaporated to dryness on the water bath in a porcelain evaporating dish. Then, 3 ml of 3% boric acid solution and 1 ml of 10% oxalic acid solution are added to the dry sample. The solution is evaporated in the same way as previously. The cool solid rest is extracted with 10 ml of diethylether. The solution is poured into a tube and its fluorescence at UV 366 nm is detected.

AURANTII DULCE PERICARPIUM: g of powdered drug is shaken with 5 ml of 6.5% kalium hydroxide solution a tube. The solution turns yellow (hesperidin).

Conclusion: Quantitative analysis of Prunus serotina flavonoids and chlorogenic acid was achieved for the first time in this work. The observed levels of the polyphenols confirm the importance of P. serotina leaves and inflorescences as an excellent sources of plant antioxidants. The HPLC method proposed for analysis of the aglycones enables reproducible and accurate determination of three of the most common flavonols – quercetin, kaempferol, and isorhamnetin. This method and its two modifications can be recommended as simple and rapid standard procedures for six important medicinal plants (Hypericum perforatum, Sambucus nigra, Calendula officinalis, Solidago virgaurea, Tilia sp., and Gingko biloba).

PARAMETERS OF STANDARDIZATION OF THE *SALVIA OFFICINALIS* LEAVES DRY EXTRACT

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Introduction: After the production of *Salvia* essential oil in Ukraine there are annually about 50 tons of waste of *Salvia* leaves and distillation liquid, while they still contain a lot of biologically active substances (BAS), in particular phenolic one. Earlier we studied chemical composition, antimicrobial and anti-inflammatory activity of the dry extract from *Salvia officinalis* leaves, having got by the complex processing after the essential oil production. Therefore, the next stage of our work was to carry out its standardization.

Aim. The aim of work was to define the parameters of standardization of the dry extract from the *Salvia officinalis* leaves, having got by the complex processing.

Previous chemical research of the extract was made by the methods of PC, TLC. The presence of such groups of BAS as monosugars, polysaccharidess, aminoacids, hydroxycinnamic acids, flavonoids and phenolic compounds was set.

Literary data shows that anti-inflammatory activity is exactly due to phenolic compounds, that why standardization of the extract we decided to conduct by their content. Standardization of the extract was conducted in obedience to requirements and methodologies of National Pharmacopeia of Ukraine. For authentication of basic BAS of the extract, we offered method of TLC. As indexes of the extract quality we certain loss in-bulk at drying (not more than 5%), content of heavy metals (0.01%) and microbiological cleanness of the extract (the presence of bacteria from *Enterobacteriaceae* family, *Pseudomonas aeruginosa*, *Staphylococcus aureus* have to be shut out). For the quantitative standardization we suggested to control content of flavonoids (more than 4%) and the amount of phenolic compounds (more than 20%). Quantitative content of phenolic compounds sum in recalculation on gallic acid was conducted by the method of direct spectrophotometry at the wave-length of 270 nm. Quantitative content of flavonoids in recalculation on on luteolin-7-O-glucoside was determined by the method of differential spectrophotometry after addition of reagent that contains 25.0 g/l boric acid R, 20.0 g/l sorrel acid R in ant acid waterless. The absorbency was measured in 30 minutes after preparation at 410 nm in relation to compensative solution. 5 series of the extract were analyzed. They fully answered the certain parameters of standardization.

Conclusions. The parameters of standardization of the *Salvia officinalis* dry extract were determined. In future after realization of validating measures it will be used for development of quality control methods.

THE SEARCH OF PROMISING SPECIES OF MEDICINAL PLANTS FOR TREATMENT DIABETES MELLITUS

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Introduction. Diabetes mellitus, a group of diseases, developing as a result of an absolute or relative (violation of interaction with target cells) hormone insulin deficiency, resulting in hyperglycemia develops – a persistent increase in blood glucose. The disease is characterized by chronic course and disturbance of all types of metabolism: carbohydrate, fat, protein, mineral and water-salt. Currently, there are 347 million diabetic patients in the world.

Aim. Investigation of prospective medicinal plant raw material for further development of phytomedicine for treating diabetes mellitus.

Materials and methods. Analyze and summarize the existing worldwide scientific information about promising medicinal plant raw material for treatment of diabetes mellitus and doses. Phytochemical research with prospective plant raw material was carried out by tests, thin layer chromatography, paper chromatography and HPLC.

Results and discussion Research *in vivo* and *in vitro* confirmed the hypoglycemic effect of plants such as: *Smallanthus sonchifolius* (Yacon, leaves 0.8 mg / kg), *Pilea microphylla* L. (Rockweed, 100mg / kg), *Cistus laurifolius* L. (Laurel-leaf cistus, leaves 250-500mg / kg), *Strychnos nux-vomica* (Strychnine tree, seeds 3.6 mg / kg), *Desmodium gangeticum* (Shalaparni, 100-250 mg / kg), *Nerium indicum* (Oleander Indian, leaves 5.5 mg / g dry weight), *Vernonia amygdalina* (Verona almond, 400mg / kg), *Morus alba* (white mulberry leaves 250-750 mg / kg), *Vaccinium angustifolium* (Lowbush blueberry, leaves 100 mcg / mg), *Prunus domestica* L. (Plum, bark 5.338 g / kg), Galega officinalis (*Galega officinalis*, grass 0.6 g / kg). Hypoglycemic action of these plants is associated with different groups of biologically active substances. Among them, there are a number of phenolic compounds, flavonoids, organic acids and alkaloids. Researchers have been found in experiments on animals by intraperitoneal administration of chlorogenic acid in dose 250 mg / kg a significant decrease in blood sugar levels and the effect was maintained for another 30 minutes after the glucose load. Thus, chlorogenic acid can beneficially affect the type II diabetes. By our previous research we received the extract from the plum leaves. And among phenolic compounds determined by HPLC chlorogenic acid dominated (2436.89 mg / 100g).

Conclusions. Thus obtained extract is promising for further study to develop on its basis new medicaments for the treatment of diabetes.

ANTIOXIDANT ACTIVITY OF EXTRACTS OF *SKORZONERA PURPUREA*

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Introduction. The considerable experience administration of herbal medicines confirms that plants are uncommon important source of biologically active substances (BAS), necessary and effective in pathological conditions of the human body. The free radical reactions takes a part in the development of many diseases, it causes the considerable changes in metabolic process of cells structural and functional integrity of cell membranes and protein structures, causes an imbalance of enzymatic and non-enzymatic components of system antioxidant defence. Substances of different groups of BAS, which called antioxidant, are used to neutralize the effect of free radicals. We know that good antioxidant properties show plant extracts and it causes continued interest to search the new plants for their production. A representative of the family Asteraceae *Scorzonera purpurea* is unexplored in phytochemical and pharmacological aspects.

Aim. The object of our study was to investigate the antioxidant activity of extracts of different morphological organs of *Scorzonera purpurea* exactly of flowers, leaves and stems.

Materials and methods. A method of remaceration was used to obtain the extraction utilizing 70 % aqueous-alcohol solution at room temperature. The antioxidant activity of the plant extracts was determined by applying the 2,2 diphenil 1-picrylhydrazyl (DPPH) radical scavenring method. For the measurement of the samples scavenging activity, in test tubes, 1.5 ml DPPH stock solution (2.2 mg was dissolved in 100 mL of methanol) was added to aliquots of 0.2 mL of ethanolic solutions of extracts. Absorbance at 517 nm was measured using UV/Vis spectrophotometer. Triplicate measurements were carried out.

The radical effect was calculated as follow:

Scavenging activity (%) = 100(Abs control-Abs sample)/Abs control.

Results and discussion. As a result of studies found that extracts of different morphological organs of *Scorzonera purpurea* manifest the high antioxidant activity. The highest level of the antioxidant effect had an extract which made of flowers 92.90 ± 0.58%. The antioxidant activity of extracts of leaves and stems was lower on 2.5 and 2% accordingly.

Conclusions. The obtained results showed that all morphological organs of *Scorzonera purpurea* are promising for production extracts with antioxidant activity.

DEVELOPMENT OF HERBAL PREPERATION "LAROCHE" OF INTEGRATED ACTION

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Introduction. The objectives of the state policy in the field of healthy eating are the preservation and promotion of health, prevention of diseases related to unhealthy diet and stress management. Currently, the creation of the new pharm products of the functional purpose is very important.

Aim. Phytoproducts based on petals of essential oil roses and fruits of vitamin wild roses are widely used in medicine and pharmacy, cosmetics and dietary food.

This morphological group of medicinal plants like roses leaves (wild roses) is of interest, which is not a pharmacopoeia of raw materials. It is therefore advisable to do the pharmacopoeia analysis and to research the evaluation of the effectiveness of pharmacological raw material in the introduction of certain types and forms of Rosa L. in the Middle Volga region.

The purpose of work is the development of phytopreparation of leaves, fruits and rose petals (wild roses), which has a complex effect in the prevention of diseases of the hepatobiliary and cardiovascular systems.

Materials and methods. Research objects are the types and forms of aromatic, attar of roses and vitamin (wild roses) grown in a region of the Middle Volga region (Rosa kamtschatica, R. brazilovskii, R.balsamica).

As medicinal plants to develop the micro-colleting and biologically active food additives the samples of air-dried leaves, petals and fruits in whole, crushed and powdered state are used.

Selection of components, structure optimization was performed taking into account the rules for the preparation of phytocomposition of therapeutic and preventive action (Kurkin, 2009; Semenova , 2014). The chemical composition of medicinal plants and the pharmacological effects of phytopreparation components were specified in the reference and scientific literature (Yakovlev, Blinova, 2002; Majewski 2010; Semenova, Shpichka, Presnyakova, 2015; Velichko, Semenova, 2015).

Results. In accordance with the principles of the system we have improved the algorithms of selection of component composition and optimization of phytopreparation applied to the object being studied. In order to regulate a science-

based approach, the coefficients (Co) of optimization of medicinal plants species included in the development herbal tea are introduced .The weight of each component was calculated according to the formula: m = Co × m of the base plant. Combinations of biologically active compounds all of morphological groups of rose raw materials (wild rose) in one assembly can lead to the increased pharmacological effect and to the spreading of its application.

Advantages of phytocomposition are an unique chemical composition: in the petals - the presence of geraniol, citronellol, nerol, linalool, phenyl ethanol; in fruits - vitamin C, flavonoids, tannins and tannin, tocopherols, catechins in the leaves - tannins, flavonoids, resins, carotenoids, vitamin C, polysaccharides. And other aspects of the use of aromatic leaves of roses (wild roses) as a new kind of medicinal plants are technically significant: the possibility of mechanized processes for collecting and processing of a new kind of medicinal plant materials - leaves of aromatic roses (wild roses); higher yields of medicinal plants per unit area as compared with the flowers (petals) roses and fruit (wild roses); the decrease in the age-producing plants on the plantation reaching the economic maturity (possible dates for harvesting of raw materials); the possibility of multiple harvesting of medicinal plant materials during the growing season; the inclusion of new groups of biologically active aromatic compounds of leaves of roses (wild rose) in the composition of preventive action.

It is necessary to note the complex pharmacological effect on hepatobiliary, nervous, cardiovascular, respiratory systems, as well as the possibility of long-term and safe use.

Conclusion. Taking into account the basic principles of herbal medicine, and science-based rules for the preparation of collecting, the selection algorithms of phytocomponents of biologically active food supplements and herbal tea based on raw materials of rose (rose hips) are proposed, its compositions with the main group of biologically active compounds and the pharmacological action of the components are optimized.

Phytocomposition "Laroche"promoting the normalization of metabolism, improving the vascular permeability and hepatoprotective properties, increasing the body's resistance by infectious diseases and increasing the secretion of bile, will be used in the field of medicine and pharmacy. Potential customers are pharmaceutical organizations, health care institutions and individual consumers.

PROSPECTS OF CREATION THE NEW PSYCHOTROPIC DRUG ON THE BASIS OF THE DRY EXTRACT FROM *LEONURUS CARDIACA* HERB

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Introduction. Modern life is full of chronic stress and emotional overload and it leads to symptoms of neurogenic and psychosomatic diseases, including diseases of the cardiovascular system. According to the results of current research, from 60 to 90% of visits to a doctor are related with stress. Choosing the sedative drugs, more than 80% of the population favored plant drugs. This is due to several reasons, such as, in particular, the combined effect is directed to the various links of the disease, a high safety profile, effectiveness, relative cheapness and availability.

Leonurus cardiaca herb is one of the most used medicinal plants with sedative effect. The most popular drug on the basis of this raw material is *Leonurus* tincture. However, it has some disadvantages: the chemical composition is changeable, so pharmacodynamics does the same; contain of ethanol is contraindicated children, pregnant women, persons whose activities require high attention.

So, this regard, the creation of standardized medicines based on *Leonurus cardiaca* herb is an important task.

Aim. The purpose of research is to carry out qualitative and quantitative analysis of the dry extract from *Leonurus cardiaca* herb and pharmacological screening of its psychotropic activity.

Materials and methods. *Leonurus cardiaca* alcohol extract has been obtained by maceration at a ratio 1 to 5, considering the absorption coefficient, which is 2. It has been infusing for three days, filtered and allowed to stand for a week. The resulting extract was evaporated at 85-95 °C under vacuum in a vacuum at pressure of 680-700 mm. Distillation residue is a thick dark-brown transparent liquid that has been left for sedimentation for 4-5 days in the refrigerator. The resulting aqueous concentrate was spray-dried with the coolant inlet temperature 160 °C and at the outlet - 80- 90 °C to a dry extract.

The dry extract from *Leonurus cardiaca* herb was investigated.

For preliminary identification of biologically active substances (BAS) we used method of thin layer chromatography (TLC).

Substances of flavonoid nature were showed with TLC and significant examples of flavonoids in the solvent system: acetic acid glacial R – water R – ethyl acetate R (20 to 20 to 60). Manifestations of chromatograms was carried out by spraying the solution dimethyl aminobenzaldehyde, after which the plate was heated

at a temperature of 100 °C to 105 °C for 10 minutes before the appearance of stains and viewed in daylight.

Such groups of BAS as hydroxycinnamic acids derivatives (caffeic, chlorogenic acid) and flavonoids (rutine, apigenin, giperozid) were found.

The study of quantitative and qualitative composition of phenolic compounds in the object was carried out by high performance liquid chromatography (HPLC) by chromatography Agilent Technologies (model 1100), which is equipped with a flowing vacuum degasser G1379A, G13111A a four-pump low pressure gradient, automatic injector G1313A, G13116A thermostat columns and diode-array detector G1316A.

Results and discussion. The studies of the dry *Leonurus cardiaca* herb extract by HPLC shows 10 compounds of phenolic nature (g/kg): caffeic acid (1.34), caffeic acid derivative 1 (5.28), chlorogenic acid (2.1), caffeic acid derivative 2 (4.68), caffeic acid derivative 3 (7.92), an unidentified substance 1 (1.29), rutine (13.04), an unidentified compound 2 (0.95), giperozide (2.14) and apigenin (2.96) .

We found 5 hydroxycinnamic acid derivatives, 2 of which were identified (chlorogenic and caffeic acid). 3 flavonoids were discovered such as rutine, apigenin, giperozid.

The total quantitative content of hydroxycinnamic acids is 21.32 g/kg: caffeic acid – 1.34 g/kg, chlorogenic acid – 2.1 g/kg; flavonoids: rutine – 13.04 g/kg, apigenin – 2.96 g/kg.

Pharmacological study of psychotropic activity was carried out with the Mouse Open Field Test. 16 nonlinear white male mice weighing 18-20 g took part in the experiment. The dry alcoholic extract was administered orally at a dose of 100 mg/kg, control group was orally administered the equivalent volume of purified water.

The study found an expressive sedative activity of the *Leonurus cardiaca* herb dry extract. It is statistically significant reducted in all types of activity by 26.7% ($p<0.05$). Locomotor activity is reduced by 29.2% ($p<0.05$), estimated research tends to decrease by 14.3% ($p<0.05$). Against the background of the *Leonurus cardiaca* dry extract also reduced vegetative support emotional reactions of mice by 13.2%. However, this reduction did not reach statistically significant values ($p>0.05$).

Conclusions. Thus, the phytochemical study shows the dry extract from *Leonurus cardiaca* herb contents phenolic compounds, flavonoids and hydroxycinnamic acids. The results of pharmacological studies have shown the prospects of creation the new psychotropic drug on the basis of the dry extract from *Leonurus cardiaca* herb.

RESEARCH OF VITAMIN COMPOSITION IN LEAVES ACORUS CALAMUS

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Introduction. Vitamins - are low molecular weight organic compounds that sorely needed for normal body functioning, because they are a part are lot of enzymes and hormones that stimulate the growth of the organism, its differentiation and morphogenesis, provide immune responses play an important role in supporting the resistance of the organism to a number of infections, poisons, radiation and other adverse external factors. Also, many of which exhibit antioxidant activity, which is one of the factors affecting life expectancy.

During the search for sources of new types of native medicinal plants, our attention caught the leaves of sweet flag (Acorus calamus L.). It has long been known medicinal plant that is widespread in Ukraine and found its use both in formal and in folk medicine, and in cooking and perfumes. In the official medicine currently used only rhizomes. They are used to treat digestive, urinary tract, oral cavity, in the treatment of oncological diseases. At the same time, in some foreign sources indicates significant similarity of quantitative and qualitative composition of biologically active substances in the leaves and rhizomes. Experimental studies have shown the following of action extracts from the leaves of Acorus as anti-inflammatory, antimicrobial, fungicidal, insecticidal, spasmolytic, antidiabetic, anticancer.

As part of a comprehensive study **aimed** to investigate medicinal herbs, our objective was to research of vitamin composition leaves of calamus.

The material for the research was sweet flag leaves, harvested near Kharkiv in 2013.

Results and discussion. The content of vitamins B was determined by fluorometry at fluorometer EF-3MA. Vitamin B_1 measured in terms of thiamine hydrochloride, vitamin B_2 - for riboflavin, vitamin PP or B_3 - to nicotinic acid. Determination of the amount of carotenoids and tocopherols conducted spectrophotometric method. Optical density of the solution was measured on a spectrophotometer "UV-46" at a wavelength of 450 nm (total carotenoids) and 520 nm (total tocopherols). All the definitions carried out according to standard techniques.

Found that in leaves calamus accumulates the most vitamin B_1 – 3.98 mg /%. Vitamin B_2 was at 1.18 mg /%. Nicotinic acid contained 1.21 mg /%. The amount of tocopherols was 1.98 mg/%, and the content of carotenoids in the leaves of sweet flag was – 2.07 · mg /%.

Conclusion. The results will be used in further studies.

MACRO- AND MICROELEMENT COMPOSITION OF UKRAINIAN VARIETIES OF GARLIC

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Introduction. Garlic (*Allium sativum* L.) – is an annual or biennial herbaceous plant from the family (*Amaryllidaceae*) Onion genus (*Allium*). It is used in Ukraine and all over the world as a food supplement for different dishes as fresh bulbs, dried slices, flakes, granules, powder.

Ukraine produces over 120,000 tons of fresh garlic yearly and is one of the world's leading suppliers of this crop. The most well-known winter and ardent varieties, cultivated in Ukraine, are "Lyubasha", "Ukrainian violet", "Ukrainian white", "Sophiyivskiy", "Winner", "Kharkiv violet", "Gulliver" etc. Garlic is widely used as a medicinal plant.

Garlic bulbs contain essential oil with specific smell (S-containing compounds), polysaccharides, amino acids, phytoncides, vitamins. The green garlic sprouts have 2-3- times higher content of ascorbic acid than the bulbs do. Fresh garlic, ethanol tinctures, oil extracts of garlic are used in folk medicine. Numerous clinical researches confirm the data about healing properties of garlic. The main pharmacologic effects of garlic medicines are antibacterial, antiviral, fungicidal, antiatherosclerotic, and also it affects the hepatobiliary system.

Nowadays famous producers of phytoremedies and food supplements on herbal basis consider this plant as one of the most important components of these remedies. «Kwai» (Germany), «Revital Garlic Pearls» (India), «Kyolic» (USA), «Allicor», «Carinat» (Russian Federation), «Allochol» (Ukraine) are the examples of such remedies.

The **aim** of our research was the determination of element content of *Allium sativum* L. Bulbs of some Ukrainian varieties.

Materials and methods. The plant material samples were collected in the summer of 2015 in Sumy region. The qualitative composition and quantitative content of of macro- and microelements in the dried plant material samples was determined by the means of atomic-emission spectroscopy at the DNU STC "Institute for Single Crystals" of the NAS of Ukraine (Kharkiv).

Results. The presence of 19 macro- and microelements, with the prevalence of K – 640 mg/100 g, Ca – 255 mg/100 g, P – 190 mg/100 g, and Na – 130 mg/100 g, was determined.

Conclusion. The results obtained can be used for the quality parameters of the plant material working out.

PHARMACOGNOSTIC STUDY OF RAW MATERIALS OF MEMBERS OF THE FAMILY COMMELINACEAE

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Introduction. The development of herbal medicine is characterized by deep theoretical research and practical developments. Conducted searches for new kinds of medicinal plants to create drugs based on them, which have high efficacy and low toxicity. From this side drew our attention to the plant family Commelinaceae. Most of the common in tropical Africa and America. Among the characteristic features of the family isolated long stem, with alternate leaves. Most leaves are arranged in two rows. The main feature leaves that they fully grasp the stem base. Side shoots have to dig the foundation sheet. Veins to sheet plates parallel arcs.

Callisia fragrant – Callisia fragnans Woodson – plant family Commelinaceae over 10 years been cultivated in Ukraine, and has long been used in folk medicine. It is a perennial herbaceous plant with rather thick stems of two types: a shortened vertical with a rosette of leaves and a horizontal elongated with immature leaves, arranged in a spiral. After reaching the mature age of plant gives liano similar spikes, at the ends of the formed sheet outlet, which is reproduction. Leaves oblong-lanceolate, large, dark green, plain, glossy. The popular name of the plant "Golden mustache" or "home ginseng".

Callisia can be used in diseases of the gastrointestinal tract, cardiovascular and circulatory system, metabolic disorders, immunomodulatory, analgesic, anti-inflammatory and antitumor agent.

Aim. In light pharmacognostical conduct research studying morphological structure of raw materials from the family Commelinaceae.

Materials and methods. The objects of the study were the leaves and shoots of plants of the family Commelinaceae, harvested in April-June and September 2015.

Results and discussion. The stems are thick enough two types: vertical shortened with rosette leaves and elongated horizontal with underdeveloped leaves arranged in a spiral. Upon reaching adulthood plants gives processes like liana, formed at the ends of leaf rosette, which happens reproduction. The leaves are oblong-lanceolate, large, dark green, single color, shiny, length of leaf lamina−20-30 cm, width− 5-6 cm. The plant contains a large number of biologically active substances as flavonoid’s and phytosterols, as iron, nickel and copper. Juice shoots contain quercetin and kaempferol, beta sitosterol.

Conclusions. So Callisia fragrant – a promising source of medicinal plants.

SEARCH FOR NEW MEDICINAL PLANT RAW MATERIALS WITH ANABOLIC ACTIVITY

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Introduction. Proteins are the most important biological substances of living organisms. They serve as the primary plastic material of cells, tissues and organs of the human body. Proteins are the basis of hormones, enzymes, antibodies and other entities that perform complex functions in human life (digestion, growth, reproduction, immunity, etc.).

Since proteins are central to the implementation of the body's vital processes, the violations of protein metabolism are components of the pathogenesis of all pathological processes. With a lack of protein in the body there are serious violations: a slowdown of growth and development of children, changes in liver, in activity of the endocrine glands and in the blood, the weakening of mental activity, decreased performance and resistance to infectious diseases.

Aim. Study of modern literature and the analysis of the role of anabolics in protein metabolism.

Materials and methods. The study of scientific literature sources from 2012 to 2016.

Results and discussion. The modern nomenclature anabolic agents include various chemical structure and origin of drugs having the ability to enhance protein synthesis in the body. It is hormonal and anti-hormonal drugs, amino acids, vitamins, coenzymes, nootropic, herbal products, bee products and others.

However, the basic therapy is represented by hormones, particularly anabolic steroids, which have a positive effect on protein metabolism, but they do have number of serious side effects (negative effects on the mental state of a person, the reproductive function in men, the adrenal cortex, cardiovascular system, liver, musculoskeletal system, skin and others), which limit their use.

In this regard, one of the major problems in modern pharmacology is the creation of new drugs that will contribute to the intensive renewal of proteins or have a direct stimulating effect on the different stages of protein synthesis.

Plant adaptogens show, as a rule, mild anabolic effect, but in its ability to increase physical and mental performance (ergotropic action) are superior to most synthetic drugs. A positive trait of plant anabolic drugs is a low toxicity, a wide range of pharmacological actions and the reasonable price. They are able to influence the metabolic processes in the body that is caused by the presence in their composition the amount of biologically active substances – flavonoids, ecdysterones,

polysaccharides, saponins, coumarins and others that enhance the pharmacological action of each other.

The range of domestic drugs has more than fifty plant drugs that can influence the body's metabolism (*Rhaponticum carthamoides, Rhodiola rosea, Aralia mandshurica, Panax ginseng, Oplopanax elatus, Eleutherococcus senticosus, Schisandra chinensis, Sterculia platanifolia*, and others). But the main for them is ergotropic rather than anabolic effect.

In Ukraine the herbal drugs with anabolic activity are almost absent. Therefore, the study of plants in order to create drugs that will implement a positive effect on protein metabolism and thus do not show pronounced negative effects remains an urgent problem of modern pharmacy and medicine.

It is known from literature sources total flavonoid preparations from different species of *Trifolium, Ononis, Medicago, Solidago* and *Psoralea* was increased the total protein content in skeletal muscles and internal organs by 30-50%. Body weight gain in the animals for 2 weeks was 60-75%, which is probably due to the stimulation of DNA and protein synthesis, and regulation of anabolic processes.

Analyzed the chemical composition of plants with different mechanisms of anabolic action. Herbal anabolic steroids can be divided into 3 groups: phytoecdysones, estrogen and hypoglycemic action anabolics.

Phytoecdysones called group of polyhydroxylated steroid compounds (*Rhaponticum carthamoides, Plantago major*). In experiments it was found that ecdysterone of Leuzea increased body weight and total protein in the liver, heart and kidneys.

Phytoestrogens – analogues of female sex hormones – have diverse structure. First of all, it may be steroidal estrogens similar to human (*Salix alba, Glycyrrhiza glabra, Prunus armeniaca*); stilbenes (*Anisum vulgare, Trifolium repens*); coumarin derivatives (*Trifolium repens, Trifolium hybridum, Medicago sativa*); isoflavonoids (*Medicago sativa, Prunus avium, Genista tinctoria*).

There are several groups of plants which include *glycokinins* having effect similar to insulin. One of these glycokinins groups has an anabolic activity (*Phaseolus vulgaris, Medicago sativa, Galega officinalis, Lactuca sativa, Elytrigia repens, Taraxacum officinale, Lactuca sativa, Apium graveolens, Juglans regia, Verbascum phlomoides*).

Conclusions. Thus, perspective is the depth study of the composition and activities of the aforementioned plants, as well as the search fornew medicinal plant raw materials which has an anabolic influence on the human body.

APPLICATION OF PARMELEE IN ETHNOSCIENCE AND TRADITIONAL MEDICINE

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Introduction. Useful properties of Parmelee have been known for a long time, even in ancient Egypt and medieval Europe. While the biological composition of the lichen has not yet been studied. However in many cases a positive effect of treatment by Parmelee was present.

Aim of our work was the study of the domestic pharmaceutical market of drugs and dietary supplements, which based on Parmelee and aspects of its medical use.

Materials and methods. Analysis of the assortment of medicines was made by using the methods of marketing research on the basis of materials of the State Register of Medicinal Products of Ukraine.

Results and its discussion. The chemical composition of Parmelee is unique. Lichen thallus contains usnic acid, a large amount of vitamin C, tannins, carbohydrates, which similar to fiber in its chemical composition. They provide the raw material swelling in hot water. Evenin and izolikenin, a minor amount of protein, fat and ash, and also potassium, calcium, phosphorus, and pigments were found in composition of polysaccharides.Usnic asid has been allocated. It is a powerful antibiotic with bacteriostatic properties in regard to tuberculosis bacteria.

The plant is widely used in traditional medicine for the treatment of the chronic cough, gastrointestinal disorders, pulmonary tuberculosis, acute colitis, toxic dyspepsia, as immunostimulatory agents. It has a calming effect on the mucous membrane of the respiratory tract. Decoction of Parmelee cleans the pus from the sores and wounds it is a good hemostatic drug.

On the Ukrainian pharmaceutical market "Parmelee herbal tea" presents, which is used as a strong expectorant, anti-inflammatory, anti-microbial agent for colds, bronchitis, tracheitis, laryngitis to liquefy phlegm and facilitates expectoration. Parmelee oral tincture is used in diseases of the respiratory tract and lung diseases (bronchitis, cough of varying intensity, bronchial asthma, tuberculosis), for the treatment of diseases of the gastrointestinal tract (gastritis, ulcers, enterocolitis). Tincture, aqueous extract powder and Parmelee "Mask Parmelee balm" is applies externally in treatment of purulent wounds, cuts, cracks, chafing.

Conclusions. Thus, based on the rich chemical composition and polyvalent pharmacological activity and sufficient resources base Parmelee is a valuable source for development of new domestic drugs.

QUANTITATIVE DETERMINATION OF TANNINS IN DIFFERENT MORPHOLOGICAL PARTS OF TATAR RHUBARB GROWN IN THE SOUTHERN BALKHASH

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Introduction. Expanding the range of medicines is possible due to the introduction into medical practice of new plants and creation on their basis of herbal drugs with high pharmacological activity and low toxicity. As promising sources of biologically active substances of natural origin have attracted the attention of the representatives of the local flora of the family Polygonaceae, including many medicinal plants. Tatar Rhubarb Rheum tataricum L. - perennial herb with a powerful rhizome, which belongs to the family of Buckwheat - Polygonaceae. Occurs everywhere in the plains and in the deserts. Commercial stocks of raw materials identified in the Balkhash lake and the Aral sea region.

For medical purposes the rhizomes are used, although all parts of the plant are rich in tannins, used in official and folk medicine. The group of tannins includes substances of vegetable origin, which are complex organic compounds that are derivatives of polyhydric phenols with diverse chemical structure beginning from the simplest to the more complex macromolecular derivatives, and the so-called phlobaphens phlobatannis. They are phylogenetically related to ancients compounds (in the pyramids and tombs of Egypt and now could be found the pictures of tanning plants and tanning materials). Tannins have astringent, anti-inflammatory and hemostatic effect, so the search for new sources of vegetable tannins in herbal drugs are highly relevant.

Aims of Research. The aim of this work was to obtain quantitative information about the contents of tannins in different morphological parts of Rhubarb Tatar grown in the southern Balkhash region.

Materials and methods. The objects of the studies used the aerial parts and roots of Rhubarb Tatar, harvested in April - May 2015 in the Southern Balkhash.

Determination of quantitative content of tannins conducted by permanganometric method.

About 0.002 kg (accurately weighed) crushed material was placed in a conical flask filled 0.00025 m^3 heated to boiling purified water and refluxed for 1800 seconds with periodic agitation. The solution was cooled to room temperature and filtered through cotton about 0.0001 m^3 of solution in conical flask of 0.0002-0.00025 m^3 volume. Pipetted 0.000025 m^3 of the resulting solution in flask of 0.00075 m^3 poured 0.0005 m^3 of purified water, 0.000025 m^3 of indigo sulfonic acid solution and titrated

with continuous stirring 20 moles/m^3 potassium permanganate solution to golden yellow color.

At the same time we conducted a control experiment.

Tannin content (X) as a percentage based on absolutely dry raw material is calculated by:

$$X = \frac{(V - V_1) \cdot 0.000004157 \cdot 0.00025 \cdot 100 \cdot 100}{m \cdot 0.000025 \cdot (100 - W)},$$

where

V – the amount of 20 mol /m^3 of potassium permanganate solution consumed in the titration of the test solution, m^3;

V_1 – the amount of 20 mol /m^3 of potassium permanganate solution consumed in the titration of the control solution, m^3;

0.000004157 – tannins amount corresponding to 6.10 mole of 20 m^3 /m^3 of solution of potassium permanganate in terms of tannin, kg;

m – raw material mass, kg;

W – loss in mass on drying of raw materials, %.

Results and discussion:

Table 1

The quantitative content of tannins in different morphological parts of Rhubarb Tatar

Raw materials	Content of tannins, %
Leaves	6.12±0.06
Stems	2.18±0.03
Fruit	15.76±0.03
Rhizome	22.96±0.04

We took the mean value of 5 determinations.

The dominant quantitative content of tannins was observed in the rhizomes, the lowest - in the stems of rhubarb Tatar.

Conclusions. Quantitative content of tannins was determined in the leaves, stems, fruits and rhizomes of Rhubarb Tatar of the Southern Balkhash by Permanganometric method. The greatest amount of tannins was observed in the rhizomes, the lowest - in the stems of Rhubarb Tatar.

The experimental results can be used in the development of analytical documents on medicinal plant raw material Rhubarb Tatar.

SECTION № 3

THE STANDARDIZATION OF MEDICINES. PHARMACEUTICAL AND CHEMICAL-TOXICOLOGICAL ANALYSIS

DEVELOPMENT OF UV-SPECTROPHOTOMETRIC METHODS OF EFAVIRENZ DETERMINATION

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Introduction. Efavirenz is a non-nucleoside reverse transcriptase inhibitor and attributed to the group of antiretroviral medicines, and used for treatment of HIV infection. At the same time it is possessed of quite a number of side effects showed by psychiatric symptoms, including insomnia, memory loss, depression, and anxiety. Use of efavirenz can produce a false positive result in urine tests for marijuana.

Aim. To develop UV-spectrophotometric procedures of efavirenz quantification in urine and to validate the developed procedures.

Materials and methods. Efavirenz isolation from urine was carried out using acetonitrile with subsequent separation of organic layer under the conditions of aqueous phase saturation by ammonium sulphate. Isolation was carried out in the acid (pH = 2), weak-acid (pH = 5) and alkaline medium (pH = 11).

Results and discussion. The development and validation of procedures of efavirenz quantitative determination was carried out with application of the normalized coordinates; the application ranges was 25 – 175%; the number of concentration levels was $g = 7$. The efavirenz concentration in urine corresponding to the point of 100% was 12 μg/ml.

The results of specificity study show that efavirenz isolation from urine using acetonitrile provides low contribution of biological matrix components into the absorbance of the sample to be analysed, and the lowest value corresponds to the experiment in the weak-acid medium.

By the results of recovery study the method with acetonitrile application in the alkaline medium is characterized by the best extraction efficiency. The values of reproducibility for recovery and blank-samples absorbance satisfy the acceptability criteria for all variants of the methods.

All examined methods are characterized by the acceptable parameters of linearity, accuracy and precision, and the obtained data are the evidence of application possibility of the developed methods for efavirenz spectrophotometric determination in urine.

Conclusions. We have developed the set of UV-spectrophotometric methods of efavirenz quantitative determination in urine using acetonitrile for analyte isolation from matrix under the conditions of aqueous phase saturation by ammonium sulphate. Acetonitrile application in the weak-acid medium is optimal by specificity and extraction efficiency.

COMPARATIVE ESTIMATION OF DIDANOSINE QUANTIFICATION IN CAPSULES BY UV-SPECTROPHOTOMETRY

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Introduction. For the present day, the rapid development of pharmaceutical science leads to the creation of new, in high degree effective pharmacologically and biologically substances on the base of which new medicines are developed that allow achieving the maximum therapeutic effect with minimum side response.

The introduction of such a products into production requires the development of methods of analytical assessment, which allows confirmation the quality of products have made.

From this point of view are very important and interesting researches about improvement of the existed methods of analysis and collaboration of the new ones for such a group of medicinal compounds as antiretroviral drugs. This group is of very high importance because of its specifity of application, which is in treatment of viral infection, including infections caused by such a viruses as virus of hepatite C and human immunodeficiency virus.

One of the modern antiviral drugs is didanosine, which is widely used nowadays in treatment of viral infections either as a separate medicine or in the various combinations with some other antiretrovirals.

For our investigation was chosen didanosine in the composition of capsules.

Materials and methods. For quantification of didanosine in the composition of capsules was applied method of UV-spectrophotometry as simple one and not-complicated in evaluation.

Assay was carried out by two techniques: by the method of standard and using specific absorbance. On the basis of the data have obtained the results of quantification by the method of standards and by the specific absorbance of didanosine in the composition of capsules have been compared by their reproducibility.

Results and discussion. As it has been stated, a relative error of separate determination for assaying didanosine contents in capsules for both techniques by the method of standards and using specific absorbance is ±3%, which does not exceed demands of the State Pharmacopoeia of Ukraine (SPhU) to the quantitative content.

Conclusions. As it has been stated in the result of our researches, the both techniques for quantification of didanosine in the composition of capsules by UV-spectrophotometry methods corresponds to the demands of SPhU; both techniques of quantification are of appropriate pharmacopoeial quality.

DEVELOPMENT OF METHOD FOR QUANTITATIVE DETERMINATION OF AMIODARONE HYDROCHLORIDE IN TABLETS

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Introduction. Amiodarone hydrochloride is a member of a new class of antiarrhythmic drugs with predominantly Class III (Vaughan Williams' classification) effects, available for oral administration as pink, scored tablets containing 200 mg of amiodarone hydrochloride. This medication is used to treat certain types of serious (possibly fatal) irregular heartbeat (such as persistent ventricular fibrillation/tachycardia). It is used to restore normal heart rhythm and maintain a regular, steady heartbeat. Amiodarone is known as an anti-arrhythmic drug. It works by blocking certain electrical signals in the heart that can cause an irregular heartbeat. Amiodarone is particularly helpful when other medicines used for the treatment of arrhythmias are unsuitable for some reason.

Aim. In chemical structure amiodarone hydrochloride is a benzofuran derivative: 2-butyl-3-benzofuranyl 4-[2-(diethylamino)-ethoxy]-3,5-diiodophenyl ketone hydrochloride. Its molecular formula $C_{25}H_{29}I_2NO_3 \cdot HCl$, with a molecular weight of 681.77.

Materials and methods. Amiodarone hydrochloride enters in tablets, such as “Cardiodaron-Zdorovye” (“Pharmaceutical firm “Zdorovye” CJSC, Ukraine), “Amiodarone” (“Lekhim – Kharkiv” JSC, Ukraine), “Cordarone” (“Sanofi aventis”, France).

Results and discussion. Official monographs of the European Pharmacopoeia and the National Ukrainian Pharmacopoeia on active pharmaceutical ingredient contain “Identification” by IR-spectroscopy and reaction of Chlorides, “Impurity H” by thin-layer chromatography, “Related impurities” by liquid chromatography and “Assay’ by potentiometric titration. According to the United States Pharmacopoeia (USP), “Assay” is conducted by liquid chromatography.

A high-performance liquid chromatography method is described in the USP in official monograph “Amiodarone tablets” for control organic impurities and assay.

The actual necessity to elaborate a simple spectrophotometric method for the analysis of Amiodarone hydrochloride in pharmaceutical formulations. UV-visible spectrophotometry is the technique of choice in research laboratories, pharmacy and pharmaceutical industries due to its low cost and inherent simplicity.

Conclusions. The objective of the work is to develop a new spectrophotometric method for its estimation in bulk and tablet dosage form with good accuracy, simplicity, precision and economy.

INVESTIGATION OF SOME ANTIRETROVIRAL DRUGS BEHAVIOUR IN THIN LAYERS OF SORBENT

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Introduction. Chromatography in thin layers of the sorbent according to the literature data, is today one of the most common methods for the determination of substances in the pharmaceutical, forensic, chemical and chemical-toxicological analysis, and is widely used to determine the purity and impurities in pharmaceutical analysis.

For chromatographic researches from the group of antiretroviral drugs was chosen zidovudine, which is nowadays is widely used for treatment of various viral infections including human immunodeficiency either as a separate substance or as a compositional part of multicomponent medicines.

That is why the constant improvement among the existed analysis methods and researches about new methods of identification and assay for zidovudine has a great interest for analysts and can have a valuable practical importance.

Materials and methods. For our researches two type of chromatographic plates: Sorbfil and Merck have been chosen.

As a detectors have been chosen such reagents as: Dragendorff reagent, FPN reagent, Van Urk reagent, Iodine vapors, UV light, mercuric sulphate with 0.05% diphenylcarbazone solution in chloroform, 1% *o*-tolidine solution and some other reagents.

As a movable phases have been chosen systems of solvents of acidic character; systems of solvents of alkaline nature and systems of solvents of neutral character.

Results and discussion. As it has been stated according to the data of the conducted investigations, the limit of zidovudine detection in all the suitable systems chosen for its identification is 2 mkg on both types of chromatographic plates mentioned above.

The most suitable systems for the identification in our experiment, appropriate for carrying out investigation about zidovudine identification by TLC method on plates Sorbfil and Merck are systems of alkaline character using Dragendorff reagent, UV light, 1% *o*-tolidine solution and iodine vapours as detectors on plates after their evaluation.

Conclusions. The systems of solvents and detectors mentioned above can be taken for identification of zidovudine by thin layer chromatography method on the plates Sorbfil and Merck.

DEVELOPMENT OF METHODS OF QUALITY CONTROL AND STABILITY STUDIES OF EYE DROPSWITHRIBOFLAVIN

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Introduction. Determination of sterility and stabilityofextemporaneous medicines is one of base and the most important tasks of pharmaceutical analysis. In this regard eye drops, especially with vitamins, are of particular interest. Stability of ingredients in eye drops depends on the chemical properties of substances, product pH, storage methods (especially the temperature), other additive and type of packaging. Sterility depends on the methods of sterilization, type of packaging and storage conditions.

For our investigation eye drops with riboflavin was chosen. As is known riboflavin is helpful with eye disorders and in particular with the treatment of some eye cataracts. Crystalline riboflavin shows no evidence of decomposition under ordinary conditions, but protection from light is advisable. Solution of riboflavin decomposes under the influence of visible or ultraviolet light. So investigation of stability of this eye drops is useful and interesting.

Aim. The aim of this investigation is to study the chemical stability and sterility of riboflavin eye drops compounding preparation.

Materials and methods. Riboflavin eye drops compounding preparation was selected for the stability and sterility study. Composition: Riboflavin 0.002, Solution of sodium chloride 0.9% -10 ml. The chemical stability study of riboflavin eye drops compounding preparation and stress testing was carried out by TLC method, UV-spectrophotometry and chemical reactions. All solvents and reagents which used in the study were analytical reagent grade, and all reagents used in the investigation were freshly prepared.

Results and discussion. For determination of stability and identification of the ingredients and degradation products chemical reactions, UV-spectrophotometry and TLC were used. For determination of sterility microbiological method was carried out.

Conclusions. During this investigation methods of the determination of stability and sterility for Riboflavin eye drops compounding preparation were developed. Quality control and stability studies were carried out.

DEVELOPMENT OF QUALITY ASSURANCE METHODS OF HYDROCHLOROTHIAZIDE IN COMPOUNDED POWDER AND SYRUP PREPARATIONS

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Introduction. Hydrochlorothiazide is a thiazide diuretic prescribed for both adults and children in the treatment of hypertension, congestive heart failure, symptomatic oedema and in the prevention of kidney stones. Compounded preparations are drug preparations in concentrations and dosage forms made to meet unique prescriber and patient needs. According to the requirements of Ukrainian legislation, batches of compounded preparations should pass quality control. Although the powders have a relatively long shelf life, the same cannot be said for liquids. It is necessary therefore to develop quality control methods and study the stability of compounded powders and syrups containing hydrochlorothiazide.

The **aim** of this study is to develop identification and assay methods for compounded formulations of hydrochlorothiazide (HCT) in powders and simple syrup using thin layer chromatography (TLC) and ultraviolet (UV) spectrometry.

Materials and methods. Powder composition: HCT - 5 mg, glucose up to 0.2 g; syrup composition: HCT – 200 mg, simple syrup qs 20 ml. Active pharmaceutical ingredients (API) used for compounding of powder and syrup were commercial tablets (Sanofi-Aventis, Ukraine LLC). 2 μL each of 5 mg/ml preparations of reference substance, powder and syrup of HCT in acetone were applied to TLC aluminium plates (silica gel $60F_{254}$, Merck KGaA). The chromatographic plates were developed over a distance of 10 cm in ethyl acetate mobile phase and observed under UV light. A UV spectrophotometer («Evolution 60s») was used to assay 0.01 mg/ml preparations of HCT from stock solutions of the reference substance, powder and syrup in 0.01 M sodium hydroxide solution. The absorbance at a wavelength of 273 nm was measured and results were compared with that of reference standards.

Results and discussion. The chromatograms showed good separation, sugar components remained on the start line while three aligned brown spots (under UV-light) were observed with R_f- 0.38, 0.38 and 0.39, corresponding to HCT of reference substance, powder and syrup. When sprayed with sublimed iodine, yellow aligned spots were seen corresponding to the above-mentioned substances. The calculated percentage content of HCT in samples of reference substance, powder and syrup were 101%, 106% and 99.94% respectively. The excipients in both powder and syrup did not significantly affect the results obtained using TLC and UV-spectrometry methods.

Conclusions. These methods could be used for quality control of HCT in compounded preparations of powders and syrups after validation.

DEVELOPMENT OF QUALITY CONTROL METHODS FOR LIQUID EXTRACT “VENOFORT”

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Introduction. For thousands of years mankind has used the resources of flora in the treatment of various diseases. Vegetable raw material such as plants, pharmacogens or derivatives (extracts, tinctures, essential oils or dried products) has been widely used in drugstores and pharmaceutical industries and they represent a substantial proportion of the global drug market. Herbal medicines have natural active constituents, they should be assessed as drugs and therefore subjected to strict controls at every stage of their idealization, evaluation and development.

Aim. The purpose of this paper is to establish the composition of biologically active substances of tincture "Venofort".

Materials and methods. The composition of the tincture "Venofort" includes *Aesculus hippocastanum*, *Sophora japonica*, *Symphytum officinale linne* and *Melilotus officinalis*.

Results and discussion. The medicinal plants of tincture, mostly contain in their composition a complex of biologically active substances represented by flavonoid compounds, tannins, alkaloids, etc.

In determining the parameters of quality control of herbal medicines, which are composed of a complex mixture of components and due to the limitations on sensitivity in ultraviolet absorption spectroscopy for the quantitative determination of compounds it is often necessary to use preliminary steps for separation and concentration of the desired elements, with a consequent increase of sensitivity. Among these techniques we can mention the liquid-liquid extraction, precipitation and solid-liquid extraction

Spectrophotometry in the UV region is one of the most used analytical techniques in terms of robustness, it has relatively low cost and large number of developed applications and can be applied in the identification and determinations of organic compounds.

Polyphenolic compounds can refer to these compounds. Therefore, it is expedient to examine the nature of the absorption of the absorption spectra of all the compositional parts of the tincture of alcohol extracts of medicinal plants.

Results of research carried on a spectrophotometer Evolution 60s in the range from 220 nm to 450 nm indicates the prevalence in the samples and total formulation contains substances of flavonoid nature.

Conclusions. The results will be taken into account in the development of quality control methods of the analyzed liquid extract “Venofort”.

MODERN CHROMATOGRAPHIC METHODS (GLC, HPLC) TO IDENTIFY MEDICINES

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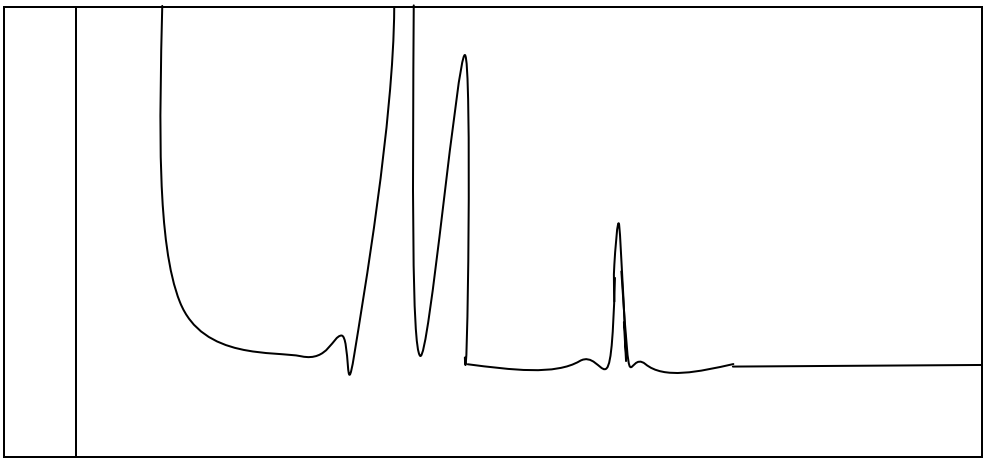
Introduction. Chromatographic methods are of great interest in a modern pharmaceutical analysis as they are able to solve the problem of separating mixtures of various ingredients – from the most simple to the most complex organic compounds. The main methods of analysis are high performance liquid chromatography (HPLC) and gas liquid chromatography (GLC). These types of chromatography have been found as methods that are used extensively in the areas such as chemistry, petrochemistry, biotechnology, medicine, production of medicines and many others.

Aim. Separating and analyzing mixtures of substances, as well as the study of physical-chemical properties of substances. Analysis of the drug "Septolete" in the form of pellets. Identification and quantitative analysis of Menthol and Thymol by using GLC and HPLC in this medicine.

Materials and methods. Peaks were recorded on the gas chromatograph the GC Chromos-1000 Laboratory with a flame ionization detector (FID). Column: SPB 5 capillary (30 m x 0.P2 mm, 0.25 μm). Column temperature: 120 °C. Gas-carrier: Nitrogen rate: 1.8 ml/min, split flow of 55:1. Mode of chromatograph: the module detectors: PID ½; Working detectors: PID-1; Analysis time: 0:12:00; Detector temperature - 230°C; Evaporator temperature – 200 °C. Standards: 1. The Menthol reference substance; 2. Reference substance of Imol; 3. Camphor (D-camphor) in order to prepare the internal standard solution and the standard solution for introduction. Reagents: 1.Chloroform; 2. Demineralized water; 3.Anhydrous Na_2SO_4.

Results and discussion.

CHROMATOGRAM



INDICATORS	METHODS	STANDARDS
Menthol	GLC	match the pattern
Thymol	GLC	match the pattern
The mass of the pellets	GFH, HPLC	1.200 g. each pellet
Uniformity of mass	GLC	±10%
Microbiological purity	GLC, Titration	3g. category
Melting point of Menthol	chemical thermometer	42-45 °C in crystalline form
Quantitative analysis - Menthol - Thymol	GLC, HPLC, Titration	Not less than 1.0 mg / Ms. the weight of pellets Not less than 0.5 mg / Ms. the weight of pellets
The presence of Benzalkonium chloride in pellets	GLC, HPLC, Titration	1.0 mg/ Ms. the weight of the pellets 15%
Dissolution "Septolete"	HPLC, GFH	No more than 60 minutes in water at the temperature, 37±1 °C

Preparation of the tested solution:

We weigh the amount of powder from the pellets, which corresponds to the 10 pellets, transfer to a separatory funnel (capacity=250 ml) and mix well with 100 ml of water. Then we extracted it 3 times, using every time 70 ml of chloroform (each time shake for 5 minutes), filtered the chloroform layer through anhydrous Na_2SO_4 into a flask of rotating evaporator. Then the chloroform was removed by distillate to dryness. The dry residue was quantitatively transferred to volumetric flask of 100 ml and was filled with chloroform to mark. Standard solution for introduction: compound of a standard solution and internal standard solution in 1:1 (V/V). The retention time of the peaks of Menthol and Thymol on the chromatogram corresponds to the retention time of the peaks in the chromatogram that were obtained from the standard solutions for introduction.

Conclusions. Modern chromatographic methods are used to analyze small quantities of a mixture of the substance which are chemically similar to each other. By using HPLC and GLC methods we were able to identify the active ingredients of the drug "Septolete", analyze Menthol and Thymol in this medicine, set their physical-chemical properties. We found the presence of Benzalkonium chloride in the pellets and prepared standard solutions for introductions. We also determined physico-chemical properties of standard solutions for introductions. Thus, GLC and HPLC are effective and reliable modern chromatographic methods in the analytical analysis which are used to identify medicines.

APPLICATION OF CHEMICAL ANALYSIS METHODS IN GEL "DIDIKLOZOL"

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Introduction. Today the important question is the creation of effective and costly drugs. We have developed a new pharmaceutical composition "Didiklozol", which will be in demand in medical practice as an anti-inflammatory and analgesic for external use. As base an ointment used Tizol gel, combines well with many medicines, facilitating transportation to the pathological center and increasing the selectivity of their action, providing sterile dosage form, and a long shelf life.

Aim. Development of specific method to identify the ingredients in the ointment. The pharmaceutical institutions use different types of quality control of medicines. Among them, the most effective and affordable is the chemical methods allows establishing the appropriate dosage forms prescribed by a physician prescription, and the quality of preparation.

Materials and methods. The object of investigation is taken dosage form, which comprises tetracaine hydrochloride 0.5 g, 0.5 g sodium diclofenac and gel Tizol to 100 g. To develop a means of detection recipe ingredients prepared 0.05% and 0.1% aqueous solutions of drugs. We research the reaction with reagents generalalkaloid, deposition, oxidation-reduction and the ability to halogenated aromatic nuclei.

Results and discussion. Research have shown that tetracaine hydrochloride and diclofenac sodium produce the same effects with analytical Tollens reagents, Marks, bromine water, potassium dichromate, potassium permanganate in an acid environment. Specific reagents on tetracaine hydrochloride are phosphomolybdic and phosphotungstic acid reagents Dragendorff and Mayer; diclofenac sodium – ferric (III) chloride, copper (II) sulfate, mandelin reagent. It is possible to develop specific responses identifying ointment ingredients.

Methods for detection of tetracaine hydrochloride:

1. Weigh ointments, equal to about 0.1 g, were dissolved in 10.0 ml of dilute hydrochloric or sulfuric acid. Subsequently, to the resultant mixture was added 5.0 ml 2-3 drops of phosphomolybdic acid. Drops yellow precipitate fosfornomolibdata tetracaine. The opening is at least 0.1 mg/ml. A similar reaction can be carried out with a solution of phosphotungstic acid. The reaction product - an amorphous white precipitate. Sensitivity reactions of 0.05 mg/ml.

2. To 2.0 ml of the mixture obtained after dissolving 0.1 g in 10 ml ointments hydrochloric acid solution with a mass fraction of 8%, was added 0.5 ml

Dragendorff reagent. Drops of yellow-orange solid. Openable minimum 0.08 mg/ml.

3. 0.1 g ointment was dissolved in 5ml of diluted hydrochloric acid and sulfuric acid is added 2-3 drops of reagent Mayer. A white amorphous precipitate. Sensitivity reactions of 0.15 mg/ml.

Identification of sodium diclofenac:

1. To 1.0 ml of alcoholic solution are added 3 drops ointments solution of iron (III) chloride and 0.1 mol/l sodium hydroxide solution to produce a pH of 5-6. It appears brown precipitate of diclofenac iron (III), soluble in acid. Sensitivity reactions of 0.35 mg/ml.

2. To 1.0 ml of the filtrate was added an ethanolic solution ointments 5-10 drops of 10% solution of copper (II) sulfate. Diclofenac precipitate copper (II) green. The opening is at least 0.40 mg/ml.

3. Weigh 0.5 g ointment was dissolved in about 10.0 ml of 95% ethyl alcohol and 10.0 ml of 2 mol/l dilute sulfuric acid. To 1.0 ml of the resulting solution was added 0.5-1.0 ml reagent Mandelina. The solution is colored cherry red color. The sensitivity of the reaction is 6.6 mkg/ml.

Tizol ($TiO_4(C_3H_8O_2)_4(C_3H_7O_3)_{10}\cdot 40H_2O$) in the formulation proposed to open a qualitatively detect the reactions of ions of titanium (IV) and glycerol:

1. 0.5 g ointment was dissolved in 8 ml of 5% hydrochloric acid solution. To 2.0 ml the resulting solution were added 3.0 ml 1% alcoholic solution of salicylic acid. Solution formed salicylate complex compound of titanium (IV) yellow.

2. 0.5 g ointment placed in a crucible, is burned and calcined for one hour at a temperature of 650 °C. The residue after burning is painted in bright yellow color. Upon cooling color disappears.

3. Titanium (IV) can be detected by reaction with a 3% solution of H_2O_2 in the presence of 2 mol/l H_2SO_4 solution. As a result of chemical interaction produced an orange coloration. Analysis of reaction due to the formation of the compound $[TiOH_2O_2]SO_4$ maximally absorbs light at a wavelength of 410 nm.

4. For the detection of glycerol 0.5 g ointment was dissolved in 5.0 ml of 95% ethanol and 5.0 ml of 10% sodium hydroxide solution. To 2.0 ml of the resulting solution was added 1.0 ml solution of copper (II) sulfate. The reaction solution turns blue-violet due to formation of sodium glycerate copper (II).

Conclusions. Developed methods of quantitative analysis chemical methods of tetracaine hydrochloride, diclofenac sodium Tizol in ointments are sensitive, simple in execution, do not require expensive equipment. Reactions can be recommended to control and analytical services for pharmaceutical analysis of a new dosage form "Didiklozol".

ANALYSIS OF RELEASING DYNAMICS FOR SOME METALS FROM KITCHEN UTENSILS TO THE ENVIRONMENTAL OBJECTS

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Introduction. Metals are the permanent components of drinking water and other foodstuffs, which we prepare using this water. It is possible even not to take into account the natural level of metals concentration in drinking water, it is enough only to remember that in everyday life we use metallic utensils contained such metals as aluminium, copper and zinc, except iron.

Aim. The aim of the work is determination of content of aluminium, copper (II), zinc and iron (II) in the samples of drinking water processed by boiling in the zinc-coated, aluminium, copper and cast-iron utensils.

Materials and methods. Quantitative determination of iron (II) was carried out by the method of chromatometric titration in the medium of sulphuric acid (direct way of titration, diphenylamine was used as an indicator).

Quantitative determination of copper (II) was carried out by the method of iodometric titration (displacement way of titration, starch was used as an indicator).

Quantitative determination of zinc was carried out by the method of compexonometric titration in the medium of ammonia buffer solution (direct way of titration, eriochrom black T was used as an indicator).

Quantitative determination of aluminium and total amount of metals was carried out by the method compexonometric titration in the medium of ammonia buffer solution (back way of titration, the standard solution of zinc sulphate was used as the second titrant, eriochrom black T was used as an indicator).

Results and discussion. It has been suggested to carry out determination of aluminium, copper (II), iron (II) and zinc in drinking water by simple titrimetric methods that do not require the special equipment and can be executed in any chemical laboratory.

Content of metals has been determined in model mixtures using the developed procedures and it has been demonstrated that metals do not interfere with quantitative determination of each other.

Determination of aluminium, copper (II), iron (II) and zinc content in the samples of drinking water processed by boiling in the zinc-coated, aluminium, copper and cast-iron utensils has become the last stage of our researches. The results are the evidence that content of the metals to be investigated exceeds the normative values.

Conclusions. Preparation of meal should be carried out in utensils with the special food coating.

VALIDATION OF A SIMPLE TITRIMETRIC PROCEDURE FOR THE DETERMINATION OF AMOXICILLIN AND AMPICILLIN IN PURE SUBSTANCE AND MEDICINAL PREPARATION

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Introduction. Penicillins are β -lactam antibiotics. Basically, penicillin is a toxin synthesized by some species of mold Penicillium genus and is harmless to humans. They are used in the treatment of bacterial infections, mainly against Gram positive bacteria. The amount of a main substances of a penicilin is recomended to be determined by the method of HPLC (SPhU) or classical iodometric titration.

Aim. The aim of a new research is to develop and validate a sensitive, accurate, reliable and specific titrimetric procedure of Amoxicillin and Ampicillin pure substance and medical preparation quantitative determination by means of potassium hydrogenperoxymonosulfate as analytical reagent with good recovery.

Materials and methods. Amoxicillin as medical preparation (500 mg, capsules, TEVA, France) and Ampicillin as pure substance meeting the requirements of SPhU with the concentration of the main substance 100% were used.

As analytical reagent the triple potassium salt of Caro's acid, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Acros Organics) was used. Its active substance is potassium hydrogen salt of peroxomonosulfuric acid, $KHSO_5$.

Results and discussion. The proposed method is based on the S-oxidation reaction of amoxicillin and ampicillin by potassium hydrogenperoxymonosulfate in acidic medium. The excess of oxidation reagent is determined by the method of iodometric titration:

$$KHSO_5 + H_2SO_4 + 2KI = KHSO_4 + K_2SO_4 + I_2 + H_2O$$

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6.$$

The oxidation-reduction interaction was determined to be quantitative and stoichiometric: 1 mol of $KHSO_5$ per 1 mol of a corresponding penicilin.

While ampicillin pure substance quantitative determination in the form of its S-oxide using potassium hydrogenperoxomonosulfate as analytical reagent RSD = 1.81%, δ = 1.42 %, for amoxicillin medical preparation RSD = 2.34%, δ = -0.58%.

Conclusions. The proposed reaction of penicillin S-oxidation using potassium hydrogenperoxomonosulfate can be applied into analytical analysis. The obtained results have good agreement with those in SPhU. The obtained data shows that the proposed method can be applied for the determination of amoxicillin, and ampicillin in pure substance medical preparation and can be used as alternative to current pharmacopoeia methods with confidence.

METHODS ANALYSIS OF PRESERVATIVES

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Introduction. Pharmaceutical preparations which need an aqueous vehicle such as eye drops are particularly susceptible to microbial growth because of the nature of their ingredients. That's why require safeguards from microbial contamination, which may affect product stability or infect the consumers. This is accomplished by the addition of anti-microbial agents in the formulation to destroy and inhibits the growth of those organisms that may contaminate the product during manufacture or use. There are several antimicrobial preservatives used in ocular preparations that may be classified as follows: quaternary ammoniums (Benzalkonium chloride); mercurials (Thimerosal); alcohols (Chlorobutanol, Benzyl alcohol); carboxylic acid (Sorbic acid); phenols (Methylparaben, Propylparaben); amidines (Chlorhexadine).

Aim. Methylparaben (Nipagine) and Propylparaben (Nipasol) are commonly used as preservatives in eye drops. These p-hydroxybenzoic acid esters are most commonly used to control bacterial growth due to their broad antimicrobial spectrum with good stability. Their typical allowed concentrations range from 0.1 to 0.2%.

Materials and methods. Nipagine enters in eye drops, such as "Taufone-Darnitsa" ("Pharmaceutical firm "Darnitsa" CJSC, Ukraine), "Pilocarpine hydrochloride" ("GNTSLS" PP, Ukraine), "Ocoferon" ("BioFarma" PP, Ukraine), "Fenistil, eye drops" ("Novartis Consumer Health" S.A., Switzerland), "Sanorine" ("IVAX", Czech Republic). Combination Nipagine with Nipasol includes in ocular drops "Oftanal" (PP "GNTSLS", Ukraine) and "Quinax" ("Alcon-Couvreur", USA).

Results and discussion. There are official monographs of Propylparaben and Methylparaben in leading world pharmacopoeias. *Monographs content "Identification" by Infrared spectroscopy and melting range of temperature, "Assay" and "Related impurities" by* liquid chromatography. Assay Propylparaben and Methylparaben in second edition of the Ukrainian Pharmacopoeia by titrimetric method analysis. But weight of sample is about 1.0 g, that is too much, that why we propose verificate liquid chromatography method, that will be apply to control substances and develop for assay parabens in eye drops a spectrophotometric method analysis, which is less weight as a substance, as well as time and available for pharmaceutical companies.

Conclusions. The purpose of this study is to incoming goods inspection and quality control of substance for quality assurance purposes finished drugs as well as for patient safety.

DEVELOPMENT OF METHODS FOR IDENTIFICATION AND ASSAY FOR STREPTOCIDE IN EXTEMPORAL OINTMENT

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Introduction. Quality control of medicinal products for today is a basic requirement to ensure the effective and safe treatment. Due to the revival and expansion of extemporaneous compounding in Ukraine, there is a need to develop methods of quality control of dosage forms, produced in a pharmacy.

Today, soft dosage forms occupy a significant part in the range in the compounding of drug preparations, which in some cases reaches 30%. The formulation of ointments is varied, and often includes several components, so the development of control methods of active pharmaceutical ingredients in extemporaneous dosage forms for today is very urgent.

The **aim** of our work is to develop methods to identify and quantitative determination of streptocide in extemporaneous ointment of the following composition:

Rp.: Streptocidi 1.0
Novocaini 0.5
Sulphur 0.5
Ung. Tetracyclini 3% - 15.0

Materials and methods. Analytical studies were performed with a spectrophotometer Evolution 60S. For operation using measuring glassware of class A and excipients meet the requirements of the State Pharmacopoeia of Ukraine.

Results and discussion. To identify the streptocide composed in the extemporaneous ointment is proposed using the reaction of diazotization. Because the novocaine will engage in the same reaction, we propose to carry out the separation of these components in the process of sample preparation. A weighed sample of the ointment was dissolved in hexane and then extracted the water soluble components. The aqueous layer was separated and proceed novocaine and tetracycline. Sulfur and streptocide suspension in hexane was treated with hydrochloric acid and proceed the streptocide. To the quantitative determination of streptocide contained in this extemporaneous ointment we suggest using the reaction of azo dye formation, followed by measurement of the colored solution at photoelectrocolorimeter.

Conclusions. The developed methods for determining the streptocide will be used in the further development of technological instructions for this dosage form.

MODERN ELECTRODE SYSTEMS FOR VOLTAMMETRIC DETERMINATION

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Introduction. Voltamperometric methods is a group of electrochemical methods, that are widely used in quantitative and qualitative analysis of substances, including medicinal, in a wide range of concentrations. Some inverted variants of voltammetry allow to obtain the lower limits of concentration of the substance at 10^{-9}-10^{-11} M. The method of amperometric titration is included in the first edition of the State Pharmacopoeia of Ukraine (SPhU).

Aim. The aim of our study was to research a wide variety and the attempt to make a classification of modern of electrode systems that are used for voltamperometric determination.

Materials and methods. Before 40s of the 20th century theoretical electrochemistry was developed mainly as an electrochemistry of the mercury electrode. In 1942 a famous scientist from Kharkiv V.G. Levich, one of the student of the L.D. Landau group, mentioned, that rotating disk electrode (RDE) differs from the others, as its surface is equally accessible in a diffusion ratio. This feature makes RDE be a unique tool for electrochemical researches over solid electrodes, because it allows to research fast electrochemical reactions. The amount of electrons that are involved in a reaction can be determined using the rotating disk electrode, that is important for establishing the mechanism of the reactions that involve organic substances. If the coefficient of diffusion of a reacting substance is known, the amount of electrons can be determined by the value of the current diffusion limit.

As the current diffusion limit on the rotational disk electrode is proportional to the concentration of the substance, thus the electrode can be used for analytical purposes. Rotational disk can be made of any solid conductive material, such as precious metals or glassy carbon that are stable at anode area and give the opportunity to research the potential anodic processes.

In 1952 the first edition of the monograph "Physicochemical hydrodynamics" was published by V.G. Levich that had been reissued in 1959. In 1958 two remarkable scientists A.N. Frumkin and L.N. Nekrasov suggested a method of the ring-disk electrode. The monograph “Rotating ring-disk electrode” by M. P. Tarasevich, E. I. Hrusheva, V. Yu. Filinovsky was published in 1987.

Three types of electrodes – an indicator (working) electrode, a reference electrode and a counter electrode – classification of the electrodes by their functions are typically used in electrolyzers for measurements. The main characteristic feature for the counter electrode is a bigger surface, compared to the indicator one. Platinum, glassy carbon and graphite are the materials that are often used for a counter electrode.

One of the most important classifications of the electrodes is by the material it’s made of. Inert electrodes that are used as a reference or a counter usually are metallic, carbon-

bearing or composite. Among metallic there are specific advantages and disadvantages that some metals have, for example mercury and a group of precious metals (such as gold, platinum, silver and others) and basic metals. Among carbon-bearing graphite, glassy carbon, pyrographite, carbositall, from carbon fiber and diamond electrodes are often used.

Composite electrodes consist of a dispersed phase and liquid medium such as carbon paste electrodes and epoxy resins or polymer - solid paste electrodes.

Saturated calomel, potassium chloride and silver chloride electrodes are often used in analytical practice as reference electrodes. A lot of efforts to increase sensitivity, selectivity and reproducibility of voltammetric measurements and attempts to avoid the toxicity of metallic mercury led to the creation of so-called disposable electrodes.

In the late 20^{th} century a huge interest was attracted to the creation of screen-printed electrodes that were printed on polymer or ceramic tapes on inkjet printer, while the dye had a trace of particles of carbon-bearing materials, silver and etc.

Results and discussion. Recently the creation of a new generation of electrodes is connected with works that are based on modifications of the electrode surface. In this case, the surface is covered with a chemical substance in a one or a few layers, polymer membrane or oxides formed of the electrode material. As a result, the ability of the electrode for voltampermetric response changes with the introduction of new specific properties. Specificity or selectivity response of the electrode increases greatly. The most important results of these studies were summarized and presented in the publication "Modified electrodes for voltamperometry in chemistry, biology and medicine" by G. K. Budnikov, G. A. Evtyugin, V. N. Maystrenko.

Currently, the amperometric biosensors are widely used as enzyme biosensors in medicine, environmental and analytical control, DNA sensors, imunosensory, microbial fabric, and sensors, and so on. Inorganic ions and organic compounds, biologically active compounds that are used in HPLC, flow-injection analysis, capillary zone electrophoresis, the microfluidic systems with electrochemical detection as gas detectors and others are determined using modified electrodes.

Another perspective direction of research is a creation of the ultra-micro electrodes. These electrodes are based on nanocomposites, nanostructures and nanoparticles. The invention of micro electrodes allows to analyze very small volumes, also making analysis possible in vivo – in a single cell of biological organism.

Conclusions. Thus, we can assume that electrochemical analysis and voltammetric methods is an important tool than can solve many problems of common chemistry, pharmaceutical, biochemical, environmental, toxicological analysis. The future pharmacist, analyst and researcher should master this powerful arsenal of modern methods of electrode systems.

PROBLEMS OF ENVIRONMENTAL POLLUTION BY DRUGS

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Introduction. Messeges about the presence medicines in the surface waters began to arrive since 1990. The following research confirmed presence of drugs in the environment around the world. Water pollution by drugs has become a serious environmental problem for the world .

Last years around the world thousands of water samples have been taken in order to study the presence of residues of drugs in the environment. Currently there were confirmed the presence of more than 150 drugs and their metabolites in the water.

The main sources of pollution are waste and sewage of pharmaceutical companies, livestock farms, domestic waste. A huge amount of drugs coming into the environment through the sewage system. Drugs withdrawal from the human body get into the sewage being in biologically active form or in the form of metabolites.

Sewage treatment plants usually are not suitable for decontamination and disposing of drugs. A large number of substances are poorly biodegradared in the treatment facilities system and get into surface water in the unchanged form.

These factors lead to the fact that uncontrolled pharmaceutical environmental pollution takes place.

Trace amounts of chemicals that are part of the analgesics, tranquilizers, antibiotics, hormones (including oral contraceptives), anti-inflammatory drugs are detecting not only in natural waters but also in drinking water. Currently their concentration is low (at 1 - 100 g/L), but long-term actions on the living organisms may have unexpected harmful consequences, both individual and species levels.

Aim. To analyze published data of environmental pollution cases by drugs and their metabolic products in order to further development identification methods of medicines various groups in the objects of biosphere.

Materials and methods. We proposed advanced approaches in order to study the environmental toxicology of drugs, including:

study of international experience in assessing the toxicity, hazards and assess risks of pharmaceutical substances as pollutants in biological systems;

study of international experience in assessing biodegradation of medicinal substances;

the drugs development responsibility extention in order to assess their potential effects on the environment at all stages of the life cycle of a medicinal product: from raw materials to products utilization;

development of new modern methods for determining drugs in different natural matrices that can affect on vital functions of alive organisms.

Results and discussion. The availability and potential hazards of pharmaceutical products in the environment and potential environmental impacts of increasingly attracts the attention of scientific and international organizations. In 2012 WHO published a report "Drugs in drinking water" as an overview of many articles and studies. In a report states that there is need for research on pharmaceutical pollution monitoring and assessment of the risks associated with long-term effects of low concentrations of drugs on alive organisms.

In Ukraine, the problem has not been studied, but a significant amount of the pharmaceutical market and the uncontrolled sale and consumption of drugs allows the design problem in the Ukraine also.

We conducted the collection and structuring the availability of pharmaceutical pollutants in different matrices (water, aquatic organisms, etc.) for the prediction of the pollution in Ukraine.

Determination of the main sources and ways of appearing drugs into the environment, forecasting the main polluting substances which may be relevant for Ukraine, it is necessary to develop analytical methods for determination of these substances in the biosphere objects.

Low concentrations of pharmaceutical pollution require the most modern analytical equipment: liquid chromatography with mass spectrometry detectors.

Conclusion. The analysis of published data on cases of environmental pollution drugs and their metabolic products was conducted.

Perspective of development methods for determining drugs in the biosphere sites to assess their risk to the environment and human health was proved.

CHEMILUMINESCENCE METHOD FOR THE DETERMINATION OF IBUPROPHEN IN PHARMACEUTICAL PREPARATIONS

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Introduction. Ibuprofen (Ibu, (±)-2-(p-isobutylphenyl) propionic acid) NSAID, phenylpropionic acid derivative has anti-inflammatory, analgesic and medium antipyretic activity. It is released in the form of covered tablets, capsules, granules, syrups, suppositories. The intensive literature survey revealed the Ibu can be quantitatively determined using spectrophotometric method, HPLC, LC, GC, MS and chemiluminescence method. For example, the CL procedures for the determination in the system Ibu - H_2O_2 – Fe (II)/(III) in the presence of Eu(III) ions; by activating effect of Ibu on CL in the system $KMnO_4$ - sulfite; CL inhibition in micellar environments in the presence of Tb^{3+} ions are known.

Aim. The development of new methods for the quantitative determination of Ibu using highly sensitive chemiluminescence method is of a great importance. The new analytical system H_2L (luminol) – H_2O_2 – Hb (hemoglobin), in which Ibu acts as an inhibitor of CL is proposed to determine Ibu in tablets.

Materials and methods. The research object is «Ibuprofen» in tablets (produced by Privately held corporation «Technolog», Ukraine).

The procedure of quantitative determination of Ibu in "Ibuprofen" tablets, 200 mg is following: approximately 290 mg of grinded tablets (accurately weighed) was dissolved in a 100 mL volumetric flask in 10 mL of 1 $mol \cdot L^{-1}$ NaOH solution. The volume of the solution was brought to the mark with double-distilled water at 293 K. The Ibu SSS solution with a concentration 2 $mg \cdot mL^{-1}$ was prepared similarly using volume-weight method. The following order of reagents mixing was used in the analysis: H_2L solution, NaOH solution, water, H_2O_2 solution, SSS solution or a solution prepared from tablets. The working HB solution was added to the chemiluminometer cell with working volume equaling 10.0 mL after all the others.

Results and discussion. It was determined that in optimal conditions Ibu had inhibitory effect on the appearance of CL in H_2L – H_2O_2 – Hb system, which was further used for the development a new procedure of Ibu quantitative determination in tablets.

Conclusions. The procedure of quantitative determination of Ibu in tablets was developed by the chemiluminescence inhibition in the system H_2L - H_2O_2 – Hb. LOQ = $3 \cdot 10^{-5}$ $mol \cdot L^{-1}$, RSD = 3.3% (n = 5, P = 0.95).

OPTIMIZATION OF CHROMATOGRAPHIC METHODS OF ANALYSIS OF PHYTOPREPARATION MACLURA POMIFERA

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Introduction. Osage orange – Maclura pomifera (Raf.) Schneid. – plant of family Moraceae, genus Maclura; large deciduous tree with a dense crown. The greatest pharmacological interest are the fruit of the plant, which are a rich source of biologically active substances. The composition of the previously developed an oil extract from the fruit of the Maclura pomifera includes flavonoids, triterpenes and phytosterols. The isoflavones osayin and pomiferin are particularly interest, they have antioxidant, immunomodulatory, anti-inflammatory action, and with the amount of phytosterols - prostate protective effect.

Aim. Development of optimal conditions for the chromatographic methods of determination of isoflavones in the oil extract of Maclura pomifera with a view to the standardization and quality control.

Materials and methods. The presence of the isoflavones in the oil extract was confirmed by ascending thin-layer chromatography. In this work we used the standard authentic samples of osayin and pomiferin ("BioBioPha Co., Ltd.", China), solvents and reagents (2% solution of aluminum chloride, vanillin reagent in concentrated sulfuric acid, 1% solution of ferric chloride) are of the category “reagent grade” and “analytical grade”. For identification we used instrumentation for TLC: chromatographic plate “Sorbfil PTLC-UV” (“Sorbfil”, Russia); UV chromatoscope, microcapillaries of 10 ul (Russia).

Results and discussion. As a result of chromatographic analysis the clear bright yellow stains of osayin and pomiferin revealed at chromatographic plate with detection of 2% ethanolic solution of aluminum chloride, followed by heating the chromatographic plate up to 105 °C for 5 minutes. Optimal mobile phases are hexane:ethyl acetate (7:3) with the values of R_f for osayin - 0.5±0.04, for pomiferin - 0.2±0.02; as well as the system of solvents chloroform:ethanol (10:0.6) the values of R_f for osayin - 0.6±0.03, for pomiferin - 0.2±0.03.

Conclusions. As a result of TLC analysis, we have developed the optimal conditions for the chromatographic methods of determination of isoflavones in the oil extract of Maclura pomifera.

QUALITATIVE DETECTION OF BROMIDE POTASSIUM BAKERY PRODUCTS

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Introduction. Bread is one of the most important and most used products in the daily human diet. Due to the fact that in the world as never before, the question of food security of the population becomes very important and the need to monitor producers of food product which obtain excess profits added to their products substances that reduce the price and increase its output. Often this process is accompanied by a significant reduction in product quality and that is the most dangerous, the risk to the health and lives of consumers.

One of these substances is potassium chromate (E 924th). Potassium bromate is added to baking products for looseness products and bleaching flour. This dietary additive is dangerous for health and life of consumers. It can cause cancer, and etc.

Aim. The aim of this investigation is to get data about presence of potassium bromate in bakery products and improving existing methods of determination of this additive in food products, in particular the development of limit-test to help determine exceeding the allowable content - 75 ppm of potassium bromate, which has the properties of a mutagen in baking products according to the World Food and agriculture organization (FAO).

Materials and methods. We investigated samples of the most popular types of bread - namely, white troughs, bread threaded, bread from a private bakery. Quality of potassium bromate in the baking goods determined by the method of iodometry. A minimal allowable concentration - 75 ppm, which may be present in these products according to the World Food and Agriculture Organization (FAO) World Health Organization Expert Committee on Food Additives (JECFA) determined by spectrophotometric method.

Results and discussion. The optical density of the solutions of the samples was - 0.425 at a wavelength of 556 nm in bakery products that were studied, and did not exceed the permissible concentration of potassium bromate according to the World Food and Agriculture Organization (FAO)).

Conclusions. Qualitative research of the potassium bromate presence in samples showed that content of this dangerous carcinogen additive does not exceed the allowed level according to the World Food and Agriculture Organization (FAO).

DETERMINATION OF TRAMADOL IN SOLUTION DROP BY TRAMADOL SELECTIVE ELECTRODE (TCE).

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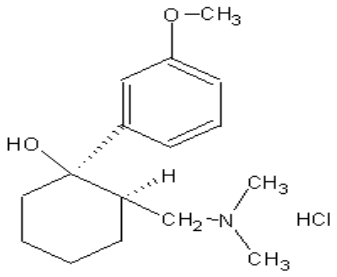
Introduction. Tramadol (tramadol hydrochloride, Melanate, Limadol, Tradonal Retard, Tramal, Tramundin Retard, Ultram, Zydol, Biovail, Crispin) - RR, SS-trans-2 [(dimethylamino) methyl] -1- (m-methoxyphenyl) cyclohexanol hydrochloride.



In the literature, there are allegations of non-medical use of tramadol hydrochloride persons with heroin addiction at doses significantly higher than therapeutic. This marked the various side effects, including the development of dependence. Moreover, in these cases, and often fatal acute poisoning, which significantly increases the risk while taking certain substances.

Aim. When the chemical-toxicological studies often have to deal with small volumes of samples analyzed, which contain small amounts of certain substances. In the pharmaceutical feasibility study is the use of small amounts of dosage forms, which are investigated.

To determine the concentration of the solution drops Tramal used in the installation shown in Fig. 1.

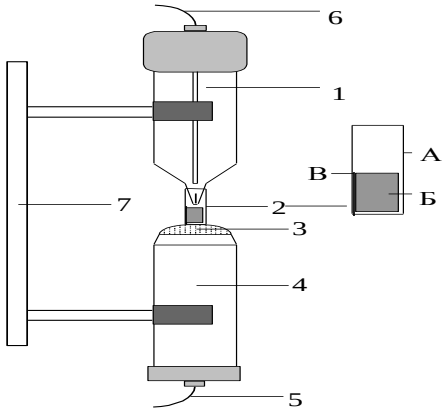


Figure 1. *Apparatus for the potentiometric determination of tramadol in solution drop:*

1 - silver chloride electrode (reference electrode); 2 - capillary nozzle (A - B PVC tube - glass tube in - capillary for potassium chloride solution); 3 - a drop of the

solution was analyzed; 4 - solid contact electrode ISE tramadol; 5, 6 - electrodes outputs; 7 – tripod

Materials and methods. EMF measurement in solutions tramal performed on digital ionomer I-130. The temperature of all solutions studied was the same. Standard solutions were prepared with different concentrations of tramadol (from 5.0 $\cdot 10^{-4}$ to 5.0 $\cdot$ 10^{-3} M), and the two standard solutions with concentrations of tramadol $C_1 = 5.0 \cdot 10^{-4}$ M and $C_2 = 5.0 \cdot 10^{-3}$ M.

As the reference electrode using a saturated silver chloride electrode EVL-1-M3. Expiration of the salt bridge solution rate in comparison modern electrodes is about 1.5 cm^3 per day ($1 \cdot 10^{-3}$ cm^3 / min). If we assume the volume of the solution was analyzed drops close to 0.05 cm^3, and in contact with the salt bridge 5 min, then during this period the solution was diluted to approximately 10%. This leads to a sharp decrease in the accuracy of ionometric analysis.

In order to reduce the expiration of a reference electrode liquid junction solution flow rate, we used a capillary nozzle 1-1.5 cm in length and 0.5 mm diameter capillary (Fig. 1). The nozzle is fixed to the capillary tube of the reference electrode. The electrode resistance of the reference electrode with the nozzle is in the range 17-20 ohms. A nozzle electrode stably by using ionomers I-115, I-130, and does not require additional shielding measurement circuits. We collect the installation, as shown in Fig. 1. membrane ISE Tramal and nozzle end of the reference electrode was applied to 1 drop Tramal solution, investigate immediately and carefully dried with filter paper. They were then applied to the membrane of ISE drop of solution investigated and summed side end nozzle drop the reference electrode. We take measurements of emf element every minute for 10 minutes.

Results and discussion. The most stable value system potentials observed for 3-7 minutes measurements. For low concentrations ($1 \cdot 10^{-6}$ - $1 \cdot 10^{-5}$ M) the stability of the potential is reduced, presumably due to the surface-active phenomena. Linearity interval electrode function for the fifth minute of measurements made (1,0±0,2) $\cdot$ 10^{-1} - (1±0,4) $\cdot$ 10^{-5} M with a slope of 56±1 mV. The minimum concentration that can be determined under these conditions is $3.2 \cdot 10^{-5}$ M. Thus, in one liter of solution will contain $9.6 \cdot 10^{-3}$g tramal, and into droplets (0.05 ml) solution of limit of detection will be about 0.48 g.

Conclusions. Tramal selective ISE ionometrical and developed methods for the determination of the drug suitable for the purposes of the pharmaceutical and chemical-toxicological analysis.

DISTRIBUTION RATIO AT A NUMBER OF FUNCTIONAL DERIVATIVES N-R-AMINE, AND THEIR QUANTITATIVE CORELATION

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Introduction. The ability to predict biological properties of compounds through their lipophilicity allows to optimize the search for new drugs and is often included in equations for calculations of the quantitative structure – activity relationships (QSAR). However, experimental methods to determine logP are time-consuming and expensive, and the values obtained often differ due to the influence of many factors.

Aim. The aim of this work is to determine the mutual correlation of the values of the partition coefficients in the series of some functional derivatives of N-R-amines calculated by different algorithms.

Materials and methods. Taking into account the data we used the available free on-line methods xlogP3, AlogPs for calculations of the partition coefficients, and the ChemBioOffice2014 software package, in particular ChemBioDrawUltra 14.0 (CBDU14) and ChemBio3DUltra 14.0 (CB3DU14), for calculations of logP and ClogP. Calculations of correlations of the values of the partition coefficients calculated for compounds were performed using the STATISTIKA 8 software. According to the requirements of mathematical statistics the correlation coefficient indicates the close relationship between the values: at values less than 0.3– relationship is absent, in the range of 0.3–0.7 it is medium, more than 0.7– it is strong.

Results and discussion. Almost all compounds are characterized by negative values of the partition coefficients; probably it is due to the presence of the polar moiety – substituted Nitrogen atom in their structure. Increase of numeric values, and hence lipophilicity, is observed in the case of increase in the number of non-polar substituents (alkyl substituents or the phenyl nucleus in compounds). Glycine, for which the calculated values (excluding logP) agree with the experimental ones, and its alkyl substituents are characterized by the maximum values of hydrophilicity. It can be also explained by the considerations previously mentioned.

Conclusions. Therefore, the results of our study allow to propose the values AlogPs obtained for further application when determining QSAR, as well as the degree of its manifestation among N-R-amine derivatives for planning a targeted search biologically active substances in this series.

TETRACYCLINE ANTIBIOTICS AND METAL SALTS INTERACTION COMPARATIVE STUDY

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Introduction. Nowadays in the modern world we can trace constant increase of comorbidity – the presence of several chronic diseases. Therefore a requirement for combination therapy is growing. At the same time number of cases of irrational multiple drug assign is growing. Consequently, drug-drug and food-drug interaction study today is an important task of pharmacy.

Antibiotic tetracycline hydrochloride is often adduced in literary sources as a classic example of interaction with metal cations. At the same time, it is described in literature, that doxycycline hydrochloride doesn't undergo this type of reactions.

Results and discussion. Considering mentioned above, the purpose of our research was comparative study of a probable interaction of tetracycline hydrochloride (TC) and doxycycline hydrochloride (DC) with salts $CaCl_2$, $MgSO_4$ и $AlCl_3$, which are constituents of antacids, food and mineral water.

Possible interaction study was carried out by absorption spectrophotometry in the UV-region of the spectrum, by measuring the optical density of the obtained solutions of TC and DC complexes with the appropriate metal salts. The purified water and 0.1M HCl were used as solvents. To reproduce the drug interaction model mixtures were prepared. Metal salts were added in stoichiometric ratios – 2:1 for $CaCl_2$ and $MgSO_4$, and 3:1 for $AlCl_3$. All solutions were prepared in a 0.002% concentration.

Analysis of the results was carried out by comparison absorption spectra of solutions TC and DC with metal salts.

In a set of experiments the following results were obtained. In a purified water medium the character of spectra for complexes DC and TC with $AlCl_3$ was changed, as well as the change in absorbance intensity. For the complexes TC and DC with $CaCl_2$ and $MgSO_4$ the character of the spectra was not change, but the change of absorbance intensity was observed.

In a 0.1 M HCl medium for complexes TC and DC in all studies the character of spectra was not changed, but the change of absorbance intensity was observed as well.

Based on the data, obtained in a set of experiments, it can be assumed, that antibiotic DC, contrary to the existing literature data, can forms chelate complexes with such cations as Ca^{2+}, Mg^{2+} and Al^{3+}. However, the mechanism of this interaction is still not find out and requires further studies.

Conclusion. As a result of the conducted study we clear up, that TC and DC interaction with metal salts can be clinically significant and requires further study of a bioavailability.

QUALITATIVE DETERMINATION OF LACTOSE IN LACTOSE FREE MILK

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Introduction. Milk – one of the most perfect foods, created by nature. It contains the most complete and balanced set of essential nutrients. Lactose, or milk sugar, is the main carbohydrate of milk. The collapse of the lactose is under the action of the enzyme lactase, which is the highest activity observed in humans at birth. It remains quite high throughout life, if milk is included in the diet constantly. At the same time, some people milk sugar can't be acquired. After consumption of milk products there irregularities in the digestive system (diarrhea, pain, bloating, nausea, vomiting). This phenomenon is due to insufficient production or lack of lactase. Especially for people who suffer from lactose intolerance, there is milk without lactose. That is why it is appropriate to develop a method of determination of lactose in lactose free milk and to check lactose content in samples of lactose free milk of domestic producers.

Aim. Our aim is to develop methods of qualitative detection of residual lactose which left after fermentation in lactose free milk.

Materials and methods. The object of our study "Milk drinking ultrapasteurized lactose free, 2.6% of fat" brand "На здоровье", produced by "Lustdorf" Ukraine was selected. lactose free milk was produced according to Specification 10.5-33548609-015: 2012.Ingredients, given on the label: cow's milk, the enzyme lactase. The label also states that the lactose content in this product is less than 0.01%.To verify the presence of lactose in the sample, it was decided to hold a series of reactions of identification of lactose and TLC.Chromatographic studies were performed on plates with a layer of silica gel G P, mobile phase composition: water-methanol-glacial acetic acid-ethylenchloride (10 : 15 : 25 : 50), as developer solution thymol in a mixture of sulfuric acid and 96% alcohol was used.

Results and discussion. The TLC method was developed and tested directly in the sample - lactose free milk without prior sample preparation, as well as the test sample after preliminary training, which included stage processing of milk lactose 70% solution of trichloroacetic acid to precipitate proteins.

Conclusions. During this investigation methods of the determination of lactose in lactose free milk by TLC was developed. Investigated sample doesn't contain lactose.

INFRARED SPECTROSCOPY FOR IDENTIFICATION OF VERAPAMIL HYDROCHLORIDE IN TABLETS

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Introduction. IR-spectroscopy is the section of spectroscopy that studies the interaction of IR radiation with substances. The method is widely used in scientific research and in manufacturing for the quality control of pharmaceutical products since it allows to determine the structure of the substance, identify and quantify organic compounds. Nowadays one of the great advantages of infrared spectroscopy is that virtually any sample in virtually any state can be studied. In pharmaceutical analysis IR spectroscopy is used for qualitative analysis of the known substances, identification by the reference spectrum or determination of the structure of the unknown substances.

Aim. Only USP propose use IR-spectroscopy method for identification of active pharmaceutical ingredients in tablets.

Materials and methods. The infrared spectroscopy method has been studied on verapamil tablets ("Verapamil", tablets, 0.04 g, "Pharmaceutical firm "Darnitsa" CJSC) with the aim of following using it in correspondent monograph of state Pharmacopoeia of Ukraine. The sample was previously ground and mixed thoroughly with potassium bromide to obtain an infrared transparent matrix in the ratio of 1:5 (Sample: KBr). The KBr discs were prepared by compressing the powder for 5 min in a hydraulic press. Scanning was carried out at the resolution of 4 cm^{-1} in the range from 4000 to 400 cm^{-1}.

Results and discussion. From the peaks obtained the following functional groups were found. In the range from 3030 and 2860 cm^{-1} a broad complex absorption was observed due to superimposing of C-H stretching vibrations of the methyl and methylene groups. At 2840 cm^{-1} there was a band due to C-H stretching vibration of the methoxy groups. In the range of 2800 – 2300 cm^{-1} a broad complex absorption was observed due to N-H stretching vibrations of the protonated amine. At 2236 cm^{-1} there was a sharp weak band due to C=N stretching vibration of the saturated alkyl nitrile. In the range of 1607, 1591 and 1518 cm^{-1} due to skeletal stretching vibrations of the benzene ring the bands were found. At 1262 cm^{-1} there was a strong band due to C-O stretching vibrations of the aromatic ethers.

The disadvantage of the method is that in addition to the characteristic bands of verapamil there are bands that are typical for organic excipients of the tablets.

Conclusions. The work on developing the method has been conducted. It will allow identifying only the active substance – verapamil hydrochloride in tablets by the method of IR-spectroscopy.

COMPARATIVE ESTIMATION OF TERBINAFINE HYDROCHLORIDE QUANTIFICATION BY TITRIMETRIC METHODS

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Introduction. One of the important tasks of the pharmacist is to determine the quantitative characteristics of drugs. Improvement of existing methods of analysis and development of new ones, which are faster, more accurate and sensitive methods for the quantitative control of drugs is an urgent problem.

Terbinafine hydrochloride is one of modern drugs of antifungal activity, which nowadays is widely used for treatment of various diseases of mycotic origin either as a separate substance or as a compositional part of multicomponent medicines.

So, constant improvement in the branch of analysis methods and researches about methods of identification and assay of terbinafine is a task of big importance and interest.

Terbinafine hydrochloride is a salt, which is formed by a weak organic base and a strong mineral acid. These salts are frequently encountered among drugs and medicinal substances.

Materials and methods. For quantification of terbinafine hydrochloride were chosen two titrimetric methods such as alkalimetry and argentometry, which are still successfully used in assay of wide range of substances.

For alkalimetric assay were used medium of 96% alcohol and phenolphthalein as an indicator. For argentometric assay was taken back method using silver nitrate as a first titrant, ammonium thiocyanate as a second one and ferric ammonium sulphate as an indicator; modification was in the presence of dibuthyl phthalate.

Both techniques have predicted a blank titration.

Results and discussion. As it has been stated, alaklimetric quantification for terbinafine hydrochloride has a relative mistake about ±0.31%; and argentometric assay in the conditions mentioned above has a relative mistake about ±0.89%.

On the basis of the obtained data we have compared results of argentometric and alkalimetric methods of quantification for terbinafine hydrochloride by their reproducibility.

Conclusions. As it follows from the conducted researches and from the data of the statistics, method of alkalimetric determination for terbinafine hydrochloride in ethanol medium and method of argentometric determination for terbinafine hydrochloride in the presence of dibuthyl phthalate can be used during pharmaceutical analysis.

IN VITRO EFFECTS OF PROPRANOLOL AND NONYLPHENOL ON MOTILITY PARAMETERS AND OXIDATIVE STRESS INDICES IN STURGEON (*ACIPENSER RUTHENUS*) SPERM

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Introduction. Pharmaceuticals in the environment has become a growing concern, especially since advancement of analytical techniques has shown that there are in fact many pharmaceuticals in our rivers and surface waters, including human beta adrenoreceptor blockers, such as propranolol, and endocrine disrupting chemicals, for example nonylphenol. Sturgeon have been classified as endangered by many international organizations. In large species such as sturgeon, it is logistically difficult and costly to conduct toxicity evaluations on broodstock-size animals, and the need for sensitive, rapid toxicity testing has led to the increasing use of sturgeon sperm as a model for toxicological studies. Therefore in the present study, we used the sturgeon (*Acipenser ruthenus*) sperm to investigate *in vitro* the potential deleterious effects of endocrine disruptor nonylphenol (NP) and β-blocker propranolol (PN) on spermatozoa motility and oxidative stress indices.

Materials and Methods. Sterlet sperm was obtained from six males (6–7 years old; body weight: 0.5-2 kg; body length: 55±9.3 cm) reared in the aquaculture facility of the Research Institute of Fish Culture and Hydrobiology at the University of South Bohemia, Vodnany, Czech Republic. The sperm samples were then exposed for 1 h to final concentrations of 1, 5, 10, 25 μM of NP and 10, 25, 50, 100 of PN at 4 °C. Spermatozoa velocity (μm/s, measuring only motile spermatozoa) and percent motile spermatozoa (%) were determined after triggering motility under dark-field microscopy (Olympus BX 50, Japan) (20x objective magnification) and analyzed with Olympus MicroImage software (Version 4.0.1. for Windows with a special macro by Olympus C & S). To evaluate oxidative stress indices TBARS method was used for measuring lipid oxidation (LO), and carbonyl protein (CP) assay was applied for assessing protein oxidation. Total superoxide dismutase (SOD, EC 1.15.1.1) activity was determined based on autoxidation of pyrogallol. Statistical comparison was made by analysis of variance (ANOVA) at a significance level of 0.05 using STATISTICA 9.0 software for Windows.

Results. Obtained results of spermatozoa motility and velocity measurements showed that both compounds significantly affected sperm physiology. The percentage of motile cells decreased up to 60±4.2% in spermatozoa exposed to 100 μM PN, compared to 84±5.7% in control. In NP treated samples 69±5.5% of spermatozoa were motile after 1 h of incubation. Spermatozoa velocity decreased

after incubation with chemicals in similar dose-dependent manner. Significant lipid and protein oxidation was observed at 50 μM PN and 5 μM NP. Activity of SOD increased up to 14,09±3,57 mU/mg protein at 100 μM PN and up to 14.04±1.74 mU/mg protein at 10 μM NP, compared to 8.86±1.74 mU/mg protein in control.

Discussion. Environmental contaminants have been shown to induce reproductive dysfunction in both wildlife and humans. Nevertheless, there is still a lack of fast and reliable tests for toxicity assessment. Since variations in spermatozoa motility might reflect quantitative and qualitative toxic effects of ectogenous contaminants, monitoring of spermatozoa motility parameters is an important approach in toxicity experiments. Furthermore, increased levels of LO and CP observed in the present study also suggest spermatozoa susceptibility to chemically induced free radical production. To counteract the damaging effects of free radicals, a variety of antioxidant enzymes are present in fish spermatozoa. However, an adaptive response of SOD to toxicant stress was shown to be insufficient to prevent damage. Taking together, our results as well as previous reports on the topic suggest that sperm *in vitro* assays may provide a fast, inexpensive and efficient tool for evaluating the effect of different classes of compounds in aquatic environment.

THE SESSION'S MATERIALS OF THE SCIENTIFIC COUNCIL ON ANALYTICAL CHEMISTRY NATIONAL ACADEMY SCIENCES OF UKRAINE

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Introduction. Scientific Council on the problem of "Analytical Chemistry" the Academy of Sciences of the Ukrainian SSR was established at the Department of Chemistry and Chemical Technology in June 1970. The Council consisted of 28 members including AS URSR academician A. T Pylypenko (the head of the council), AS URSR academician M. S. Polouektov, prof. I. V. Pyatnitsky. The Members of the AS URSR Council were included in Scientific Council of AS SRSR and its different sections (AS URSR acad. M. S Polouektov and K. B. Yatsimirsky, AS URSR corresponding member V. A. Nazarenko, prof. I. V. Pyatnitsky). In 1997 the Scientific Council of NAS of Ukraine resumed its activities.

Aim. The aim of our work was to study the materials of the sessions of the Scientific Council on Analytical Chemistry of NAS of Ukraine in recent years.

Materials and methods. The corresponding member of NAS of Ukraine, Doctor of Chem., professor of the department of analytical chemistry of Kyiv National University V. N. Zaitsev is the head of the council now. The Council also has the Executive Secretary, the Bureau and has regional offices - Western, the Kiev, Southern, Eastern, Central and four sections of the Council: "General Questions", "Methods of Analytical Chemistry", "Objects of Analysis", "Chemical Metrology, Standardization".

Results and discussion. Since 2002, the annual sessions of Scientific Council on Analytical Chemistry take place and annual reports of the Council are published. Four times a year the journal «Methods and objects of chemical analysis» is published. The great contribution to the work of the scientists of the Kharkiv Scientific Council on Analytical Chemistry should be noted. Corr. Member of NAS of Ukraine, Doctor of Chem., professor V. P. Georgiyevskiy, that has been a member of the Bureau for many years, and professor O. I. Gryzodub, the head of the Eastern Council's sections, Doctor of Chem. In 2006 , Doctor of Chem., professor V. V. Bolotov, Doctor of Chem., associate professor (now professor) M. Ye. Blazheyevskiy were included as members to the Council along with the others Kharkov scientists.

Conclusions. The study of materials of the Scientific Sessions of the National of Sciences Council of NAS of Ukraine on Analytical chemistry - is an important task for every future scientist-analyst, that allows to evaluate development of modern trends and directions of discipline. Analytical chemistry is one of the fundamental disciplines in the training of specialists of various fields including pharmacy.

THE CHOICE OF OPTIMAL CONDITIONS FOR CHEMICAL-TOXICOLOGICAL ANALYSIS OF CETIRIZINE BY THIN-LAYER CHROMATHOGRAPHY

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Introduction. Cetirizine hydrochloride is long acting antihistamine. The drug is used to treat allergic reactions. The product is ranked third in sales among the population of Ukraine. Cetirizine hydrochloride in overdose and self-treatment affects the central nervous system and causes severe intoxication, because the choice of highly sensitive and selective methods of study of cetirizine in biological objects is an important issue. In carrying out the modern chemical-toxicological analysis of drugs are widely used thin-layer chromatography-method (TLC), which leads to its use for screening of toxic substances, cleaning substances from biogenic impurities, identification and quantitative determination.

Aim. The choice of optimal conditions of analysis of cetirizine hydrochloride by TLC-method, suitable for chemical and toxicological studies.

Materials and method. TLC analysis of cetirizine was carried out by ascending, dimensional thin layer chromatography. For selecting optimal chromatographic conditions of cetirizine as thin layers of adsorbents used chromatographic plates, which are widely used in studies of biological objects: Sorbfil PSTH-AF-A (silica STH-1A, 5-17 microns, thickness - 110 mm, a binding agent – silicasol, type bases - aluminum foil, plates size - 10x10 cm); Sorbfil PSTH-P-B-UV (silica STH-1B, 8-12 microns, 100 mm, silicasol, PETF-E (Polyethylene and Teflon), 10x10 cm); Glass plates by "Merck" (Germany) (silica gel 60 F254, 10-12 microns, glass, 10x20 cm).

Chromatographic behavior of cetirizine was investigated by TLC in 9 solvent systems, which are recognized standard by the International Committee for systematic toxicological analysis of the International Association of Forensic Toxicologists - chloroform-acetone (80:20), ethylacetate, chloroform-methanol (90:10), ethylacetate-methanol-25% ammonia solution (85:10:5), methanol, acetone, methanol-25% ammonia solution (100:1.5), methanol- n-butanol (60:40), cyclohexane-toluene-diethylamine (75:15:10).

For selecting optimal chromatographic conditions of cetirizine were studied 4 solvent systems, which are used in general organic TLC screening substances - chloroform-acetone-dioxane-25% ammonia solution (47.5:45:5:2.5), toluene-acetone-ethanol-25% ammonia solution (45:45:7.5:2.5), ethylacetate-methanol - 25% ammonia solution (85:10:2.5), chloroform-n-butanol-25% ammonia solution

(70:40:5). TLC analysis was performed according to the procedure: at the start line of the chromatographic plate by a distance of 1-2 cm from the edge at a point applied with the calibration capillary 20.0-50.0 μg of study medication using its 0.01% alcoholic solution of cetirizine. The spot diameter should be less than 0.5 cm. Chromatography was performed in a chamber volume of 500 cm^3, into which 50.0 ml of an appropriate solvent system were added with subsequent saturation of the chamber solvent vapors at least 30 minutes; path length of the front of the mobile phase - 7 cm. Chromatography was terminated when the solvent reached the finish line. Chromatographic plate was dried at room temperature, after which identification was carried out by using UV light and Dragendorff's reagent for Mounier.

Cetirizine spots were identified by comparing the chromatogram obtained for the sample solution with a corresponding spot on the chromatogram obtained for a reference sample (reference solution). The comparison was made by staining, size and value retention - *Rf* for both spots.

Results and discussion. As a result of TLC studies were established the most optimal conditions for the identification and purification of cetirizine in the presence of biogenic impurities: solvent systems - methanol or methanol-25% ammonia solution (100:1.5); chromatographic plates – glass plates by "Merck" ($R_{f\ \text{cetirizine}}$ = 0.57-0.59).

The results of TLC analysis may be recommended for directional investigations of biological material on cetirizine for preliminary studies - chromatographic plates - Sorbfil PSTH-AF-A, Sorbfil PSTH-P-B-UV and system of organic solvents – acetone ($R_{f\ \text{cetirizine}}$ = 0.50-0.51), for confirming studies – system of organic solvents – methanol-25% ammonia solution (100:1,5) and chromatographic plates - Sorbfil PSTH-AF-A ($R_{f\ \text{cetirizine}}$ = 0.80-0.82), Sorbfil PSTH-P-B-UV($R_{f\ \text{cetirizine}}$ = 0.71-0.73).

In screening studies combined poisonings is recommended to use the system - acetone and chromatographic plates - Sorbfil PSTH-P-B-UV, glass plates by "Merck" ($R_{f\ \text{cetirizine}}$ = 0.31-0.34) to confirm the presence of cetirizine in a biological object.

Conclusions. The choice of optimal conditions of analysis of cetirizine hydrochloride by Thin-Layer Chromathography – method (systems of organic solvents, stationary phase, location reagents), suitable for chemical-toxicological investigations has been conducted.

For directional chemical-toxicological analysis of cetirizine are recommended: stationary phase - chromatographic glass plates by "Merck", the systems of organic solvents - methanol or methanol-25% ammonia solution (100:1.5) ($R_{f\ \text{cetirizine}}$ = 0.57-0.59). The location reagents of cetirizine - UV light and Dragendorff's reagent for Mounier.

DEVELOPMENT OF DETERMINATION METHOD FOR CONCENTRATION OF α-LIPOIC ACID SOLUTIONS IN RESEARCH OF BIOVAILABILITY PROCESS FOR SOLIDS DISPERSION

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Introduction. α-lipoic acid is a coenzyme that participates in the oxidative decarboxylation of pyruvic (consisting of pyruvate dehydrogenase complex) and α-keto acid (composed of α-ketoglutarate dehydrogenase). It is involved in the regulation of lipid and carbohydrate metabolism, affects on cholesterol metabolism, improves liver function and has a detoxifying effect in cases of poisoning by heavy metals salts. It is used as prophylactic and therapeutic purposes in the treatment of atherosclerosis of the coronary vessels, liver diseases, diabetic and alcoholic polyneuropathies.

Aim. Specialists of the department of Industrial Technology of Drugs work on creation of the medicinal product with α-lipoic acid on the basis of solid dispersions. In order to establish the possibility of developing assaying methods of α-lipoic acid in solution in the bioavailability studies of solid dispersions of α-lipoic acid, we studied its absorption spectra in different solvents.

Results and discussion. Absorption spectrum of alcoholic solution of α-lipoic acid is characterized by two absorption bands. The wide high-intensity band at 200-240 nm is common to many organic substances, containing functional groups with lone pairs of electrons. In this case the absorption due to electronic transitions in the carboxyl group. α-lipoic acid solutions have a pale yellow-green color. The absorption spectrum is illustrated by the presence of wide, but not intensive absorption band maximum in the range 332-335 nm (λ_{max} 334 nm), due to the presence in its structure a disulfide bond in the 1,2-dithiolan cycle.

The absorption spectrum of α-lipoic acid in 0.1 M aqueous solution of hydrochloric acid, which simulates the acid medium in the stomach, by its nature is very similar to the spectrum of an alcohol solution and differs from it only by the slight hypochromic effect.

One of the main requirements that are responsible the use of spectral methods for the quantitative determination of substances, is its submission of the light absorption of the solution to the Bouguer-Lambert-Beer law. Such verification is reduced to the plotting the absorbance of the solution concentration. Absorbance of α-lipoic acid in 0.1 M hydrochloric acid solution at a maximum at 334 nm obey the law of Lambert-Bouguer-Beer law over the entire concentration range from 1.25 to 12.50 $\cdot 10^{-2}$%. Specific absorption rate in this case consist 6.148±0.106.

Conclusions. The method for determining the concentration of α-lipoic acid solutions will be used in selecting the optimal compositions of solid dispersions with its contents.

DEVELOPMENT OF METHOD FOR QUANTITATIVE DETERMINATION OF FLAVONOIDS IN THE RESEARCH OF BIOAVAILABILITY PROCESS OF WITH POWDER ROOT OF SCUTELLARIA BAICALENSIS

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Introduction. Scutellaria Baicalensis – a perennial herb of the family Lamiaceae, whose roots and rhizomes contain 4-4.5% of flavonoids: baicalin, baicalein (trioksiflavon), wogonin (deoxy-metoksiflavon), up 2.5% pyrocatechols, resins, starch and tannins. Scutellaria has hypotensive, sedative, tonic, antispasmodic, anticonvulsant effects. Also it has anti-inflammatory, antithrombotic, antiallergic, exhibits antiviral and antibacterial activity. However, it is known that flavonoids poor solubility in both water and lipid results in low absorption on oral administration.

Aim. On the department of Industrial Technology of Drugs as part of the doctoral thesis Slipchenko G. N. developing a new dosage form – capsules with powder rhizomes and roots Scutellaria baicalensis. Evaluation of the bioavailability is one of the important stages in the process of development and improvement of technology of medicinal forms. Solubility of drugs is their most important characteristic. Other things being equal, it is largely characterized by the pharmacological activity of drugs and used for non-experimental prediction of bioavailability. It is planned study of Scutellaria flavonoids solubility in 0.1 M hydrochloric acid, which simulates the acidic intestinal environment and in biorevalent environments. Biorevalent medium is the dissolution medium, as close as possible to the internal fluids of the human body (digestive and gastric juices) on the chemical composition and physico-chemical properties (pH, osmolarity, buffering capacity, surface tension). Use of such media allows approximating the results of in vitro tests to in vivo performance and extending the range of studies involving dissolution of a drug.

Results and discussion. During the test "Dissolution" in contrast to conventional buffer solutions using biorevalent media may simulate the effect of food intake on the rate and completeness of drug dissolution. Moreover, the use of these media for products related to the 2 and 4 classes of biopharmaceutical classification system, clearly demonstrated similar correlations in vitro dissolution profiles and pharmacokinetic curves in vivo.

In the course of work to develop a methodology for determining the concentration of bioflavonoids in the solution based on the spectral characteristics of baicalin extract studied and a model compound – bioflavonoid baikalin selected analytical absorption maximum absorbance defined boundaries of subordination of its solutions Bouguer-Lambert-Beer.

Conclusions. The results of these studies will be used in the development of optimal technology of the new medicinal form.

DEVELOPMENT OF DERIVATIVE TLC-PURIFICATION PROCEDURE FOR DETERMINATION OF DOXYLAMINE IN BIOLOGICAL FLUIDS

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Introduction. One of the vital problems in the process of developing the analytical procedures for application in chemical and toxicological analysis is ensuring the necessary degree of specificity in relation to the components of biological matrix. The special importance this question acquires in the context of analysis of the biological objects exposed to the processes of putrefaction, burning, storages under various conditions for a long term, multiple freezing/thawing, etc. The solution of this problem lies in the plane of developing the effective purification methods for extracts from biological material.

Aim. The aim of the paper is to develop the purification procedure for extracts from blood and urine containing doxylamine by means of the method of derivative TLC, and to estimate the possibilities of application of the offered purification method in relation to the biological liquids exposed to the putrefaction processes.

Materials and methods. Doxylamine of pharmacopoeial purity was used in the experiment.

The model and also blank-samples were analysed for each developed procedure; the blank-samples were prepared in the following way: 5 samples (20.00 ml) of the blood obtained from the different sources, 1.00 ml of distilled water were added into them.

Validation of the procedures of doxylamine quantitative determination was carried out with application of the normalized coordinates; the application range was 25 – 175%; the number of concentration levels was g = 7. The doxylamine concentration in urine corresponding to the point of 100% was 32 μg/ml.

Results and discussion. Doxylamine isolation from biological liquids has been carried out using amphiphylic solvent (acetonitrile) under the conditions of aqueous phase saturation by electrolyte (ammonium sulphate); this approach enjoys wide popularity in modern forensic and toxicological analysis.

Isolation has been carried out in the weak-acid medium (pH = 5) that results in decreasing of co-extraction processes of biological matrix components in a number of cases. It is necessary to note that application of amphiphylic solvents and saturated solution of ammonium sulfate allows to maintain the isolation efficiency of substances of base character in the weak-acid medium at the same level as in the alkaline medium – it is conditioned by shift of pH real value in alkaline side for mixtures of electrolytes saturated solutions with amphiphylic solvents.

Purification of the extracts from blood and urine containing doxylamine has been carried out using the method of derivative TLC; generally this method provides obtaining the derivate for the substance to be investigated by means of the certain chemical reaction, its elution in the certain mobile phase, visualisation by the certain developer and determination of the value of R_f.

The offered method of derivative TLC-purification consists of applying the extracts from biological liquids on the start line of chromatographic plate (at the same time the standard sample is applied on the plate), eluting the chromatographic plate sequentially with the application of two mobile phases and eluting doxylamine by 0.01 mole/l hydrochloric acid solution from the chromatographic plate area corresponding to the spot of standard sample. Besides, it is provided obtaining the quaternary N-chlorammonium base for doxylamine in the way of processing the sample to be investigated and the standard sample by the excess of sodium hypochlorite solution in the saturated sodium hydrocarbonate solution on the start line of chromatographic plate after eluting the plate in chloroform (mobile phase 1). It is suggested to use the mixture of hexane and diethyl ether (2:1) as a mobile phase 2, and to carry out developing the spot of standard sample by 1% *p*-aminodiethylaniline sulphate solution.

Quantitative determination of doxylamine in eluates was carried out using extraction-photometric, UV-spectrophotometric and HPLC-procedures.

Determination and estimation of specificity and recovery for the developed procedures has been carried out, and the results allow to state the acceptable values of the parameters for all variants of final analytical operations.

For the possibilities estimation of applying the offered method of derivative TLC-purification in relation to the biological liquids exposed to the putrefaction processes 4 series in 6 blank-samples of biological liquids were prepared and exposed to storing at 25 ºC for 1, 2, 3 and 4 weeks respectively. For each series 3 blank-samples were spiked by analyte after respective expiry date, and then the analysis of all series were carried out.

The results of specificity and recovery determination for the developed procedure of derivative TLC-purification of extracts containing doxylamine in relation to the components of biological matrix exposed to the putrefaction processes allow to state the acceptability for all bioanalytical procedures.

Conclusions. The method of derivative TLC-purification of extracts from blood and urine containing doxylamine has been developed; the method allows to increase the elution degree of doxylamine from the chromatographic plate and decrease the amount of co-extractive substances in the obtained eluates. Possibilities of application of the offered method of derivative TLC-purification in relation to the biological liquids exposed to the putrefaction processes has been confirmed.

RESEARCH OF THE POSSIBLE INTERACTION OF FAMOTIDINE WITH METAL SALTS BY UV-SPECTROPHOTOMETRY

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Introduction. Famotidine, 3-[[[2-[(Aminoiminomethyl)amino]-4-thiazolyl]methyl] thio]-N-(aminosulfonyl)propanimidamide – $C_8H_{15}N_7O_2S_3$ – H_2-antihistaminic preparation. By blocking of histamine H_2-receptors it inhibits both basal and stimulated acid secretion; it also inhibits the activity of pepsin. It is not fully absorbed from the digestive tract, bioavailability is 40-45%, increases under the influence of food and decreases with the use of antacids. Binding to plasma proteins is 15-20%.

The aim of this work is to study the effect of metal salts on the physicochemical properties of famotidine. Such interaction plays an important role in the manifestation of the biochemical and pharmacological properties of the drug, its pharmacokinetics and side effects. Thus, the formation of complexes can reduce bioavailability and inhibit the digestion of famotidine at the stage of absorption. It is also important because famotidine as the anti-ulcer agent is often used in combination with antacids that contain a significant amount of metal salts. Also, metal salts may be contained in a sufficient amount of other medicines and some kinds of food.

Materials and methods. Considering the solubility of the drug 0.1 M hydrochloric acid solution was used as a solvent. The interaction of the drug with metal salt samples was not accompanied by any visual effects. To further investigate the possible of drug interactions the weight amount of about 0.1000 g of famotidine and weight amount of metal salts (calcium, magnesium, aluminium), which were taken in the stoichiometric ratio of the rate of 1 mole of bivalent metal equivalent to 2 mole of famotidine, and 1 mole of trivalent metal equivalent to 3 mole of famotidine, were placed into 100.0 ml volumetric flask, dissolved in 0.1 M hydrochloric acid solution and brought to the mark with the same solvent. The aliquot of 2.0 ml of the resulting solution was diluted with the same solvent to the 100.0 ml volume. Absorption spectrophotometry in the ultraviolet range of wavelengths from 220.0 nm to 350.0 nm was chosen as a research method. As the blank solutions the 0.1 M hydrochloric acid solutions of the same metal salts were used.

Results and discussion. In carrying out spectrophotometric readings differed little from the control data. In all cases, the absorption maximum was at the range of 265.0-267.0 nm. The addition salts of calcium significantly increased the intensity of the absorption, while magnesium salt contributed to its decline. The most significant decrease in the absorption rate was observed in the presence of aluminium salts, suggesting a possibility of its chemical interaction with famotidine.

Conclusions. The obtained results confirm the importance further research of interaction of famotidine with the antacids and other metal salts containing drugs.

CHOOSING THE CHROMATOGRAPHIC CONDITIONS FOR DETERMINATION OF GLIBENCLAMIDE

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Introduction. Treatment of diabetes mellitus type 2 is based on the usage of oral anti-diabetic drug, which belong to different compound classes. Sulfonylureas derivatives are the leading group of anti-diabetic drug. Glibenclamide has been considered as the second generation of sulfonylureas. It has been widely used in treatment of type 2 diabetic patients. Lifelong application, growing number of patients with diabetes mellitus, side effects – are the factors of toxicological hazards of this drug. Thus, the development of the suitable methods for the chemico-toxicological analysis of glibenclamide is an actual problem. Thin layer chromatography is one of the most widely applied methods in the chemico-toxicological analysis, which use in the stages of preliminary and confirmatory researches. **The aim of this work** was to choose the chromatographic conditions for determination of glibenclamide acceptable for toxicological investigations.

Materials and methods. Analysis has been performed on chromatographic plates Merck silica gel 60 F_{254} and Sorbfil, and mobile phases such as: 1) chloroform-acetone (80:20); 2) ethyl acetate-methanol-25% ammonia (85:10:5); 3) ethyl acetate; 4) chloroform-methanol (90:10); 5) chloroform-ethanol (90:10); 6) chloroform-cyclohexane-glacial acetic acid (40:40:20). For the detection of adsorption zones such reagents have been used: ferric-iodine complex, *chlor-zinc-iodide solution,* Bushard's reagent and 12.5% solution of copper sulfate in alkaline medium.

Results. It has been found that glibenclamide have satisfactory chromatographic mobility in all used mobile phases. But, in phases 1, 2, 4-6 glibenclamide adsorption occurs in the second, fourth and fifth chromatographic zones, where localized derivatives of barbituric and salicylic acid, 1,4-benzodiazepine and pyrazolone-5. Consequently, system 3 was defined as the most suitable for the analysis. The adsorption of glibenclamide occurs with R_f values of 0.47 for Merck and 0.42 for Sorbfil. For the suitability checking of the used phases, chromatographic procedure carried out with the standard substance – caffeine. After processing of corresponding zones with aforementioned reagents the visualization products of glibenclamide stained in brown color, while – with 12.5% solution of copper sulfate gives green color on blue background products of visualization.

Conclusions. The proposed chromatographic conditions can be used for determination of glibenclamide in the extracts from biological objects for poisoning of this anti-diabetic drug.

INVESTIGATION OF DOXAZOSIN IN THE ROTTING BIOLOGICAL MATERIAL

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Introduction: Doxazosin is a postsynaptic α_1- adrenoreceptor antagonist. It used for treat high blood pressure and urinary relation associated with bening prostate hyperplasia. This medicine in case of overdose and self treatment can break the function of heat, liver, kidneys or cause death. The choice of high sensitive methods of investigation of doxazosin in biological objects is necessary.

Aim: the investigation of techniques of extraction and purification from impurities and quantitative determination of doxazosin in liver tissue of corpse during decay.

Materials and method: The model mixture consist of 10.0 g of liver tissue and 200×10^{-6} g doxazosin. They were storaged for 7, 14, 21 and 28 days at temperature 5 ºC. In parallel, a control experiment was carried out. Extraction out of biological material was performed in several stages – centrifugation, the protein fraction was precipitated by ethanol (96%), extraction of impurities with hexane, and thin layer chromatography (TLC).

Hexane purification was performed at pH 2.0. TLC-purification was performed at conditions: stationary phase - Sorbfil, mobile phase - chloroform-acetone (80:20).

Quantitative determination was performed by UV- spectrophotometric method. Conditions: spectrophotometer SF-46, quartz cell of 1.0 cm; λ_{max} = 250 ± 2 nm; reference solution was obtained from the control experiment.

Doxazosin concentration in solution (C, mg / ml) was calculated from the equation of the linear dependence of absorbance and concentration (P = 8.988 A).

Results: At the beginning the content was 10.0±4.8% of substance; after 21 days of storage in decay tissue of the corpse can be found 3.5%; after 28 days – doxazosin not possible to determine.

Conclusions: We had defined shelf life of doxazosin in decay biological material. The results can be recommended for using in chemical-toxicological analysis.

DEVELOPMENT OF TANDEM PROCEDURE FOR ZOPICLONE DETERMINATION IN SEWAGES OF PHARMACEUTICAL PLANTS

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Introduction. Realization procedure of toxicological examinations requires to give the results of analyte content determination in the sample obtained with the help of at least two methods of analysis, which are based on different principles. Therefore elaboration of so-called tandem procedures allowed to carry out substance determination in the same sample simultaneously by means of two methods of analysis is actual.

Aim. The purpose of our paper is development and validation of tandem extraction-photometric/UV-spectrophotometric procedure of zopiclone quantitative determination in sewages of pharmaceutical plants.

Materials and methods. Doxylamine of pharmacopoeial purity was used in the experiment.

Results and discussion. Tandem extraction-photometric/UV-spectrophotometric procedure of zopiclone quantitative determination is based on using acid dye methyl orange formed ionic associates with zopiclone in the acid medium, which are extracted by chloroform. Under these conditions the chloroform layer becomes yellow. The amount of methyl orange is equivalent to the amount of zopiclone in ionic associates under these conditions.

It has been suggested to carry out decomposition of ionic associates and reextraction of methyl orange and zopiclone in 0.1 mole/l hydrochloric acid solution simultaneously and to measure the absorbance of methyl orange and zopiclone in the obtained aqueous solution by spectrophotometer.

We have carried out validation of the offered tandem procedure in the variant of the method of calibration curve using model solutions.

The obtained data specify that the offered tandem procedure of zopiclone quantitative determination is characterized by satisfactory linearity, accuracy and precision for all variants of range of the methods application and for both variants of the used wave length that makes it suitable for zopiclone quantitative determination in sewages of pharmaceutical plants.

Conclusions. The tandem procedure for zopiclone determination in sewages of pharmaceutical plants has been developed; the offered procedure allows to determine simultaneously zopiclone both by its own absorbance in UV-range of spectrum and by absorbance of methyl orange in visible range of spectrum that provides additional reliability of analysis and satisfies the requirements to researches realization in toxicological analysis.

DETERMINATION «DOHLOKS» IN CHEMICAL–TOXICOLOGICAL RESEARCH OF BIOLOGICAL OBJECTS

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Introduction. The article describes a method for determining the toxicity of the preparation "Dohloks" pesticide widely used in agriculture .

«Dohloks-dimpilat» (international name), a pesticide widely used in agriculture to kill harmful insects, to control ants, cockroaches, etc. The chemical composition of this organophosphorus and carbamate compounds. In Kazakhstan, the drug «Dohloks» is widely used imported against the Colorado potato beetle. There was one case of poisoning of a woman who had drunk the purpose of of suicide drug «Dohloks» and was found without signs of life. On this case of in Almaty branch of forensic medicine center was carried of chemical-toxicological examination on suspicion of poisoning with this pesticide.In the present we report here the results of chemical-toxicological studies of internal organs and blood for the detection of «Dohloks» in the carcass of of the dead woman.

Key words: organ phosphorus compounds, preparation «Dohloks», chromatography-mass spectrometry, chemical-toxicological research.

Materials and methods. In carrying out the chemical-toxicological studies internal organs were used: the stomach, liver, kidney and blood. To isolate the organophosphorus compounds are used the following procedure, 50 g of the stomach, liver, kidney individually filled with 150 ml of a mixture of alcohol-acetone-diethyl ether-water at a ratio of 2 : 2 : 1 : 1 containing 0.5-0.8 g of oxalic acid to pH 2 to universal pH paper. Insisting under periodic stirring for 4 hours. The solvent mixture was centrifuged, then placed in a freezer before of hardening fat. Skimmed and vaporized extraction from stomach, liver, kidneys was extracted with chloroform in portions 30.70 ml. Obtained overall of the chloroform extract of each object separately was evaporated and placed in a volumetric flask of of 50 ml, bring the volume of up to the mark with chloroform. 1) A portion (10 ml), the chloroform extract from organs and their preparation «Dohloks» were examined for cholinesterase sample that was positive. 2) 10 ml of chloroform extraction after evaporation of warm air up to 1 ml was applied on the chromatographic plate with a layer of neutral silica gel KSK.

Results and discussion. Chromatography system: hexane-dioxane (1: 1), then the plate was treated with a solution of ammonium molybdate solution and brilliant

green (Stenersen method) [1] where observed the appearance of blue spots with R_f 0.65 in all cases (stomach, liver, kidney) sobpadayuschee with an Rf value of 0.65 «witness» - «Dohloks». One of the evidential and highly sensitive method is gas chromatography-mass spectrometry. In connection with this we have conducted chemical-toxicological research of blood dnnym method. Used for this purpose 5 ml of blood, which is mixed with 5 ml of concentrated hydrochloric acid, and hydrolysis was carried out in a water bath for 20 minutes in a fixed glass vial. After cooling, alkalized with 25% ammonia a solution of, extracted with chloroform-isopropanol (8: 2), three times with 5 ml, then 3 .mu.l prepared extracts from the stomach, liver, kidneys and blood were injected into the evaporator-liquid gas chromatography-mass spectrometer Agilent 6890 Inetrt XL MSD 5975B under the following conditions: capillary column «DB-1» 12 m long with an internal diameter of 0.2 mm, the speed of the carrier gas (helium) 1 ml / min flow division 1:30. Column oven temperature programming: 3 minutes at 100 °C heating 30 °C / min to 310 °C and 310 °C preservation for 15 min. The temperature of the evaporator and the transition chamber mass spectral detector 275 ° C. Izonizatsii energy of 70 eV. The data were processed comparison method mass spectra library Polgrevskoy in spectors medicines, drugs, pesticides and their metabolites (PMW TOX3.1), whose database includes about 5000 names[2]. As a result of the processing of data extracts from the stomach, liver, kidney and blood was identifirovan «Dohloks» ion peak with the parameter space 4,14 m/z. At the same time we introduced «witness» - the original «Dohloksa» a solution of. The peak was obtained with a retention time of 4.135 min, a molecular ion peak area «Dohloksa» amounted to 4,14 m/z. additional ions amounted Parameters: 4,16 m/z, 4,18 m/z, 4,38 m/z.

Conclusion. Thus, in the a result of the chemical-toxicological studies of biological objects- stomach, liver, kidneys and blood in all cases it was found «Dohloks-Dimpilat».

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THE DEFINITION OF NUMERIC INDICATORS FOR THE ROOT OF HARPAGOPHYTUM PROCUMBENS

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Introduction. During after years the most pressing health challenges around the world are quality, efficacy and safety of medicines. In most developed countries of Europe, USA and Japan the main activity of the regulatory bodies in the field of medicines is, in particular, the standardization in the field of quality control (Institute of Pharmacopoeia). In Ukraine in this area the world's leading scientific institution is the State enterprise "Ukrainian scientific Pharmacopoeial center for quality of medicines", which is the main developer of the normative document in the field of quality control of drugs – the State Pharmacopoeia of Ukraine (SPU). One of the directions of SPU is the development and introduction of monographs on herbal medicinal raw materials. In this case, the priorities of plant objects in this case are medicinal plants widely used in Ukraine. On the domestic pharmaceutical market registered medicines on the basis of the root of Harpagophytum procumbens, which are used in medical practice for the treatment of diseases of the musculoskeletal system. The quality of the root of Harpagophytum procumbens is regulated by the monograph of the European Pharmacopoeia (EPh) 8.0 "Devil's claw root". The availability of medicines on the basis of harpagophytum on the pharmaceutical market of Ukraine, its widespread use and medical and pharmaceutical practice leads to the development of domestic normative documents.

The **aim** of this work was to study the numerical performance for the root of Harpagophytum procumbens (supplier "Starwest Botanicals", USA), as one of the stages of standardization of raw materials.

Materials and methods. EPh monograph "Devil's claw root" regulates the determination of numeric indicators such as loss in weight on drying (not more than 12.0%) and total ash (not more than 10.0%).

The results of the research. In the course of the research it was found that the loss on drying in the analyzed sample consisted of 8.82±0.23%, the content of total ash amounted to 3.45±0.31%.

Conclusions. Analyzing the results the obtained experimental data we can conclude on the compliance of plant material – root of Harpagophytum procumbens to the demands of European Pharmacopoeia monograph “Devil's claw root” on such indicators as “loss on drying” and “total ash”. Therefore, the data obtained will be used in the development of the monograph State Pharmacopoeia of Ukraine “Harpagophytum procumbens roots”.

DEVELOPMENT OF METHODS IDENTIFICATION AND QUANTITATIVE DETERMINATION OF EXTEMPORANEOUS PREPARATIONS

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Introduction. More and more often are met situations when the patient's health care needs can not be satisfied with the help of factory production drugs. For example, if a patient has an allergy to one of the components or excipient; or if the patient is elderly or a child can not swallow the tablet, and / or it needs a smaller dose than it is available.

Aim. Continuing researches of the Department of Pharmaceutical Chemistry NUPh on development of quality control methods, we chose the extemporal production of powders, which are often appointed to patients and which composition as active ingredients include paracetamol, phenylephrine hydrochloride, rutin and ascorbic acid.

For use of these powders as inside blank pharmacy it is necessary to develop rapid analysis techniques for the selected recipe.

Materials and methods. A review of the literature has shown that for the analysis of active ingredients of pharmaceutical dosage forms it is appropriate to use the method of absorption spectrophotometry in the ultraviolet and visible region.

To determine the routine, we propose to use photocolorimetry method based on the reaction of formation of chalcone after interaction with an alcoholic solution of sodium hydroxide solution. Maximum optical density of yellow colored product of reaction is observed at wavelength of 418 nm. To reduce the error accuracy of quantitative determination method, we suggest to use method spectrophotometry by a standard method.

The attempt to use this method for the analysis of phenylephrine hydrochloride and ascorbic acid is not succeed, so a mixture of these components we offer to determine by titrimetric methods. For a quantitative estimation of phenylephrine hydrochloride is used a method of acid-base titration. Titrate alcoholic solution of formulation with 0.1M sodium hydroxide solution using phenolphthalein as an indicator. Ascorbic acid can be quantitatively titrated by iodometry.

Conclusions. We are working to develop methods to identify all of the API and the quantitative determination in the test dosage form.

DEVELOPMENT OF AN EXTRACTION-PHOTOMETRIC METHOD FOR DETERMINATION OF GLICLAZIDE

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Introduction. Gliclazide is an oral hypoglycemic agent which is widely used for the treatment of non-insulin-dependent diabetes mellitus. It belongs to the sulfonylurea class of insulin secretagogues, which act by stimulating β-cells of the pancreas to release insulin. Due to mechanism of action, gliclazide may cause hypoglycemia, cardiovascular events and other pathological complications. Herewith, observed tendency of patients with this complications to suicide attempts. These factors cause the development of the side effects, which lead to the acute or lethal poisoning. In accordance with legislation of International judicial practice of poisoning of chemical substance for determination of toxicant in the biological objects a forensic toxicology investigation should been conducted. The extraction-photometric method is sensitive and rapid photometric method which is used for determination of mentioned drug. The method is quite selective as the drug contains basic moiety which preferentially interacts with acidic dye and the drug-dye ion-pair can be extracted into the organic solvent before measurement.

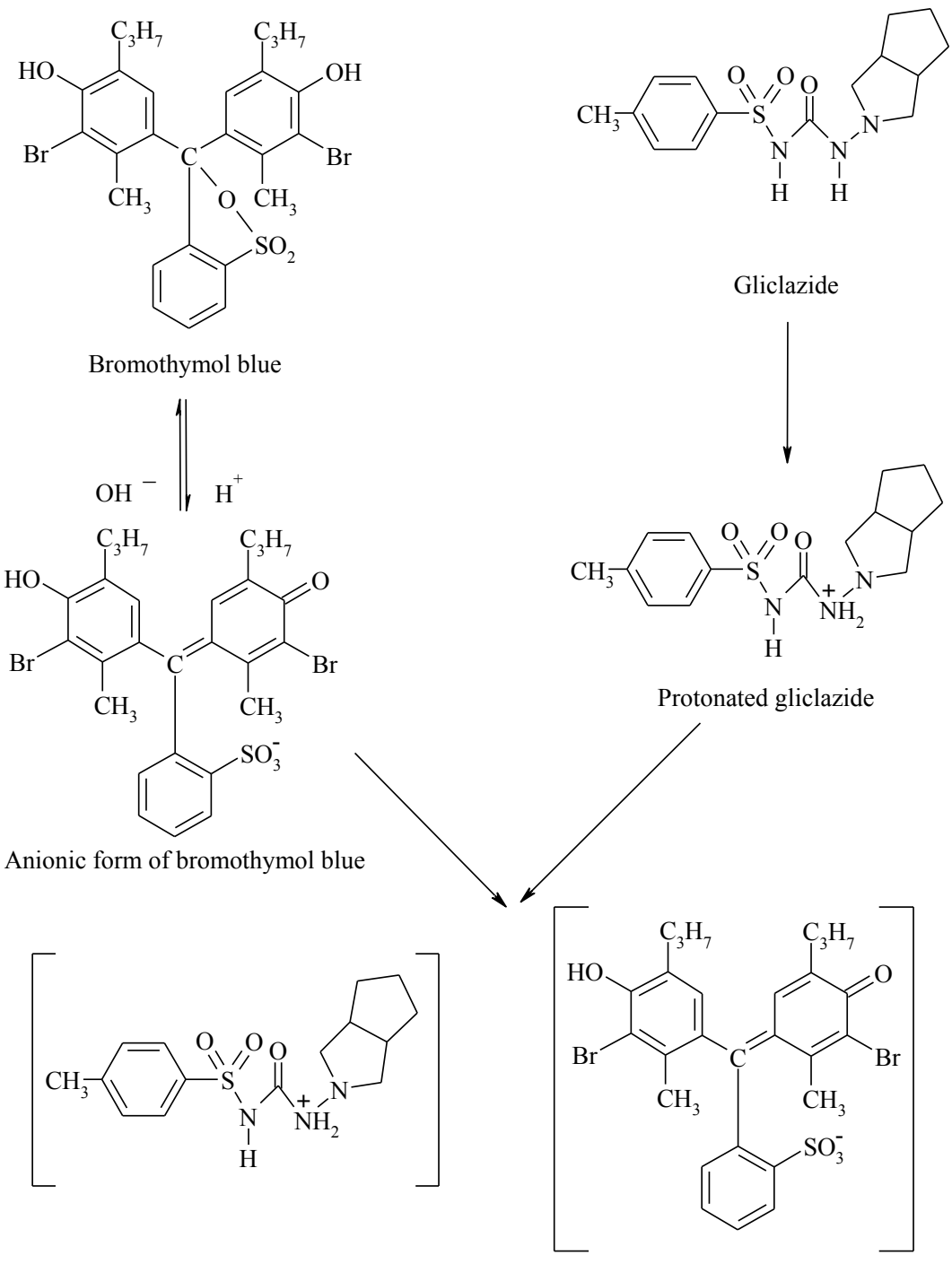
The aim of present paper was to develop highly sensitive, rapid, simple visible photometric method for the determination of gliclazide.

Materials and methods. A spectrophotometer (KPhK-2) with matched 1.0 cm quartz cuvettes for all absorbance measurements was used. A laboratory ion meter I-160 M was used for pH measurements. For the researches of gliclazide methanol solution (50 μg/ml) and 0.1% aqueous bromothymol blue were used.

Results and discussion. Development of extraction-photometric method was composed by exploiting gliclazide analytically useful functional groups and its ability to form ion-pair complex with acidic dye bromothymol blue. Experiments were carried out to assess various wavelengths and buffer solutions at different pH values. The studying of the absorption spectrum of the chloroform solution of the gliclazide ion-pair complex with bromothymol blue in the range of 364-490 nm was conducted. It has been found that absorption maximum was observed at 400 nm.

For foundation of pH at which maximum absorption of extraction of ion-pair complex can formed, series of phosphate buffer solutions with different pH (2.5 to 4.0) were used. The value of pH 3.0 was determined as the most suitable for the formation of ion-pair complex.

Reaction of ion-pair complex can be represented by scheme:



Consequently, the proposed method which is based on the formation of ion-pair complex between gliclazide and bromothymol blue at pH 3.0 followed by extraction of the complex by chloroform, and measuring the absorbance of yellow drug-dye complexes at 400 nm.

Conclusion. Extraction-photometric method for the quantitative determination of gliclazide which is based on the reaction of ion-pair complex with bromothymol blue has been developed. Hence, the proposed method can be used for the determination of gliclazide in the extracts obtained from biological objects.

THE STUDY OF THE VALIDATION CHARACTERISTICS OF THE QUANTITATIVE DETERMINATION METHODS OF PYRIDOXINE HYDROCHLORIDE AND ASCORBIC ACID IN COMPOUNDING PREPARATIONS

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Introduction. Today there is a real need of compounded preparations which contain water-soluble vitamins, especially for pediatrics, geriatrics or treatment of patients with complex comorbidities. Development and validation of quality control methods for compounded preparations have great practical value in terms of quality improving of medicines. It is important that quality control methods for compounded preparations meet modern requirements of State Pharmacopoeia of Ukraine, Orders Ministry of Health and are reproducible in conditions of pharmacies and quality control laboratories.

The **aim** of this work was the development, improvement and validation of quantitative determination methods of the ascorbic acid and pyridoxine hydrochloride in two-component powders. Powders composition: Pyridoxine hydrochloride 0.005, Sugar 0.2.; Ascorbic acid 0.1 g; Glucose 0.3 g. According to the published data for quantitative determination of pyridoxine hydrochloride in powder two titrimetric methods (alkalimetric and argentometric) were chosen. For analysis of ascorbic acid alkalimetric and iodometric methods were selected.

Results and discussion. Before methods validation model samples of compounded powders were prepared. The exact sample weight of pyridoxine hydrochloride (0.035 g, 0.043 g, 0.05 g, 0,058 g, 0.065 g) was put in mortar and thoroughly mixed with 2.50 g of sugar. Model samples of ascorbic acid powders were prepared by the same scheme (0.80 g, 0.90 g, 1.00 g, 1.10 g, 1.20 g of ascorbic acid and 3.00 g of glucose). During the method validation basic parameters were studied: accuracy, precision (repeatability), linearity and range. During the validation of alkalimetric method determination of pyridoxine hydrochloride it was found that the method is linear in the range 70-130%, the linear equation $Y=0.98 \cdot X+2.68$, Z_{intra} – 100.47%, SD_z – 0.83%, Δ_{intra} – 0.52%. Metrological results of argentometric method determination of pyridoxine hydrochloride is: $Y=0.99 \cdot X+1.13$, Z_{intra} – 100.53%, SD_z – 0.49%, Δ_{intra} – 0.83%. Metrological characteristics of iodometric and alkalimetric methods determination of ascorbic acid are: $Y=1.03 \cdot X+0.75$ and $Y=1.0 \cdot X-1.82$, Z_{intra} – 101.15 and 100.89%, SD_z – 0.44 and 0.46%, Δ_{intra} – 0.77 and 0.81% respectively.

Conclusion. Experimental results of method validation prove the possibility of using given methods in pharmaceutical analysis in accordance with modern requirements to the quality control.

COMPARISON OF SPECTRAL CHARACTERISTICS OF FAMOTIDINE IN DIFFERENT SOLVENTS

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Introduction. Nowadays the presence of accessible and recreated methods of quality control of drugs is very important. Preliminarily the investigations of possibility of famotidine identification by using coloured reactions of interaction between the substance and the solutions of metal salts were undertaken by us. Besides that, the physico-chemical methods of analysis are commonly used to standardize and control the quality of active pharmaceutical ingredients of organic nature. USP and Ph.Eur. suggest using the absorption spectrophotometry in the ultraviolet and visible region of spectrum for famotidine identification. This method can be applied due to the presence in the famotidine's structure of chromophores: double bounds and the thiazoline core. Taking into account famotidine chemical properties, its absorbance will depend on pH of test solution that is specific enough by itself and it can be used for identification.

Aim. The aim of our investigation was to research changes in characteristics of famotidine's spectra depending on the value of pH of the environment.

Materials and methods. The measurement of the absorbance of the test solutions was carried out on a spectrophotometer in the range of spectrum from 220.0 nm to 350.0 nm wavelength. 0.001% solutions of famotidine in corresponding solvents were prepared for this study. 0.1 M hydrochloric acid solution; 0.1 M sodium hydroxide solution and water were used as solvents. Corresponding solvents were used as the compensation solutions.

Results and discussion. The results of carried out investigations showed the spectra, that were measured in 0.1 M HCl and water differ between themselves insignificantly. The absorption maxima are observed at 220.0±2 nm. In spectrum of famotidine alkaline solution, unlike solutions in other solvents, bathmochromic changes are observed. It also should be noted that famotidine sodium salt has more expressed absorption maximum, in contrast to the ionized acidic form of famotidine, and it is observed at λ_{max} = 228.0±2 nm. The changes of spectral characteristics in different solvents can be related to the presence of the sulfonamide group. As a result of interaction with the hydrochloric acid solution due to tertiary N-atom famotidine forms salt that hydrolyses in water solutions. This fact causes insignificant difference of spectra, which were measured in 0.1 M hydrochloric acid solution and water. In the case with NaOH, salt appears due to a substitution of the H-atom on the Na-atom in a sulfonamide group by the Sulphonamides type, which causes changes of electronic density in the molecule of famotidine and changes in the spectral picture.

Conclusions. The results of experimental data show that it is reasonable to use 0.1 M NaOH as a solvent for identification and for assay, as the absorption maximum of famotidine in those conditions is the most expressed and specific.

DETERMINING THE CONCENTRATION OF DIPHENHYDRAMINE IONS IN AQUEOUS SOLUTION BY DIPHENHYDRAMINE SELECTIVE ELECTRODE.

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Introduction. In recent years, for electro active substances widely used heteropoly (GPA) Keggin's structure having the general formula: $HMe_{12}O^{n-}_{40}$, where X - central atom (P, Si) E - metal ion (Mo (VI), W (VI)). SBS with organic cations to form sparingly soluble in water but soluble in organic solvents compound. This allows their use in plasticized membranes ion-selective electrodes (ISE). As plasticizers we have used dibutyl phthalate (DBP) or dioctyl phthalate (DOP) in the preparation of membranes.

Aim. We found that the best electro analytical properties has an electrode containing plasticized membrane as electro active substance ionic associate with diphenhydramine phosphorustungstate ($PW_{12}O^{3-}_{40}$), as well as a plasticizer - DOP.

Materials and methods. The method is based on use of two standard solutions of the drug, which is in the range of concentration of the solution was analyzed. EMF measurement circuit (1) was performed with a digital I-130 ionomer. As the reference electrode use a saturated silver chloride electrode. First, the first measured EMF E_1 standard drug solution C_1 at a concentration less than the concentration of the solution was analyzed C_A. Thereafter, the solution was analyzed by EMF, E_A. Finally, the measured EMF in the second standard solution with a concentration C_2, which is greater than the C_A (C_1 and C_2 are selected so that the $C_2 / C_1 = 10$). Calculate the slope of the electrode function ISE, in the accepted range of concentrations of standard solutions: $S = E_2 - E_1$. Find the difference voltage (delta E) between EMF (E_A) and EMF (E_2): $\Delta E = E_A - E_2$.

Results and discussion. Aqueous solutions diphenhydramine different concentrations (from $5.0 \cdot 10^{-4}$ to $5.0\ 10^{-3}$ M), and the two standard solutions with concentrations of diphenhydramine $C_1 = 5.0\ 10^{-4}$ M, and $C_2 = 5.0\ 10^{-3}$ M.

Ionometric proposed method based on the use of the developed ion-selective electrode to determine diphenhydramine in aqueous solution with an uncertainty not exceeding 1.38%.

Conclusions. Diphenhydramine selective electrode and ionometrical developed methods for the determination of the drug suitable for the purposes of the pharmaceutical and chemical-toxicological analysis.

QUANTITATIVE DETERMINATION THYMOL IN SYRUP "KALINOL PLUS" OF THE HPLC METHOD.

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Introduction. Syrup "Kalinol plus" (state registration number: LS№15-00336) production «Azerfarm Ltd" plant, composed of thyme extract, sugar syrup, potassium bromide and 80% ethanol. In medical practice, used as a mucolytic and expectorant in acute and chronic inflammation of the air ways. The main active components are a syrup thymol extract and potassium bromide. Most drugs with extract of thyme essential oil or thyme, standardized not only the total number of essential oils, but also thymol or carvacrol.

Aim. Despite the widespread use of HPLC method for analysis of essential oils obtained from plants, direct determination of thymol and carvacrol in the various dosage forms of this method is unacceptable. In connection with the above stated , the use of the HPLC method to determine the number of separate components in a multicomponent herbal preparations composition is of paramount importance.

The present study focuses on the quantitative determination of thymol in the preparation " Kalinol plus" by HPLC. Experimental studies were carried out in the UV-detector chromatography HPLC-«Agilent-1100" (USA). Stationary phase column «Zorbax SB-C18», 5 micron particle size. Temperature of column 30 °C, solvent flow rate of 1 ml / minute, standard sample volume 10 mcl. The time of analysis 15 minutes.

Materials. Preparation of the test solution. 1.0 g of syrup (accurately weighed) "Kalinol plus" was placed in a volumetric flask of 25 ml, 20 ml of solvent and agitated until dissolved and then for 5 minutes, the resulting solution was kept in an ultrasonic bath, further the solution is made up to the required amount of the same solvent, under stirring.

The resulting solution was centrifuged for 5 minutes at 10000 rpm. Preparation of the reference solution of 50 mg (accurately weighed) was placed in a thymol volumetric flask of 100 ml, was added to 20 ml of solvent and agitated until complete dissolution, then the solution is made up to the required amount of the same solvent, under stirring.

Methods: 50 mg of thymol standard sample was placed in a volumetric flask of 100 ml, was added thereto about 20 ml of solvent and agitated until complete dissolution and then the solution is made up to the required amount of the same solvent. The volumetric flask was placed 50 ml of 2 ml of the standard solution,

approximately 20 ml of mobile phase and agitated, then the volume was adjusted to the desired amount of the same solvent. The volumetric flask was placed 25 ml of 5 ml was added thereto about 20 ml of solvent and agitated, then adjusted to the desired amount of the same solvent to give a solution with a concentration of 0.004 mg/ml.

1.0 g (accurately weighed) Syrup "Kalinol plus" was placed in a volumetric flask of 25 ml, were added 20 ml of solvent and agitated to ensure complete mixing. The volume was adjusted to the required volume with the same solvent to thymol concentration 0.004 mg / ml. Solution then was degassed for 5 minutes in an ultrasonic bath. The resulting solution was centrifuged for 10 minutes at 10000 rpm.

Results and discussion. Studies have found that the rate peak thymol 28,701 relative area units per 12,789 minutes, the peak area in the chromatogram of the test substance are well separated, have no obstacles in the definition of the solvent, excipients and the main active ingredient.

The results are shown in Figure №1.

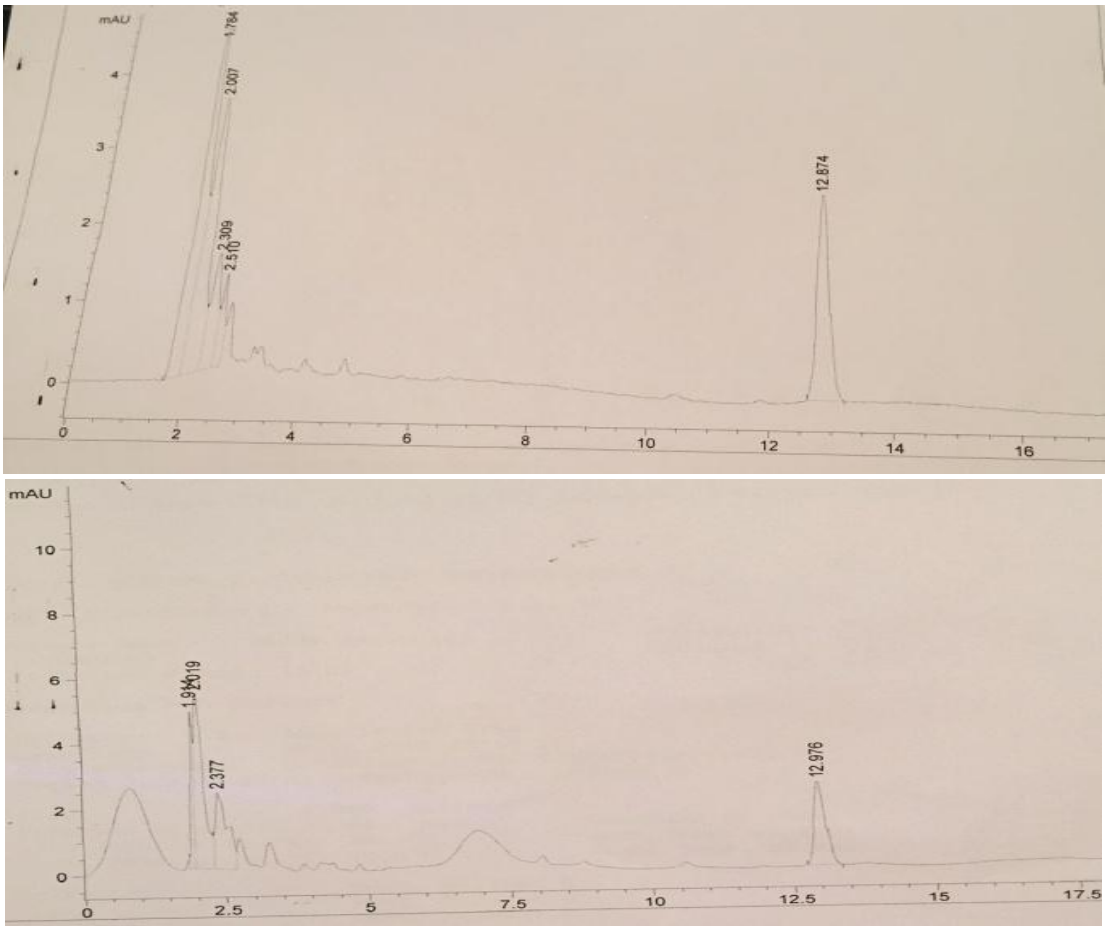

***Figure 1**. The chromatograms thyme extract and model mix.*

USE OF THE REACTIONS WITH THE HEAVY METAL SALTS FOR IDENTIFICATION OF OMEPRAZOLE IN PALLETS

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Introduction. Omeprazole is one of the most prescribed drugs from the proton pump inhibitors group that is used in therapy of passionately-destructive diseases of the digestive system. Omeprazole decreases the level of the stimulated and basale secretion of hydrochloric acid (dose-dependently), reduces secretion of pepsin and general volume of gastric secretion, it has also the expressed antihelicobacter effect. This medical drug is included into the standard chart of gastric and duodenum ulcer treatment.

The State Pharmacopoeia of Ukraine does not have a monograph to regulate the order of quality control of medical forms with the omeprazole. So it is necessary to develop and introduce it, because the medical forms with omeprazole are often prescribed and they require the presence of normative documents for their quality control.

Not all laboratories of drugs quality control have the proper hardware-based equipment and other, so the issue of the development and introduction of the chemical methods of quality control, which would be specific but at the same time economical enough and easily recreated, are urgent issues nowadays.

The chemical structure of omeprazole (the presence of acid center of the nitrogen atom of pyrrole core) determines the possibility of motion of the identification reactions for omeprazole with the heavy metal salts, such as copper sulfate, cobalt chloride, iron (III) chloride et al – with formation of complex salts with the characteristic colouring by the principle of sulfanilamides.

Aim. The aim of our research was checking the possibility of interaction between omeprazole and heavy metal salts and defining the most characteristic among themfor this drug.

Materials and methods. On the pharmaceutical market of Ukraine the substance of omeprazole is supplied as pallets, because it is unsteady and hydroscopic. Therefore the possibility of influence of auxiliary substances should be taken into account during the development of the possible identification reactions.

With regard to physical and chemical properties of omeprazole pallets (bad solubility in water and mineral acids solutions) for the improvement of solubility pallets were preliminary grounded in the mortar. The weight amount of pallets powder was dissolved in a 0.1M sodium hydroxide solution and in the future result solution was used as the investigated solution. Control experiments were carried out

in the same conditions without adding any weight amount of testing samples, to make sure that observed analytical effects are not hydroxides of the corresponding metals.

All reagents that conform to the State Pharmacopoeia of Ukraine which are harmonized with the European ones were used in the study.

Results and discussion. After adding the cobalt chloride solution to the test solution with the omeprazole in drops, light blue coloured precipitate was formed, unlike the control experiment, where precipitate had dark blue-green colour.

During the interaction between the test solution and the iron (III) chloride solution, we observed formation of the light brown precipitate that differed from the characteristic darkly-brown precipitate of control experiment.

With the copper sulfate solution in the test solution, we observed formation of blue-green color precipitate; at the same time in the control experiment we observed formation of brightly-blue precipitate.

For the interaction between the omeprazole solution and the silver nitrate solution conditions of slightly alkaline environment to prevent the formation of silver oxide precipitate, which would mask other analytical effects, were created previously. For this propose, omeprazole was dissolved in the 0.1 M sodium hydroxide solution, the result solution was neutralized to the slightly alkaline reaction of the environment, using phenolphthalein as an indicator. Upon adding silver nitrate solution to the test solution in drops, we observed formation of yellow-white volumate precipitate. Formation of white amorphous precipitate was observed in the control experiment. The formed precipitates of silver salt of omeprazole and silver oxide differ in structure and colour, which is well noticeable, while viewing of them on a black background.

After adding the lead acetate solution in drops to the omeprazole solution, which was neutralized to the slightly alkaline reaction of the environment, using phenolphthalein as an indicator. Formation of white lamellar precipitate was observed. In the control experiment without addition of the omeprazole weight amount after adding the lead acetate solution visual changes were not observed.

Conclusions. Thus, based on the obtained results, it is possible to make the conclusion that coloured reactions with heavy metal salts solutions can be used for identification of omeprazole in pallets. The optimal conditions for the reaction between silver nitrate and lead acetate are previous neutralization of alkaline omeprazole solutions to the slightly alkaline reaction of the environment, using phenolphthalein as an indicator. With solutions of cobalt chloride, iron (III) chloride, iron sulfate and lead acetate, analytical effects are observed very clearly which differ from the control tests. Analytical effect of interaction between omeprazole and silver nitrate is well noticeable in comparing to the control test, while viewing of them on a black background.

IDENTIFICATION OF PESTICIDES OF THE NEONICOTINOID GROUP IN WHITE CABBAGE BY THIN-LAYER CHROMATOGRAPHY

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Introduction. The residual amounts of pesticides in foods and their impact on human health poses the problems of rational use of these group of chemicals. At present people have no opportunity for substitution pesticides to protect harvest. Due to using chemicals we can obtain different agriculture plants without losing from insects, weeds, fungus and so on.

The nicotine sulphate was widespread pesticide for a long time, but its application was suppressed because of their high toxicity for mammals. The neonicotinoids are analogs in structure to nicotine sulphate.

Today these chemicals are the popular and safe pesticide group among the insecticides. Neonicotinoids are toxic for different insects; these chemicals are toxic for mammals to less degree because of differences in receptor sensitivity of insects and mammals. The example of neonicotinods of the first generation is the imidacloprid, the second generation is the thiamethoxam.

The problem of studying of their accumulation in the food is important due to the growing popularity.

The **aim** of investigation. The aim of this work is the identification of a number of neonicotinoids – imidacloprid and thiamethoxam, in white cabbage by thin-layer chromatography.

Materials and methods. The choice of this object due to its high prevalence and, consequently, the potential possibility of getting neonicotinoids in the human body during growing this vegetable. The available analytical method for the most laboratories is the thin-layer chromatography (TLC). The other advantages of this method are the simplicity, rapidity, economy.

Results. In the first stage of the study the optimal chromatographic conditions of the separation of neonicotinoids were chosen. As the stationary phase silica gel was using (the "Sorbfil PTLC-U-A-UV" plates). During changes of eluting power of mobile phase its optimum composition has been determined – hexane-isopropanol-acetonitrile in the ratio of 60:35:5 (two-dimensional chromatography). Detector was the vapors of iodine.

The extraction of pesticide from plant objects is important phase before using analytical method. Realization of sample preparation was the next stage of study. The purpose of this stage was to learn the impact of ballast substances for identification of analytes.

Model mixtures of the pesticides in cabbage (the content of Imidacloprid – 5 mg/kg, thiamethoxam – 0.5 mg/kg) were prepared.

Three procedures of the neonicotinoids isolate have been considered, resulting the optimal method were defined (table 1).

Technique I includes infusion of the sample with acetonitrile; the transfer of ballast substances in the hexane layer in the presence of saturated solution of sodium chloride and extraction of analytes with chloroform.

Technique II is the insisting of the sample with acetone, followed by re-extraction of analytes into chloroform in the presence of a saturated solution of sodium chloride. The residue after evaporation of chloroform was dissolved in acetonitrile and additional cleaning from ballast substances by the hexane extraction was carried out.

Technique III is analog of technique II except for the stage of additional purification from ballast in the hexane layer. The reason is due to the absence of the fat in white cabbage, the removal of which is necessary for the analytical process.

Table 1

Influence of ballast substances to the identification of neonicotinoids

$R_f \times 100$ analytes, zones of ballast substances	Technique I	Technique II	Technique III
Imidacloprid	46		
Thiamethoxam	27		
Zones of ballast substances	38 75 93	31-41 57-73	31-41 57-73

Conclusion. During the experimental work it was established that the insisting of the sample with acetonitrile, purification of the extract with hexane and extraction of neonicotinoids in the layer of chloroform led to distinct zones of ballast substances which overlap at region imidacloprid location.

This fact makes difficult the identification of Imidacloprid by technique I.

Also it was shown, that the insisting of sample should be performe with acetone and extraction the analytes should be performe in the chloroform layer, the dry residue should be dissolve in acetonitrile (technique III).

No need for further cleaning of the acetonitrile phase by hexane was identified because of obtaining similar results by using techniques II and III, and significant losses of the analytes during use of the technique II.

DEVELOPMENT OF QUANTITATIVE DETERMINATION METHOD FOR FUROSEMIDE IN COMPOUNDED SYRUPS

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Introduction. Furosemide is used in the management of oedema associated with congestive heart failure, nephrotic syndrome and hepatic cirrhosis. Nowadays compounded oral dosage forms, containing diuretics such as furosemide, hydrochlorothiazide and spironolactone are widely used in pediatric practice. This is due to the lack of similar finished pharmaceutical products, low cost and simplicity of application. Syrups and powders are preferred dosage forms. Syrups are used in pediatrics for masking medicines taste. The advantage of convenience in administration and higher bioavailability, when compared to oral solid dosage forms, make syrups more appropriate for children. Development of analytical methods for quality control and stability study of extemporaneously prepared medicines are one of the most important tasks of the contemporary pharmaceutical analysis.

Therefore, the **aim** of our work was to develop method for quantitative determination of furosemide in compounded syrups.

For the purpose of this study 5mg/ml suspensions of pharmaceutical substance furosemide (Ipca Laboratories Ltd batch 5074HRII), furosemide tablets (Arterium "Київмедпрепарат") and crushed furosemide tablets in simple syrup USP were prepared. The absorbance of 0.005mg/ml solutions of these samples in 0.1M sodium hydroxide were measured at a wavelength of 271nm, using an Ultraviolet(UV) spectrometer ("Evolution 60s").

Results of the assay after five measurements showed percentage content of 100.3±0.4%, 104.1±0.7% and 103.2±0.4% for samples of the pharmaceutical substance, furosemide tablets and the compounded syrup of furosemide. Intraday stability (over 7 hours 30 minutes) for furosemide in the tablet and syrup samples showed percentage content of 102.8±1.2% and 103.5±0.6% respectively.

Conclusions. This method could be used for quantitative determination of furosemide in syrups since the excipients in tablets and simple syrup did not significantly affect the results obtained using UV-spectrometry. To further prove the possibility of using this method in pharmaceutical analysis subsequent validation is required.

DEVELOPMENT OF THE METHODS OF IDENTIFICATION AND QUANTIFICATION OF 3-METHYLPYRIDINE-2-AMIDE 1-HEXYL-4-HYDROXY-2-OXO-1,2-DIHYDROQUINOLINE-3-CARBOXYLIC ACID

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Introduction: Roughly one-third of the world's population has been infected with *M. tuberculosis*, with new infections occurring in about 1% of the population each year. However, most infections with *M. tuberculosis* do not cause TB disease, and 90–95% of infections remain asymptomatic. In 2012, an estimated 8,6 million chronic cases were active. In 2010, 8.8 million new cases of TB were diagnosed, and 1.20–1.45 million deaths occurred, most of these occurring in developing countries. Of these 1.45 million deaths, about 0,35 million occur in those also infected with HIV. Due to this high record of tuberculosis and its high mortality rate, there is need for the development of new antituberculosis drugs that can improve the life standard of the affected people.

Aim: To develop the methods of identification and quantification of 3-methypyridine-2-amide-1-hexyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid and the procedures required.

Method and materials: For identificationof3-methypyridine-2-amide-1-hexyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid are

- Reaction with $FeCl_3$ because of the presence of phenolic hydroxyl group
- Reaction with cyanogen bromide, the pharmacopoeial reaction for pyridine cycle.
- Reaction with 2,4-dinitrochlorobenzene, the non-pharmacopoeial reaction for pyridine cycle

The method proposed for the quantification of this new substance, 3-methypyridine-2-amide-1-hexyl-2-oxo-4-hydroxyquinoline-3-carboxilic acid is non aqueous acidimetry.

The titration is carried out with titrant perchloric acid in the medium of acetic acid and the endpoint is determined potentiometrically by a potentiometer.

The results: the results were subjected to quantitative review as the procedure was repeated can therefore makes it possible to conclude that they are reliable, making it possible to assay the substance by the non-aqueous acidimetry method. Also, the identification of the substance was successfully proven.

Conclusion: this substance can be quantified by non-aqueous acidimetry, and can be identified by the proposed reagents with visible products and reactions.

OPTIMIZATION OF THE WAYS OF FUROSEMIDE IDENTIFICATION

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Introduction. The search of new cost-effective methods of analysis of medicinal substances is being carried out at the Pharmaceutical Chemistry Department of National University of Pharmacy. Furosemide (4-chloro-2-[(furan-2-ylmethyl)amino]-5-sulphamoylbenzoic acid) is a drug that possesses diuretic properties. Furosemide is included in the European Pharmacopoeia (EP), the Britain Pharmacopoeia, and the State Pharmacopoeia of Ukraine. There are different methods of identification of furosemide. The EP suggests usage of both instrumental and non-instrumental methods of dentification of this substance. They include infrared absorption spectrophotometry, ultraviolet (UV) and visible spectrophotometry. Non-instrumental method is the identification of a primary aromatic amino group after hydrolysis using naphthylethylendiamine to obtain an azo dye.

Aim. The target of our work is the optimization of identification for a widely used pharmaceutical substance furosemide to discover and find the most suitable and appropriate methods of identification of furosemide based on its structure and properties.

Materials and methods. We used the analytical balance Axis ANG-200 and the measuring glass wear of class A. For the spectrophotometric investigations we used spectrophotometer Evolution 60S; the methods of chemical identification.

The object of our investigation being the pharmaceutical active ingredient furosemide was checked for the possibility of other ways of the identification alternative for the mentioned above.

We have checked that furosemide in the reaction for a primary aromatic amino group (diazotization by sodium nitrite in the presence of hydrochloric acid and next diazotization) gives a characteristic red colour when alkaline solution of β-naphthol is used to obtain an azo-dye. This possibility of this reagent usage was proved instead of naphthylethylene diamine dihydrochloride suggested by the EP when a violet-red colour develops.

The ability of aromatic carboxylic acids to form coloured products with the salts of heavy metals is used in pharmaceutical analysis. It was observed that furosemide forms the coloured precipitates with such reagents and we consider the aromatic carboxylic group to form the salt. At first we obtained the sodium salt of furosemide: 0.1 g of furosemide were shaken with 3 ml of 0.1 M sodium hydroxide solution during 1-2 min and then filtered. Then the salt of a heavy metal was added.

We obtain a light-green precipitate with copper sulphate solution, the pink precipitates with the salts of cobalt (II) (chloride and nitrate were used), and a brown-red precipitate with ferric chloride solution.

We have checked the spectral characteristics of furosemide in different solvents. The solution suggested by EP for this determination is a solution of sodium hydroxide, because the substance is practically insoluble in water but dissolves in dilute solutions of alkali hydroxides. Taking into consideration the fact that furosemide is sparingly soluble in ethanol 96% we have checked the UV characteristics in this solvent. Furosemide has functional groups of acidic character along with the groups of basic character so we checked its UV characteristics also in 0.1M hydrochloric acid solution.

Test solutions. A) 50 mg of furosemide were dissolved in a 4 g/l solution of sodium hydroxide and diluted to 100 ml with the same solution. 1 ml of this solution was diluted to 100 ml with a 4 g/l solution of sodium hydroxide. B) 50 mg of furosemide were dissolved in ethanol 96 per cent and diluted to 100 ml with the same solution. 1 ml of this solution was diluted to 100 ml with ethanol 96 per cent. C) 50 mg of furosemide were dissolved in 0.1M hydrochloric acid solution and diluted to 100 ml with the same solution. 1 ml of this solution was diluted to 100 ml with 0.1M hydrochloric acid solution.

The spectra were obtained in the spectral range 200-400 nm. The obtained spectra have three defined absorption maxima: A) at 228, 270, and 333 nm, B) at 235, 283, and 335 nm; C) at 231, 273, and 336 nm. The ratios of the values of absorbance in the second and the first maximum were calculated and are A) 0.56; B) 0.55; C) 0.61.The absorbance ratio for the determination in sodium hydroxide solution corresponds to EP.

The results of absorbance measurement in the range of concentrations of analyzed substance where they submit the combined *Beer-Lambert-Bouguer* law were used to calculate the specific absorbance. The average value of specific absorbance $A_{1cm}^{1\,per\ cent}$ was determined.

Results and conclusion. The obtained results suggest the alternative ways of furosemide identification and give the possibility to identify furosemide reliably. The described variants of identification can be used depending on the presence of resource base of certain laboratory.

The results of validation studies show that the specific absorbance was calculated with good accuracy and can be used for the quantification of furosemide by the method of specific absorbance.

QUANTIFICATION OF FUROSEMIDE BY THE METHOD OF SPECTROPHOTOMETRY

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Introduction. The investigations that are carried out at the Pharmaceutical Chemistry Department of National University of Pharmacy are targeted on the search of easy and least time consuming methods of analysis of pharmaceutical preparations. Furosemide (4-chloro-2-[(furan-2-ylmethyl)amino]-5-sulphamoyl-benzoic acid) is a most commonly used loop diuretic prescribed for the treatment of acute and chronic diseases of different etiology. The assay of furosemide by the European Pharmacopoeia, the Britain Pharmacopoeia, and the State Pharmacopoeia of Ukraine is carried out by the method of non-aqueous acid-base titration that needs the special equipment and usage of organic solvents.

Aim. The aim of our work was to check the possibility of usage of ultraviolet spectrophotometry for the quantification of furosemide and to develop a new practical procedure for its assay. The work was also targeted on the search of suitable solvents for the spectrophotometric determination.

Materials and methods. We used the analytical balance Axis ANG-200 and the measuring glass wear of class A. For the spectrophotometric investigations we used the spectrophotometer Evolution 60S. The statistical studies were carried out by the common procedure.

The electron absorption spectra of furosemide in different solvents were studied. It was found that its spectra in ethanol, sodium hydroxide solution and hydrochloric acid solution have three absorption maxima in the range 200-400 nm. The ratios of the values of absorbance in the second and the first maximum were calculated.

The specific absorbance of furosemide in alcoholic solution in the maximum at 283 nm was calculated. Its metrological characteristics were determined.

The procedures for the spectrophotometric quantification of furosemide by the methods of specific absorbance and the method of standard were developed. The validation characteristics that prove the possibility of the suggested methods for the assay of furosemide were obtained.

Results and conclusion. The simple UV spectrophotometric method for the assay of furosemide has been developed. It is proved to be easy enough and provides good accuracy of the results that is why it can be used in the pharmaceutical analysis for the quantitative analysis of furosemide.

DEVELOPMENT OF THE METHODS FOR QUALITY CONTROL OF BRONCHOFORT TINCTURE

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Introduction. Medicinal plants containing essential oils take one of the leading positions at the pharmaceutical market due to the wide spectrum of the pharmacological action such as the antiseptic, antibacterial, analgesic, regenerating, expectorant, diuretic and sedative action. Many essential oils improve the circulatory system work, have a beneficial effect on digestion, excrete toxins and wastes from the body, strengthen the immune system, normalize the endocrine profile. These features are explained by complexity of the chemical composition and the mechanism of the therapeutic effect.

Aim. The Department of Industrial Drug Technology works on development of the tincture under the conditional name of Bronchofort for using it as an agent for the treatment of the upper respiratory tract (laryngitis, tracheitis, pharyngitis and bronchitis). The composition of the tincture includes chamomile flowers (*Matricaria recutica* L.), leaves of southern blue gum (*Eucalyptus globulus Labil)*, thyme herb (*Thymus vulgaris* L.) and common yarrow herb (*Achillea millefolium* L.). The choice of these plants is stipulated by the presence of different classes of essential oils possessing the anti-inflammatory, antibacterial, expectorant, sedative, analgesic actions. Therefore, the aim of our work is to develop the methods for quality control of biologically active substances in Bronchofort tincture.

Biologically active substances of medicinal herbs in the composition of the tincture indicate that the most compounds are aromatic in nature and contain hydroxyl groups in their structure. In order to develop the methods for quality control of the tincture under research at first it is advisable to study the character of absorption spectra of all alcoholic solutions of the components and the total drug.

Materials and methods. The absorption spectra of alcoholic solutions of the tinctures under research were recorded on an Evolution 60s spectrophotometer in the region from 220 nm to 400 nm.

Results and discussion. It has been found that all of them are characterized by the presence of two absorption maxima at the wavelengths of 272-284 nm and 322-331 nm, it may indicate the presence of substances with the polyphenolic structure, as well as hydroxycinnamic acids.

Conclusions. Therefore, when developing the methods for quality control the content of biologically active substances in Bronchofort tincture should be calculated with reference to gallic acid or hydroxycinnamic acid.

DETERMINATION OF AFLATOXIN B1 IN DIFFERENT TYPES OF TEA BY THIN-LAYER CHROMATOGRAPHY

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Introduction. Mycotoxins are the second metabolites of microscopic fungi. These substances are widespread contaminants of food raw materials, human food and animal feed, therefore mycotoxins may work harm to human health and damage to animal husbandary. Mycotoxins are highly toxic substances and, in some cases it have mutagenic, teratogenic, carcinogenic properties, and so control for maintenance mycotoxins is important.

The **aim** of investigation. The aim of this experimental work was the determination of aflatoxin B1 in different grades of tea by thin-layer chromatography (TLC).

Materials and methods. The objects of the study were different types of tea (Indian black, Ceylon black) and gastric mixture of medicinal herbs (production by "Krasnogorskleksredstva", Russia).To conduct the study by the method of additives the standard solutions of aflatoxin B1 (10 μg/ml) were taken. It was adjusted 0.15 μg of the standard aflatoxin B1 (1.5 times of the maximum permissible concentration).

For the detection of aflatoxin B1 in objects extraction and purification of the extract were carried out. The method of sample preparation involves a single extraction with acetone; the acetone extract is diluted with water. Purification from ballast substances is carried out with lead acetate and hexane; the next stage was extraction of analyte from aqueous-acetone solution in layer of chloroform and concentration of the sample.

Results. Chromatographic determination of aflatoxin B1 was performed by method of one-dimensional ascending TLC on plates with ultraviolet light detection (Sorbfil PTSH-P-UV) in 6 systems of solvents (table 1).

Table 1

Chromatographic mobility of aflatoxin B_1

№ p/p	Solvent system	R_f*100 Aflatoxin B1
I	Chloroform-isopropyl alcohol (99:1)	14
II	Chloroform-acetone (9:1)	23
III	Chloroform-methanol (97:3)	45
IV	Chloroform-acetone-isopropyl alcohol (78:22:10)	70
V	Chloroform-acetone-isopropyl alcohol (33:6:1)	47
VI	Chloroform-acetone-isopropyl alcohol (8:1:1)	55

In these work we used the fluorescence properties of aflatoxin B1 for its detection. Aflatoxin B1 has blue fluorescence under influence long-wave ultraviolet light 365 nm. Also to confirm the presence of the analyzed compound iodine vapor was used. The colour and intensity of the fluorescence of the aflatoxin spots on chromatogramm is not changed under action of iodine vapour unlike other luminous compounds. Spraying plates with solutions of mineral acids change the color spots glow of aflatoxins to yellow. We counted coefficients of the mobility (Rf*100) and evaluated the compactness of the obtained spots.

The optimal zone of aflatoxin B1 on the chromatographic field was found in the solvent systems 2-6. In these conditions the work to assess the impact of ballast substances of different types of tea on the identification of the analyte was carried out (table 2).

Table 2

Identification of aflatoxin B1 in different types of tea

The object	Solvent system	Rf*100 ballast	Rf*100 aflatoxin B1
Ceylon black tea	IV	0-18 22-33 68-75	70
	II	0-19 59-66 74-80	23
	III	0-19	45
Indian black tea	IV	5-80	67
	VI	5-80	55
	V	0-48 60-74	47
Gastric mixture of medicinal herbs	IV	0-93	59
	III	0-93	67

Conclusion. The analysis of gastric mixture of medicinal herbs revealed a significant effect co extraction substances. This fact complicates the use of this technique for identification of aflatoxin B1.

The difficulty of determining aflatoxin B1 on the chromatographic plate is observed when extract was obtained from the investigated sample of Indian black tea. Ballast prevent to identification analyte.

Experimental work with the sample of Ceylon black tea showed the suitability of the systems II and III for identification of aflatoxin B1 in this object.

DETECTION ETMOZIN BY REACTION STAINING AND BY TLC

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Introduction. Aetmozinum - 2 karboetoksiamino-10-(3-morpholino-propionyl) phenothiazine hydrochloride - refers to antiarrhythmic drugs of class I (hinidinopodobnyh action), used in the beats, paroxysmal tachycardia and atrial fibrillation paroxysms occurring in coronary heart disease, arrhythmias and other etiology. Etmozin includes preparations of the list B. Forensic medical diagnosis of intoxication etmozin is a difficult task. This is one hundred clinical picture of poisoning with medication is uncommon. Moreover, it does not cause a specific morphological changes in the organism. Therefore, the development of methods of forensic chemical analysis etmozina is an urgent task.

Aim. The aim of our work is to develop a detection etmozina conditions in the presence of other drugs with similar pharmacological effects, with color reactions and TLC.

Materials and methods. Color reactions are performed on the white ceramic plates, using a 0.05% solution in ethanol etmozina obschealkaloidnye and reagents: Stamps, Mandelina, Erdman, Lieberman, Fred. To detect etmozina TLC glass plates used for high-performance thin layer chromatography (HPTLC, silica KSKG fraction 5:20 mkm, thickness of 130±25 mkm), Sorbfil plate (silica gel CTX-IA, fraction um 5:17 mkm), glass plates firm Merck (Germany) (silica gel GF-254) solvent system movable neutral and alkaline character.

Results and discussion. Of all studied color reagents for the most sensitive etmozina detection reagents were Mandelina and Lieberman (10 mcg in the sample). The most optimal solvent systems, which lead to reliable values of the quantity Rf (0.2-0.8) are HPTLC plates, hexane: ethyl acetate-ethanol-ammonia (30: 10: 5) (Rf = 0.40), hexane-toluene-diethylamine (20: 15: 5) (Rf = 0.58). Sorbfil plates, hexane: acetone: ammonia (20: 20: 1) (Rf = 0.45) and chloroform-cyclohexane-diethylamine (5: 4: 1) (Rf = 0.42). Heel etmozina showed showed reagents Dragendorff, Lieberman and Mandelina. The most sensitive reagent proved Dragendorff (detection limit of 0.5 micrograms of the drug in the sample).

Conclusions. The results of this analysis can be used in forensic chemical analysis etmozin.

IDENTIFICATION TUSUPREKSA BU CHROMATOGRAPHY IN THIN LAYERS OF SORBENT

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Introduction. Tusuprex (Oxeladin) – citrate α, α – dietilaminoetoksietil-phenylacetic acid - antitussive drug used in medicine and in the treatment of bronchitis, tracheitis, acute stage proceeding in a dry cough. Compared with codeine tusupreks has a softer effect, does not inhibit breathing, does not cause drug dependence and addiction, so after a long phasing out its use is not required. Application tusupreksa with hypnotics and sedatives may enhance their effect. This drug is of interest in chemical-toxicological respect.

Aim. Our aim is to develop tusupreksa detection conditions in the presence of other drugs that have similar pharmacological action, by chromatography sorbent in thin layers (TLC).

Materials and methods. We used glass plates for high performance thin layer chromatography (HPTLC, silica KSKG fraction 5:20 mkm, thickness of 130±25 mkm), Sorbfil plate (silicagel SLC-IA, fraction 5:17 mkm), glass plates from Merck (Germany) (silicagel GF-254) solvent system movable acidic, neutral and alkaline character.

Results and discussion. The most optimal mobile solvent systems for identification are tusupreksa system: methanol – ammonia (100:1.5), (R_f = 0.44), 1-butanol - acetic acid - water (66:17:17) (R_f = 0.54), hexane - toluene - diethylamine (75:15:10) (R_f = 0.55), toluene - ethylacetate - diethylamine (30: 20: 1.5) (R_f = 0.59). We investigated the possibility of separating tusupreksa with other drugs with similar effects. The separation achieved in the systems methanol – ammonia (100:1.5), ethylacetate - methanol - diethylamine (30:20:1.5). To display tusupreksa in thin layers of sorbent used various developers. It is set at a number of developers: bromophenol blue, iodine vapors, reagent Dragendorff in various modifications. Most sensitive is the Dragendorff reagent, whereby 0.1 mkg of the drug in the sample was detected.

Conclusions. The research results can be used during the chemical-toxicological analysis tusupreks.

ANALYSIS OF DOSAGE FORMS CONTAINING VITAMIN B6 BY IONOMETRIC METHOD

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Introduction. Pyridoxine hydrochloride - is a watersoluble vitamin of the B group. Its application improves the absorption of polyunsaturated fatty acids, delays the congestion of cholesterol, lipids and calcium on the walls of blood vessels, which prevents the development of atherosclerosis. In the human body, vitamin B6 is phosphorylated and forms of pyridoxal phosphate, pyridoxamine and pyridoxal usually in an amount of 2-3% per day of the total pyridoxine. This leads to a lack of pyridoxine in the body, as well as appearance of hypovitaminosis and deficiency disease, which are manifested in the form of dermatitis, epileptic seizures, and bone marrow hypofunction. In this regard there is actual development of simple and rapid techniques of pyridoxine hydrochloride analysis.

The literature describes methods of analysis of pyridoxine hydrochloride using as a titrant silver nitrate solution with a visual and a potentiometric indication of equivalence point. However, the proposed methods are not specific because do not allow to analysis of pyridoxine hydrochloride by biologically active moiety of the molecule. Now this approach is low acceptable.

Materials and methods. Based on this, the most perspective is the method of direct potentiometry (ionometry). The literature describes the pyridoxine-selective electrode based on ion associate of pyridoxine hydrochloride and sodium tetraphenylborate. However, this electrode has low electrode characteristics, making it difficult to use in the assay. Therefore, for the development of simple and rapid methods potentiometric analysis of pyridoxine hydrochloride in dosage forms, the task of developing and research pyridoxine-selective electrode based on ion associates with of pyridoxine heteropolyanions Keggin structure ($XMe_{12}O_{10}$,где X(P,Si);Me(Mo(VI);W(VI)) has been put.

Preliminary studies have shown that as the electrode-active substance is necessary to use of pyridoxine ion associate with phosphorus tungstic acid. The composition of the solidstate membrane pyridoxine-selective electrode is (w%): polyvinyl chloride 26±4, dibutyl phthalate 50±5, ionic associate of pyridoxine with phosphotungstic acid 17±3, activated carbon 4%.

Results and discussion. As a result of studies, it was found that the electrode function of the made pyridoxine-selective electrode is linear in the range of

concentrations of (6,0±0,2) · 10^{-5} - (1,0±0,1) 10^{-2} M with a slope of 56±2 mV, which corresponds to the characteristics of the ion-selective electrode (ISE) for the singly charged ion. Electrode response time is 20-30 seconds and potential drift of the week does not exceed 3-5 mV. Working resource of the electrodes is not less than 6 months. Consequently, pyridoxine-selective electrode may be used for potentiometric analysis of pyridoxine hydrochloride in solid and liquid dosage forms. Potentiometric analysis of pyridoxine hydrochloride in the following dosage forms: injectable solutions with a concentration of 1% of pyridoxine hydrochloride, 2.5% and 5%, and tablets containing of pyridoxine hydrochloride and 0.01 g 0,002g has been carried out by using the developed pyridoxine-selective electrode. For analysis electrochemical circuit with salt bridge was used consisting of two electrodes: pyridoxine-selective electrode and reference electrode. As the reference electrode – the silver-chloride electrode was used EVL-1 MZ. Measurements of electromotive force carried out on the ionomer I-130. Analysis was performed by tightinterval testing of two-point calibration curve. For this purpose, we set the concentration range in which the dispersion of the points of dispersion with respect to So^2 straight line does not exceed 0.5 mV. To do this, we calculated the parameters a and b, and the value of So^2 for the equation E = a + b · lg by ordinary least squares. It was found that this concentration range is 10^{-2}-10^{-3} M.

To perform the measurements two standard solution of pyridoxine hydrochloride was prepared. The concentration of the first standard solution (C_1) is equal to 10^{-2}M of pyridoxine. The second standard solution was prepared by ten-fold dilution of the first, the concentration (C_2) is 10^{-3} M of pyridoxine. The sample solution was prepared so that the concentration of pyridoxine hydrochloride fell into within a range of concentrations of the tightinterval calibration curve: 10^{-2}-10^{-3} M. Next electromotive force of circuit in standard (E_1 and E_2) and the sample solution (E_x) was measured. The concentration of pyridoxine hydrochloride (C_x) is calculated by formula:

$$Cx=C_1\text{-antilg}(Ex-E_1)/(E_1-E_2)$$

Conclusions. The results of ionometric analysis of pyridoxine hydrochloride in the dosage forms are characterized by sufficient precision and reproducibility. Proposed method analysis is simple and rapid and does not require the use of expensive reactants and reagents. The relative uncertainty of the analysis does not exceed 2%, which corresponds to the requirements of technical documentation of the dosage forms.

PECULIARITIES OF IDENTIFICATION OF SODIUM BENZOATE AND SODIUM SALICYLATE IN COMPOUNDS WITH THE TEST-SYSTEM WITH CUPRUM (II) SULPHATE

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Introduction. The use of test-detection and test-systems techniques can simplify and speed up the procedure of the inner pharmacy extemporal medicines (EM) components quality control to a great extent. While conducting former experiment test-systems based on filter paper modified through physical immobilization with heavy metals salts (Fe^{3+}, Cu^{2+}, Co^{2+}) were used. The objects of studies were medicinal substances in mono-component dosage forms which combining with salts mentioned above can make coloured chelate complexes.

Aim. The aim of this work is to check and prove the possibilities of using test-system based on the filter paper modified with the aqueous solution of $CuSO_4$ for identification of sodium benzoate and sodium salicylate in mono-component solutions and in compounds.

Materials and methods. Test-system modified with heavy metal salt $CuSO_4$, 2% aqueous solutions of sodium benzoate and sodium salicylate and their compound in relation 1:1.

Results and discussion. As a result of the conducted study it was defined that the test-system under investigation allows to identify sodium benzoate and sodium salicylate in mono-component aqueous solutions. While examining the components compound it was defined that an intensive grassy green colouring with the spot of fur in the middle occurs on the surface of the test-system. This effect allows to identify simultaneous presence of both preparations under investigation in a solution.

Conclusions. Test-system based on filter paper with cuprum (II) sulphate enables to identify investigated substances in mono-component solutions and in compounds.

DETERMINATION OF THE SPECIFIC ABSORPTION OF THE 5-HYDROXYMETHYLFURFURAL FOR QUANTITATIVE DETERMINATION OF INULIN BY UV-SPECTROPHOTOMETRIC METHOD

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Introduction. Spectrophotometric method by specific absorption is recommended for quality control of various pharmaceutical substances in State Pharmacopoeia of Ukraine (SPhU), European, British, International Pharmacopoeias and Pharmacopoeia of USA. Spectrophotometric method by specific absorption is characterized by simplicity of execution, economic and does not require the use of standard samples.

Aim. 5-hydroxymethylfurfural (5-HMF) – is the product of the inulin substance after acid hydrolysis. The aim of our work is experimental determination of the specific absorption of 5-HMF.

Materials and methods. The substance of inulin manufactured by Alfa Aesar No. A18425 batch number H5597 was used in the experimental researches. The analytical balance AV 204 S/A METTLER TOLEDO was used. Reagents, measuring glass-ware of class A (first class) and excipients meeting the requirements of the SPhU were used for the work. The spectrophotometer "SPECORD 200" was used in the work. The measurements were performed with 1-cm cells at (20±1) °C.

Results and discussion. The specific absorbance of 5-HMF obtained in the course of hydrolysis has been determined experimentally. The absorption maximum of 5-HMF is at the wavelength of 285 nm. The results of determination of the specific absorption ($A_{1см}^{1\%}$) of 5-HMF are shown in Table.

Tab. The results of determining of the specific absorption ($A_{1см}^{1\%}$) of 5-HMF.

№	Introduced inulin, g/ml·10^{-5}	The optical density, A*	$A_{1см}^{1\%}$	Metrological characteristics
1	2.56	0.5978	252.92	$\overline{X}$=258.16
2	2.88	0.6880	258.72	S = 3.00
3	3.20	0.7679	259.91	$S_{\bar{X}}$=1.34
4	3.56	0.8415	258.93	$\Delta\bar{X}$=2.86
5	3.84	0.9229	260.31	$\bar{\varepsilon}_{\bar{X}}$=1.11%

* – the average value of three measurements

Conclusions. According of the results of study of the dependence of absorbance on the concentration of inulin substance in the solution the specific absorption of 5-HMF for substance inulin is 258±2.86.

«KROKUEMO» WITH ANALYTICAL CHEMISTRY

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Introduction. The proposed work is devoted to the analysis of the results of the dates of the license integrated examination "Krok 1" by students of the National University of Pharmacy in 2015.

Aim. The object of the study were the results of the license tests by students of specialty "Pharmacy" full-time education with a basic high school education and pharmaceutical schools. Analysis of the results of delivery of the license integrated examination "Krok 1" by students on discipline analytical chemistry from 2010 showed a rather low rating results in comparison with other disciplines - in the range of 6-8 place from 8, indicating that certain systemic difficulties in the study of analytical chemistry on II curriculum, and in the process of preparing for the exam "Krok 1".

Materials and methods. In order to improve the results of the license exam on the discipline of the study was carried out a survey of students IV course of the specialty "Pharmacy" and III course specialty "Pharmacy-SSE".

Results and discussion. We developed a questionnaire, in which respondents were asked:

- to assess the complexity of the discipline analytical chemistry as such;
- differentiate the degree of difficulty of mastering test for analytical chemistry in blocks qualitative, quantitative and instrumental analysis methods;
- identify the best answer to the algorithm tests for analytical chemistry (memorizing correct answer, use the system knowledge on the subject; search for "tips" in the formulation of the test; intuitive response);
- determine the most appropriate algorithm for the student to prepare for the test (sequential test study of each discipline, part of the exam, a comprehensive training in booklets of previous examinations; computer testing to obtain maximum results).

We, too, were interested in the time factor in preparing for the tests and sources of information (training and monitoring).

Conclusions. In the course of the survey were interviewed 355 students, representing 90% of pass rate. The survey was not anonymous for the purpose of correlation of the responses received to the results of the exam. The results are presented in the form of statistical data and recommendations for students who have yet to take part in the "Krok 1" licensed integrated examinations.

SELECTING THE CONDITIONS OF ANILOCAINE'S CHROMATOGRAPHIC DETERMINATION IN BIOLOGICAL OBJECTS EXTRACTS

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Introduction. Anilocaine is a local anesthetic of the amide type, that was synthesized in the Perm State Pharmaceutical Academy. It is effective in different kinds of anesthesia, such as surface, infiltration, conduction and spinal. Following formulations, based on anilocaine were developed and brought to the medical use: 1% and 2% injectable solution, 5% topical solution, "Anicol" ointment, bandages long-acting. The implementation of suppositories, films, drugs, anesthetic gel, aerosol in medical and veterinary practice suppositories, is planned in the future.

Purpose. It is necessary to conduct a step of pharmacokinetic study in the introduction of new drugs in medical practice. In this connection, there is a need for highly efficient and sensitive methods of substances detection in human's and laboratory animals biological material. High performance liquid chromatography is the most popular method of pharmacokinetics. Selecting of chromatographic conditions for determination analocaine in extracts from biological objects by micro high performance liquid chromatography is the purpose of this work.

Materials and methods. The high pressure liquid chromatographic system consisted of HPLC model "Milchrom A-02" contains UV-detector. Chromatographic analysis was performed using ProntoSIL 120-5 C18 AQ analytical column (75×2 mm).

Results and discussion. Chromatographic analysis was carried out at 40 °C temperature. Optimal separation of anilocaine and endogenous components were achieved by gradient elution of C18 column. The mobile phase was a mixture of 0,1% trifluoroacetic acid: acetonitrile pumped at a flow-rate of 0,1 mL/min. Detection was set at a wavelength of 210 nm. The retention time of anilocaine was about 9.5 min. In developed chromatographic conditions extracts from biological objects (urine, blood plasma, liver, kidney laboratory animals) were analyzed. No additional peak due to endogenous substances that could have interfered with the detection of anilocaine was observed. The resolution (R) between the peak of anilocaine and the nearest peaks is at least 6, indicating the excellent separation.

Conclusion. The described chromatographic conditions are precise and rapid and can be used for pharmacokinetic studies of anilocaine drugs.

USE OF RAMAN SPECTROSCOPY TO IDENTIFY THE PARACETAMOL

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Introduction. At the present time the Raman spectroscopy is one of the promising direction in pharmaceutical practice. Raman spectroscopy is the method of study the vibrational, rotational, and other low-frequency modes of the tested substance in the range from 100 to 4000 cm^{-1}, based on the phenomenon of inelastic (Raman) scattering of monochromatic light in the visible, near UV or near-IR.

Aim. Develop a new methodology for assessing the quality indicators of medicines on the basis of Raman spectroscopy, and substantiate the significance of its implement into practice of pharmaceutical analysis.

Materials and methods. For obtaining Raman spectrum is used the device Raman spectrometer, which is produced by US company «Enhanced Spectroscopy» of the brand «R532». The measurement was carried out at room temperature.

The object of the analysis were paracetamol tablets. For studying the spectrum of the drug analysis was conducted with its working standard sample (Hebei Jiheng (Group) Pharmaceutical CO., LTD., China). The data is transmitted from the device to a computer via a USB port.

Results and discussion. This study shows that the Raman spectrum of the tablet paracetamol appropriate of its working standard sample. Their characteristic peaks is situated (2926, 3061, 3322 cm^{-1}) in the same area as the standard of paracetamol (Fig.1).

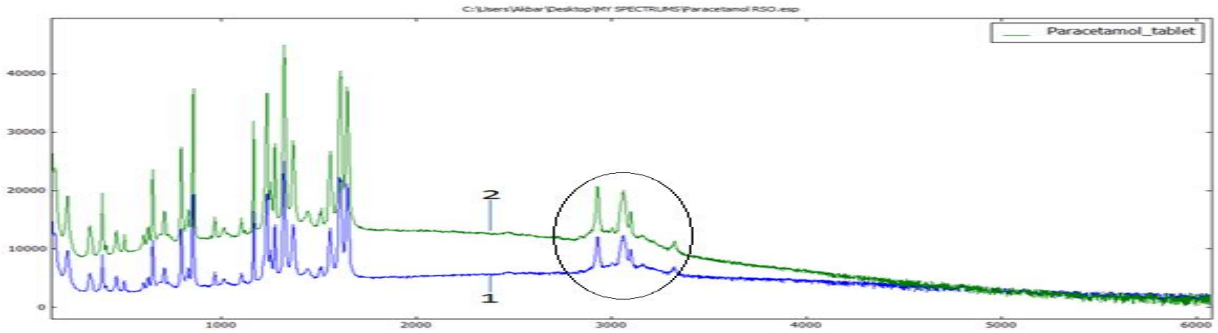

Figure. 1*- spectrum of the standard sample; 2-spectrum tablets.*

Conclusion: For the first time were obtained Raman spectra of a standard sample paracetamol. It has been found that in Raman spectrum of the paracetamol tablets there are peaks characteristic for its working standard sample. The obtained data can be used in the pharmaceutical industry for the verification of cleaning equipment process in the manufacture paracetamol.

STANDARDIZATION OF ALLTROMBOSEPIN CAPSULES

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Introduction. Currently the whole world is strong interest in herbal medicines. Among the vegetable raw materials bulb onion (Allium cepa L.) has great prospects. "Alltrombosepin" was obtained by fermentation of bulb onion. Preclinical studies showed that it has antiaggregant action.

Aim. Selection of composition and technology for Alltrombosepin capsules and development of their standardization methods.

Materials and methods. The substance and capsules of Alltrombosepin; research methods for Alltrombosepin substance and capsules.

Results and discussion. The optimum composition of the capsule mass selected on the base of study of technological properties of Alltrombosepin powder and 6 compositions of the capsule mass is: Alltrombosepin substance - 100 mg, aerosil - 15 mg, starch - 33.5 mg, calcium stearate - 1.5 mg. Qualitative parameters of Alltrombosepin capsules were studied in accordance with SP XI. The results obtained are shown below: orange color hard gelatin capsule with size №2 filled with from grayish-yellow to light-yellow powder possessing a sharp specific taste and smell. The average weight of the capsule contents must be 0.15±10%. Humidity. 5.0 g of a powder was dried at temperature 100±5°C to constant weight. The weight loss on drying must be not more than 15%. Disintegration. Not more than 20 min. Heavy metals. Approximately 1.0 g (accurately weighed) of the capsule contents must pass the test for heavy metals. Reference was prepared using a reference solution of lead (not more than 0.01%). Identity. 0.15 g of preparation was dissolved in 10 ml of water and the solution was filtered. To 3 ml of the solution was added 2 drops of 0.1 mol/l potassium permanganate solution. Color of potassium permanganate solution disappeared (unsaturated organic sulfur compounds).Assay of the sulfur organic compounds. 20 capsules were weighed. About 1.5 g (accurately weighed) of preparation was placed into a test tube, suspended in 10 ml of 70% ethanol. The solution was subjected to a processing on ultrasonic bath for 10 min and centrifuged at 3000 rpm. The precipitate was resuspended in 10 ml of 70% ethanol and the extraction was repeated in the same conditions. The solution obtained was united and transferred into a 25 ml volumetric flask and diluted to volume required with 70% ethanol and stirred. The solution preliminarily was subjected to a mineralization in the presence of sodium zinkate, then it was analyzed by spectrophotometric method. After the absorbance of the solution was measured by a spectrophotometer at a wavelength of 665 nm in a cuvette with a layer thickness of 10 mm. In parallel, the absorbance of 3,3'-dithiodipropane acid RS solution was measured. As a blank solution was used a solution consisting of a mixture of all the reagents used for the analysis, without extract. The amounts of organic sulfur compounds in the preparation based on on 3,3'-dithiodipropane acid must be at least 0.1 mg per capsule.

Conclusions. For the first time the quality control methods were developed for Alltrombosepin capsules.

APPLICATION OF HPLC AND GLC IN THE ANALYSIS OF METRONIDAZOLE

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Introduction. Metronidazole is attributed to the group of antiprotozoal medicines and widely used for treatment of infectious diseases, at the same time it is possessed of quite a number of side effects showed by classic symptoms of acute intoxication, especially when interacting with alcohol.

Aim. The research purpose is to develop the conditions of metronidazole detection and identification by the methods of high-performance liquid and gas-liquid chromatography.

Materials and methods. Metronidazole of pharmacopoeial purity was used in the experiment; its solutions in ethanol with the concentration from 1 μg/mL to 0.1 μg/mL were prepared.

Conditions of HPLC-analysis (the volume of injection – 100 μL): device – MiLiChrome® A-02; column – ∅2×75 mm, reversed phase ProntoSIL-120-5-C18 AQ; temperature – 40ºC; eluent A – 0.2 mole/l $LiClO_4$ – 0.005 mole/l $HClO_4$; eluent B – CH_3CN; flow – 100 μL/min.; gradient elution mode – linear from 5% to 100% CH_3CN for 40 min., then 100% CH_3CN for 3 min.; detector – UV-spectrophotometer (210, 220, 230, 240, 250, 260, 280, 300 nm).

Conditions of GLC-analysis (the volume of injection – 2 μL): device – HP 6890 Hewlett Packard; column – HP-1 ∅0.32 mm × 30 m, 0.25 μm, the thickness of layer of 100% dimethylpolysiloxane of 1 μm; temperature of the column thermostat – 70ºC (3 min.), increasing the temperature with the rate of 40ºC/min. to 180ºC (keeping for 2 min.), increasing the temperature with the rate of 40ºC/min. to 250ºC (keeping for 3 min.); injector temperature – 280ºC; detector – flame-ionization; detector temperature – 280ºC; volume rate of carrier gas (helium) – 1.5 ml/min; stream dividing – 1:2.

Results and discussion. Under the given conditions of HPLC-analysis the retention time for metronidazole is 5.85 min. The spectral ratios relation to λ = 210 nm are determined, and it has been shown that detection at λ = 280 nm or 300 nm is optimal. Limit of detection is 0.3 μg/mL (calculated by the ratio of «signal/noise»).

Under the given conditions of GLC-analysis the retention time for metronidazole is 9.077 min. Limit of detection is 0.1 μg/mL (calculated by the ratio of «signal/noise»).

Conclusions. The conditions of metronidazole detection and identification by the methods of high-performance liquid and gas-liquid chromatography have been experimentally fitted.

APPLICATION OF TLC IN THE ANALYSIS OF SECNIDAZOLE

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Introduction. Secnidazole is attributed to the group of antiprotozoal medicines and widely used for treatment of infectious diseases, at the same time it is possessed of quite a number of side effects showed by classic symptoms of acute intoxication, especially when interacting with alcohol.

Aim. The research purpose is to develop the conditions of secnidazole identification by the method of chromatography in thin layers of sorbent.

Materials and methods. Secnidazole of pharmacopoeial purity was used in the experiment; its solutions in ethanol with the concentration of 1 μg/ml and 0.1 μg/ml were prepared.

The chromatographic plates Sorbfil® PTLC-PH (silica gel STC-1HP, PETP, silica sol, 8 ÷ 12 μm fraction, 100 μm layer thickness) purchased from IMID LLC (Russia) were used as the thin layers.

Results and discussion. The chromatographic dealing of secnidazole has been studied in 18 mobile phases: 1. chloroform – acetone (8:2); 2. ethyl acetate; 3. chloroform – methanol (9:1); 4. ethyl acetate – methanol – 25% NH_3 (85:10:5); 5. methanol; 6. methanol – *n*-butanol (6:4); 7. methanol – 25% NH_3 (100:1.5); 8. cyclohexane – toluene – diethylamine (75:15:10); 9. acetone; 10. chloroform – dioxane – acetone – 25% NH_3 (47.5:45:5:2.5); 11. toluene – acetone – ethanol – 25% NH_3 (45:45:7.5:2.5); 12. chloroform – *n*-butanol – 25% NH_3 (70:40:5); 13. chloroform; 14. chloroform – methanol – CH_3COOH conc. (90:10:1); 15. toluene – CH_3COOH conc. (3:1); 16. toluene – methanol – CH_3COOH conc. (9:1:1); 17. ethyl acetate – methanol – CH_3COOH conc. (85:10:2.5); 18. chloroform – methanol (1:1).

When using the mobile phases 3, 5, 8, 9 the investigations were carried out also at the plates processed previously with 0.1 mole/l KOH solution in methanol and then dried at 110°C for 30 min. In the mobile phase 6 the plates were previously processed with 0.1 mole/l NaBr solution.

UV-light before and after processing with the vapour of HCl; the Dragendorff reagent modified by Munier and 0.1 mole/l KOH solution in methanol were used for developing the spots of secnidazole at the plates.

Conclusions. The chromatographic mobility of secnidazole has been studied under the conditions of TLC-screening using general and some separate systems of solvents. The reagents for the secnidazole spots development on chromatographic plates have been offered; their sensitivity has been ascertained.

DEVELOPMENT OF THE NON-AQUEOUS ALKALIMETRIK METHOD OF THE QUANTIFICATION OF 6- HYDROXY-4-OXO-1,2-DIHYDRO-4*H*-PYRROLO[3,2,1-*ij*]QUINOLINE-5-CARBOXAMIDE

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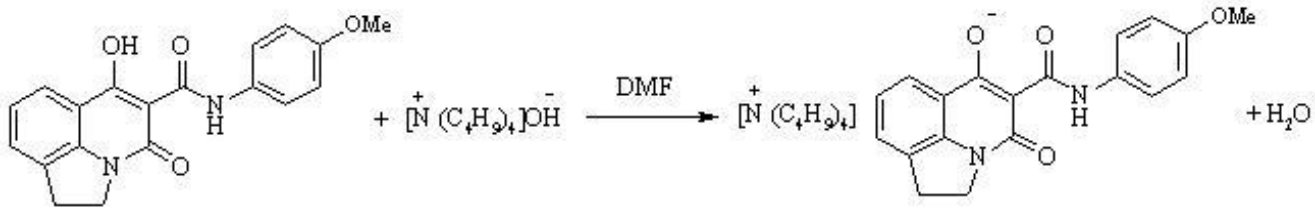
Introduction. The pharmacological properties of a series of amides of 6-hydroxy-4-oxo-1,2-di-hydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-5-carboxylic acid, which have been studied previously, allow us not only to establish certain regularities of relationship between chemical structure and pharmacological activity, but also to find practically non-toxic compounds with a high diuretic effect. Among the obtained substances the highest diuretic activity 6-hydroxy-*N*-(4-methoxyphenyl)-4-oxo-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline-5-carboxamide has.

Aim. Therefore one of the important objectives of our study was to develop a method for the quantitative determination of the most active compound in accordance with existing modern requirements for the introduction of drugs into medical practice.

Materials and Methods**.** Based on the chemical properties of the obtained compound we have chosen the method of non-aqueous alkalimetric titration. Titration was carried out in a non-aqueous solvent medium of dimethylformamide (DMF), universal organic solvent.



Results and discussions. As a titrant solution, the tetrabutylammonium hydroxide in 2-propanol was used, the end point is determined potentiometrically. A standardization of titrant solution and assay is performed in the same conditions for exclusion of additional errors.

Conclusions. The results were subjected to quantitative determination of statistical processing. The sample can be called reliable if options included in it are not burdened blunder.

DEVELOPMENT OF METHODS FOR IDENTIFICATION AND ASSAY FOR DRY EXTRACT OF LUPULI STROBILI IN COMPOSITION OF CAPSULES

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Introduction. Hop ordinary (Humulus lupulus L.) – a medicinal plant, widely used in officinal and folk medicine and cosmetology. Medicines from the hop cones have diverse pharmacological properties – sedative, analgesic, hypnotic and anti-inflammatory. The main compounds that determine the biological activity of hop cones are bitterness, flavonoids, phenolic compounds, as well as essential oil.

Aim. Specialists of the department of Industrial Technology of Drugs under the guidance of prof. Ruban E. A. are working to develop a new drug – the capsules with the dry extract of hop cones. After analyzing the proposal of the State Pharmacopoeia of Ukraine criteria, we concluded that the capsules with dry extract of hop cones are needed to standardize on such parameters: description, identification, uniformity of capsule contents weight, disintegration, microbiological purity, quantitative content of active ingredients.

Results and discussion. For identification of capsules with the dry extract of hop cones we propose to use the reaction to flavonoids (reaction of formation chalcones), phenolic compounds (with ferric (III) chloride) and use a thin-layer chromatography method in the system: butanol R – anhydrous acetic acid R – water R (4: 1: 2). The chromatogram of the test solution after spraying aluminum chloride solution should be observed for at least two bands: yellow band similar at position to the band on the chromatogram of the reference solution of the rutin and darker stripe yellow-orange band above the first band. The presence of other bands of varying intensity and staining is allowed.

For the assay of active substances in plant extracts non-specific physico-chemical methods of analysis are commonly used. These methods allow determining the full amount of related substances and conditional recounting them on any standard compound from this group. The obtained results are conditional, but allow to regulate the content of group of biologically active substances and thereby to standardize the extract. To quantify the amount of flavonoids we proposed a method based on interaction with the aluminum chloride, recalculated on the rutin, the presence of which was previously confirmed by TLC. The relative uncertainty of the average determination by this method is 2.061%.

Determination of the amount of polyphenolic compounds is carried out by adsorption UV-spectrophotometry at 270 nm, with the conditional recalculation result to gallic acid. The relative uncertainty of the average determination by this method is 2.124%.

Conclusions. The results of these studies will be used to create analytical documentation on capsules with dry extract of hop.

DEVELOPMENT OF METHOD FOR NITROFURAL QUANTITATIVE DETERMINATION IN COMPOUNDING OINTMENT

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Introduction. The large group of diseases, including dermatological diseases, is associated with damage of the certain type of microorganism. That's why antimicrobial products are widely used in medical practice. The main requirements for them are high activity and its retention in biological liquids; wide spectrum of antimicrobial activity; quick action at different pH value; high solubility; sufficient surface activity; and chemical resistance. Antimicrobial agents should not cause local irritation, sensitization and interrupt the process of wound healing.

General toxicity of the antimicrobial substance is taken into account for its evaluation. Antiseptic agents are divided into two groups: organic and inorganic origin. The first group includes Nitrofural, which is often used in many compounding dosage forms preparation, including ointments.

Aim. Development of the method for Nitrofural quantitative determination in compounding ointment in the presence of Procaine hydrochloride and Hydrocortisone butyrate.

Materials and methods. Spectrometer EV60 was used for the analysis. Absorption spectroscopy method was used for the quantitative determination of Nitrofural. The method is based on its ability to form a colored solution after reacting with Sodium hydroxide.

Results and discussion. Hydrocortisone butyrate absorption maximum is close to the absorption maximum of Nitrofural. Therefore, it will affect the accuracy of Nitrofural quantitative determination in the ointment by the absorption spectroscopy method. The ointment sample was dissolved in ether concidering the ability of Hydrocortisone butyrate to pass into the ether extract. Then, the extract was washed with water for three times. To complete Nitrofural extraction, Sodium chloride was dissolved in water. To form the colored compound, the solution of Sodium hydroxide was added to prepared water extract. Quantitative determination of Nitrofural was carried out using the absorption spectroscopy method at a wavelength of 440 nm.

Procaine hydrochloride also passes into the water extract but it will not affect the results of analysis, since its reaction with Sodium hydroxide will not lead to the formation of colored products.

Conclusion. As a result of research, the scheme for sample preparation and quantitative determination of Nitrofural in compounding ointment in the presence of Hydrocortisone butyrate and Procaine hydrochloride was developed.

IODOMETRIC DETERMINATION OF CEFEPIME IN THE REACTION WITH POTASSIUM HYDROGENPEROXYMONOSULFATE

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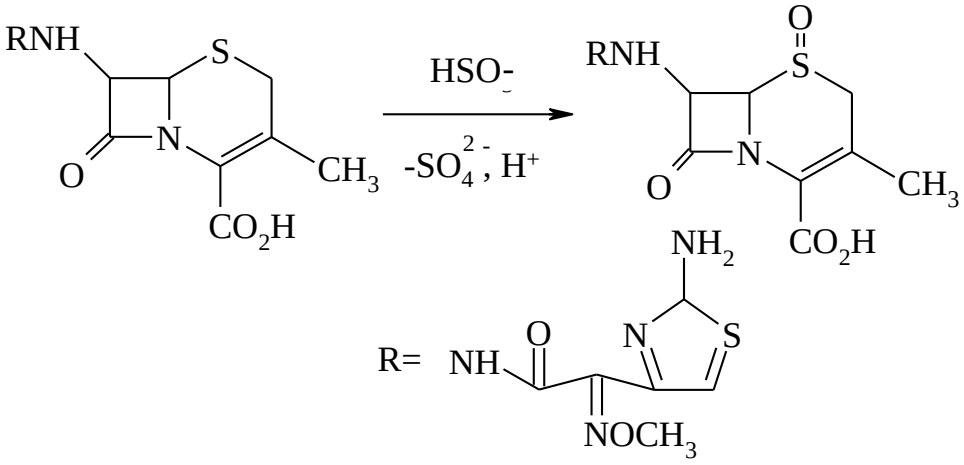
Introduction. Cefepime is a fourth-generation cephalosporin antibiotic. Cefepime has an extended spectrum of activity against Gram-positive and Gram-negative bacteria, with greater activity against both types of organism than third-generation agents. For the Cefepime assay State Pharmacopoeia of Ukraine (SPU) recommends to use the method of HPLC.

Aim. The development of a new procedure of quantitative determination of Cefepime content in pure substance and medical preparation by the oxidimetric method using potassium hydrogenperoxomonosulfate as analytical reagent was proposed.

Materials and methods. *Cefepime* pure substance and medical preparation (SPU requirements) were used. As oxidant potassium hydrogenperoxymonosulfate ($2KHSO_5 \bullet KHSO_4 \bullet K_2SO_4$), Acros Organics (Oxon) was used. The choice of the reagent was determined by its rather high oxidative activity, E_0 = 1.84 V, availability, and satisfactory solubility in water.

Results and discussion. The proposed method is based on quantitative S-oxidation reactions of Cefepime by potassium hydrogenperoxomonosulfate in an acidic medium. The excess of oxidant-reagent was determined by iodometric titration.



The time of stoichiometric interaction does not exceed 1 min. The limit of detection is 0.02 mg mL^{-1}. For Cefepime pure substance RSD=1.67 % (accuracy δ=1.02 %), for powder for injections RSD=2.65 % (accuracy δ=-0.17 %).

Conclusions. Cefepime S-oxidation reaction by means of potassium hydrogenperoxomonosulfate can be applied into analytical practice. The proposed method is high sensitivity, precision and reliable. The absence of expensive device, toxic solvents and special facilities as in HPLC method are the advantages of the procedure. It is simple and rapid in application.

METROLOCAL ASSESSMENT OF THE REFRACTOMETRICY METHOD FOR QUANTITATIVE DETERMINATION OF PHARMACY COMPOUNDING SOLUTION

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Introduction. In the pharmaceutical analysis refractometry method is used to identify of substances, assess their purity and for quantitative analysis. The refractometry method is used widely in the practice of pharmacy control to assess the quality of the preparation of concentrated solutions, liquid dosage forms made for the future compounding.

Monograph 2.2.6 of State Pharmacopoeia of Ukraine (SPhU) "The refractive index (refractive index)" is harmonized with the requirements of the European Pharmacopoeia (EPh) and gives a description of the method, the instrument calibration rules, standard terms and conditions for carrying out tests to refractometric analysis and requirements for the refractometric equipment that must be met. The national part of this monograph contains additional conditions for the application of the method for quantification of the substance in the solution: the accuracy of the measurement of the refractive index must be not less than $\pm 2\times10^{-4}$. Allowed calibration with purified water, for which the refractive index is $n_D^{20} = 1{,}3330$, the value of the temperature coefficient must not exceed ($\frac{\Delta_n}{\Delta_t} = 0{,}000085$).

Aim. The aim of our work is experimental determination of the metrological characteristics of refractometry method for the quantitative determination of model solution of sodium hydrogencarbonate 5% according to the requirements of SPhU.

Materials and methods. The analytical balance AV 204 S/A METTLER TOLEDO was used. Reagents, measuring glass-ware of class A (first class) and excipients meeting the requirements of the SPhU were used for the work. The refractometer RL 3 was used in the work. The refractometer RL 3 is characterized by the scale of the refractive index from 1.3 to 1.7; scale division is equal 0.001; the accuracy of determination - $\pm 2\times10^{-4}$ meeting the requirements of the SPhU. The substance of sodium hydrogencarbonate manufactured by Biesterfeld Siemsgluss International GmbH" Hamburg, Germany No. 060125 meeting the requirements of the BPh 98/USP30/SPhU was used in the experimental researches. The measurements were performed with at ambient temperature 20 °C±0.5 °C.

The validation parameters - linearity, precision, accuracy, reproducibility was investigated throughout the range of application methods performed by a standardized procedure. In the process of determining the refractive index of purified

water (n_0) and model solution (n) with concentration (C_x) was measured three times. The content of sodium hydrogen carbonate C_x is calculated by the formula: $C = \frac{n-n_0}{F}$, in which C – the concentration of substance: n - the refractive index of solution; n_o - the refractive index of purified water; F - the value of the refractive index growth of sodium hydrogencarbonate with increasing concentration by 1%.

Preparation of the test solution. 4.9411 g (exact sample) RS placed in a volumetric flask of 100 ml, added 40 ml of purified water and stirred until dissolved sodium hydrogencarbonate, dilute with water to volume, and mix.

Preparation of model solutions. Model solutions were prepared according to the range of concentration from 60 to 140% of the concentration specified (60, 80, 100, 120, 140%). Sample weights 3.0330 g; 4,0150 g; 4.9411 g, 5.9680 g and 7.0265 g were accurately weighed. Prepared like a test solution.

Results and discussion. The results of quantitative determination of sodium hydrogencarbonate 5% in aqueous solution by refractometry allow to conclude that if content tolerances is ±2% it is not possible to conduct a correctly quantitative definition by this method. The validation characteristics of the refractometry method (Table) for quantitative determination of hydrogencarbonate 5% in aqueous solution have been investigated. These results allow recommending the refractometry method for quantity control of sodium hydrogencarbonate with the permissible limits of ±5%.

Table

The results of the statistical evaluation of the metrological characteristics of methods of quantitative determination of sodium hydrogencarbonate by refractometry.

Test data			Theoretical data			
Relative confidence interval of single results			Maximum permissible uncertainty of the method, $max\Delta_{As}\%$		Prognosis of total uncertainty, $\Delta_{As}\%$	Permissible limits, B%
Lab. 1	Lab. 2	Inter laboratory				
$\Delta_{x,r}^1$	$\Delta_{x,r}^2$	$\Delta_{x,r}^{intra}$	±2%	±5%		
3.3	1.6	3.0	0.64	1.6	3.2	10

Conclusions. The prognosis of total uncertainty $\Delta_{As}\% = 3{,}2\%$ exceeds the maximum permissible uncertainty for the permissible limits of ±5%. For correct quantitative determination of sodium hydrogencarbonate by refractometry is recommended to use with the permissible limits of ±10% or to use refractometer with limit of permissible error of the refractive index which is not higher $\mathbf{n_D}$ - $\pm 1\times10^{-4}$.

SECTION № 4

TECHNOLOGY PHARMACEUTICAL, PERFUMERY AND COSMETIC PRODUCTS

THE RELEVANCE OF DRUG DEVELOPEMENT TO TREAT TYPE 2 DIABETES

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Introduction. Diabetes mellitus (DM) is endocrine disease, which is characterized by a chronic increase in blood sugar levels due to absolute or relative deficiency of insulin, which is the hormone of the pancreas.

The disease leads to disruption of all types of metabolism, vascular damage, nervous system and other organs and systems.

Type 2 diabetes include relative insulin deficiency. It is no less alarming the fact that type 2 diabetes is on the third position among the immediate cause of death after cardiovascular diseases and cancer.

For this reason, the main goal is to treat the disease as much as possible full compensation of carbohydrate metabolism disorders.

Currently, an effective treatment of type 2 diabetes is aimed to prevent pancreatic β-cells by depletion of glucose an optimal balance in the organism, preventing and / or slowing the progression of complications that lead to disability and early death of patients.

Purpose of the research. The relevance of drugs development to treat type 2 diabetes.

Materials and methods. It was used systematic, structural, and logical analysis, comparative analysis and graphical method of data generalisation.

Results and discussion. The following groups represent pharmacological preparations for type 2 diabetes correction, which are used in the clinic nowadays: sekretogeny insulin (sulfonylureas), biguanides (metformin), insulin sensitayzery (rosiglitazone, pioglitazone).

The prevalence of this disease and the variety of pathogenic variants determine the relevance of the search and development of new oral antidiabetic drugs. Recently, in the treatment of insulin-dependent diabetes it has been prefer medicines that can not only compensate for diabetes, but also to delay its development and progression of its complications.

Nevertheless, for a number of drugs, there are significant limitations in the use, because of the risk of side effects.

Conclusion. The results of the research of the domestic pharmaceutical market and frequency of disease indicative of the need for new can not only regulate glucose homeostasis, but also warning the risk of type 2 diabetes complications.

THE RELEVANCE OF CREATION OF THE ALLOPATHIC AND HOMEOPATHIC SUPPOSITORIES WITH ANTI-ALLERGIC EFFECT FOR CHILDREN

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Introduction. Creation of new children's medicines in the rectal dosage form suppository is the necessary task of contemporary pharmacy practice. Suppositories is one of the perspective solid dosage forms thanks to some advantages. They are high bioavailability, reducing the risk of side effects, no unpleasant taste and smell, снижение риска побочных эффектов, отсутствие неприятного вкуса и запаха, the ability to apply the drug in case of failure to take medications «per os» and others. The given dosage form successfully is used not only in traditional medicine, but also in homeopathic.

Today the prevalence of allergic diseases is observed. Recently allergy has become one of the most pressing biomedical problems in the world. The rapid growth of the number of allergic diseases among children are most upset. Every fifth child suffers from allergies, including 40.4% of respiratory allergy, 24.2% – allergic skin lesions, 23.4% – polynosis.

The aim. The aim of this work is to demonstrate the relevance of the creation of new drugs anti-allergic action applied in allopathic and homeopathic medicine.

Materials and methods. Research carried out by the analysis of the literature data.

Results and discussion. According to the literature review today the pharmaceutical market of Ukraine there are no medicines in the dosage form of suppositories for children.

Over the past few years, growth trends number of allergic diseases occur throughout the world, including such as atopic dermatitis, allergic rhinitis and asthma. Unfortunately, in Ukraine due to the imperfection of medical statistics the prevalence of allergic diseases, their medical and social consequences are unknown.

In connection with the situation in front of doctors and patients the problem of choice of effective treatments and medicines appears, especially antihistamine profile. The choice of drugs should be based on the principles of evidence-based medicine, that is research-based evidence obtained as a result of properly conducted studies.

Conclusions. From the above it can be concluded that the new antiallergic medicines for treating various allergic diseases necessary to develop, and new medicines to children used in allopathic and homeopathic must be created.

PHARMACO-TECHNOLOGICAL TESTS OF FAST DISSOLVING TABLETS WITH ANTIMICROBIAL ACTIVITY

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Introduction. Fast dissolving tablets are becoming popular as one of the dosage forms. Such tablet disintegrates rapidly when placed on tongue, releases the drug that dissolves or disperses in the saliva. Some medicines have already been presented on the market by several pharmaceutical companies. Suitable drug candidates for such systems include antimicrobial medicines.

Ofloxacin is a synthetic broad-spectrum antibiotic which used to treat many infections. The bioavailability of this drug in the tablet form is approximately 98 %. The composition of fast dissolving tablets with ofloxacin was formulated at Industrial Phamacy department. The research work was supervised by Associate Professor Sichkar A.A.

Aim. The evaluation of the prepared tablets for all pharmaco-technological parameters.

Materials and methods. The following research methods are used for tablets according SPhU: determination of the resistance of tablets to crushing, the friability, disintegration time. The immersion liquid is purified water at 37±2 ºC. The wetting time of the tablets was measured by special procedure.

Results and discussion. The tablets of ofloxacin were white in color with a yellowish tint and smooth surface. Weight variation of all formulations was found to be within the range of 398 mg to 403 mg.

A tablets require certain value of hardness to withstand the mechanical shocks during packaging and at the time of application. The resistance of prepared tablets to crushing varied from 45 to 50 N which show good mechanical strength with sufficient hardness. The friability of all the formulations with ofloxacin were found to be less than 1.0 % which was within the official acceptable limits. The results show resistance to loss of weight that indicates the tablet's ability to withstand abrasion in packaging and handling. The wetting time for all the formulations was found to be less than one minute for the optimized one which indicates faster disintegration of the tablet. The disintegration time of the tablets varied from 50 to 58 seconds. The tablets with increasing superdisintegrants amount may disintegrate quicker.

Now tablets are studied during storage.

Conclusions. The fast dissolving tablets with ofloxacin were estimated for all pharmaco-technological parameters which were found to be within the acceptable limits.

URGENCY OF CREATION DERMATOLOGICAL OINTMENT FOR TREATING DIAPER DERMATITIS

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Introduction. Diaper dermatitis is caused by overhydration of the skin, maceration, prolonged contact with urine and feces, retained diaper soaps, and topical preparations and is a prototypical example of irritant contact dermatitis. Signs and symptoms are restricted in most individuals to the area covered by diapers.

Diaper dermatitis commonly affects infants, with peak incidence occurring when the individual is aged 9-12 months. One study determined that at any given time, diaper dermatitis is prevalent in 7-35% of the infant population.

Urgency of this problem is defined not only by the continued growth of said disease, but by the inconsistency in evaluating different pathogenetic mechanisms of its development and, consequently, not always effective treatment results of existing medicines.

Aim is theoretical substantiation of active substances' choice for creation a new dermatological ointment for diaper dermatitis treatment.

Results and discussion. In terms of pharmacological properties most promising for use in the form of ointments with anti-inflammatory, anti-allergic and antimicrobial activity are medicinal herbs such as licorice root, grass herd, rosehip oil and essential oils of chamomile and tea tree. Extemporaneous prescriptions of ointments containing these plant components widely used in dermatological practice.

Extemporaneous ointments with chosen natural substances today prepare on the petrolatum base. For preparation ointments with these components on emulsion bases there are no data on the compatibility of the components, rational technology and stability.

In terms of the above and considering the rules of extemporaneous ointments preparation, we have developed composition of emulsion ointment with licorice root, essential oils of chamomile and tea tree, and its extemporaneous technology.

All these natural components have anti-inflammatory and anti-allergic properties due to their chemical composition (flavonoids, polysaccharides, triterpene saponins, sugars, etc.). The components of our proposed ointment emulsion base (corn oil, beeswax, emulsifier and hydrophilic phase) and their concentrations were determined based on rheological, osmotic and biopharmaceutical research.

Conclusions. Proposed ointment with licorice root, essential oils of chamomile and tea tree is promising for use as a medicine for the treatment of diaper dermatitis.

THEORETICAL SUBSTANTIATION OF ACTIVE SUBSTANCES' CHOICE IN DENTAL GEL "DENTAVIR-PHYTO"

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Introduction. In dental practice called stomatitis any inflammation of the mucous membrane in the mouth. The disease can occur in people of all ages perfectly. The most common cause of stomatitis is the lack of hygiene of oral cavity. However, the sores can appear and for other reasons, so it is also divided into several types: fungal, herpes, bacterial, etc.

Medicines of local action are a compulsory component of treatment of any kind of stomatitis. The purpose of their use – removing inflammation, pain and accelerating healing of ulcers, prevent infection. Today more and more of dentists in treating stomatitis recommend the usage of medicines based on natural plant material, the advantages of which are in focused therapeutic effect and the almost complete absence of side effects.

Aim is theoretical substantiation of active substances' choice for creation a new dental gel under conditional name "Dentavir-phyto".

Results and discussion. Among the known medicinal plants that can be used in the treatment of stomatitis, worth noting licorice, sage, peppermint and others. Licorice root extract was used in 1970 primarily only for the treatment of stomach ulcers. It is known that a licorice for 4000 years used as a reparative agent. Therapeutic opportunities of licorice root extract are due to the fact that licorice has anti-inflammatory and analgesic properties.

The most serious side effect of stomatitis is a sharp pain in the mouth, which can affect the quality of life (affect eating, language). Scientists have shown that in addition to the healing of ulcers in stomatitis licorice root extract helps reduce pain in just three days of treatment.

Sage is not by chance got its name, which comes from the word "salvia" – sun care. This plant is considered sacred in ancient times, honored her great physicians like Hippocrates and Dioscorides, and everything that sage has a strong disinfecting action, used in our time. Sage with stomatitis is used as an antimicrobial and astringent mean, which helps neutralize inflammation and dries oozing sores.

Mint for thousands of years is widely used in Western and Eastern medicine to treat various diseases; eliminates the pain and inflammation in caries, gingivitis and stomatitis.

Conclusions. So promising medicinal plant raw materials for creation of dental gel for the treatment of stomatitis can be licorice root extract, sage and peppermint.

ENCAPSULATION OF IODINE IN THE β-CYCLODEXTRIN BY "HOST-GUEST" METHOD

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Introduction. Iodine deficiency disorders are urgent public health problem for many countries of the world including the Republic of Uzbekistan. The elimination of iodine deficiency means the decision of one of the social problems of mankind. In this regard, creation of a iodine containing organic agent that will significantly replenish daily ration fed iodine in the organism is actual for normalization of iodine metabolism and prevention of iodine deficiency.

Aim. Selection of iodine encapsulation conditions in the β-cyclodextrin (β-CD) by "host-guest" method.

Materials and methods. Iodometric titration, method for the preparation of the "host-guest" complex.

Results and discussion. Experiments on the selection of conditions showed that the optimum ratio of β-CD and (I_2: KI) 6,5: (1:10); temperature – 25 °C, reaction time – 3 h. These conditions allow obtaining the desired product with the best yield (83.8%); with increasing of temperature complex yield is reduced. This is probably due to the volatilization of iodine at elevated temperature. At temperature below 25 °C, apparently, the active iodine molecules required to overcome the energy barrier of the reaction are unsufficient.

Complexes were prepared by the following procedure: crystalline iodine and potassium iodide weighed in a ratio of 1:10 were dissolved in 50 ml of purified water. Separately 6.5 g of β-CD was dissolved in a conical flask with a capacity of 250 ml in 150 ml of purified water. The flask was set on a magnetic stirrer and while stirring the contents of the flask a J_2: KJ solution was added drop wise; After the completion of addition of reagents, stirring was continued for another three hours. Then the mixture was left at 0 °C for 12 hours to allow iodine encapsulating in β-CD completely. The formed complex gave a brown precipitate. The precipitate was separated by vacuum filter and washed with 100 ml of 0.001 mol/l potassium iodide solution. The desired product – iodine-β-cyclodextrin is a shiny brown crystalline powder, insoluble in water possessing a weak smell of iodine.

Conclusions. Thus, for the first time the optimal conditions for obtaining the iodine-β-cyclodextrin complex were selected.

DEVELOPMENT OF MINERAL ENTROSORBENTA BASED ON BENTONITE CLAY OF NAVBAKHOR DEPOSIT OF THE REPUBLIC OF UZBEKISTAN

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Introduction. One of the areas of use of bentonite clays is a creation of enterosorbents to absorb toxins in the human body.

Aim. Colloid-chemical approach to the technology of enterosorbent obtained on the base of bentonite clays of Navbakhor deposit (field).

Materials and methods. The objects of research were an alkaline bentonite of Navbakhor deposit (field) and smectite substance (Pharm Medic).

Samples of clay minerals were purified from water-soluble salts of sand by elutriation in distilled water at a ratio of solid phase:liquid 1:20.

Then, the solid phase was separated from the liquid by means of centrifugation (repeated several times if necessary). The isolated solid phase was dried in an air heater dryer at 413 K to air-dry state. After the samples were subjected to dispersion in a laboratory ball mill and sieved through a sieve with hole size of 0.1 mm. These samples were subjected to chemical and structural analysis and their nature of surface and porosity were studied.

The chemical composition of the samples was determined by means of the silicate and atomic absorption analysis.The structure of the samples was studied using: x-ray phase differential-thermal, microscopic analysis and the method of adsorption of water vapor in the vacuum system with Mak Ben spring quartz balances.

Results and discussion. The obtained sorbent codenamed Navbahtit is a light-gray powder with slight earthy odor; ρH of 2% suspension – 7.0-8.6; bentonite number -80 ml; colloidality - 90%. Initial experiments to obtain Navbahtita substance showed that the process efficiency is influenced by several factors: the amount of water (hydromodul) used in the purification process, the multiplicity of purification, the multiplicity of centrifugation. The optimum values of these three factors were found by means of mathematical planning of experiment. As a result the optima factors were found: hydromodul - 1:20, the multiplicity of purification – 2, the rate of centrifugation – 8000 rpm.

Conclusions. Thus, for the first time the technology of purification of alkaline bentonite clays of special layer of Navbakhor deposit of the Republic of Uzbekistan was developed.

DETERMINATION OF PHARMACO TECHNOLOGICAL PROPERTIES OF ALVERINE CITRATE

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Introduction. The actual problem of modern medicine and pharmacy is the necessity of broad and effective elimination of spastic disorders that occur in many people who suffer from digestive diseases. One of the most effective solution to this problem is the creation of new and effective medicines with active pharmaceutical ingredient of broad therapeutic action.

Among of myotropic spasmolytics, which are used in the treatment of different functional disorders of the gastrointestinal tract, can be distinguished Alverine citrate. The main indications for its application are the elimination of spasms of smooth muscles.

Purpose. Therefore the objective of work was research of pharmaco-technological indicators of Alverine citrate in order to develop of composition and technology of spasmolytic action drug.

Materials and methods of research. The results determine of shape and size of Alverine citrate particles are indicate that studied sample is polydisperse powder with the particles of anizodiametric shape in the form of shapeless lumps and their fragments. Surface of the particles is smooth. Based on the obtained data, we can assume that Alverine citrate will have poor fluidity and predict the expediency introduction of auxiliary substances.

The analysis of technological characteristics showed that the active pharmaceutical ingredient has poor fluidity, a significant difference in the parameters of bulk density before and after shrinkage depending on dismount of cylinder indicates the ability of a powder to clumping with a formation of systems that are quite resistant to destruction and that are undesirable in the technological process of capsules dosage forms, because it can lead to uneven dosing.

So the next step of our research was establishing the particle size of Alverine citrate. The degree of crushing was studied by sieve method. Distribution by factions occurred unequally: tiniest fraction was 9.89%, the highest – 0.46%. At the request of SPU particle size of powders for internal use should be 0.16 mm. This faction in the sieve analysis was about 64%. That is was necessary to conduct additional crushing of substance. After grinding Alverine citrate the size of the majority particles (about 95%) is in the range of 0.2 to 0.1 mm.

Conclusion. Thus obtained results are advisable to use in the development of composition and technology of capsules with Alverine citrate.

STUDYING OF THE RANGE OF MEDICINES FOR TREATMENT OF PSORIASIS

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Introduction. Psoriasis – a chronic inflammatory disease of skin which is characterized by monomorphic papular rash; damage of joints and nails. The disease etiology still remains not found out, can be hereditary, virus, neurogenetic or exchange. Process is characterized by a long chronic current with the periods of remissions and aggravations which are quite often preceded psychological an overstrain, catarrhal diseases.

There are also many kinds of display of this illness. From them the most significant exudative arthropathic erythroderma psoriasis. Rashes on skin are usually presented by the symmetrized, flat, roundish or oval, cyanotic-pink papules size about lentil, covered with silver-white scales which, increasing can merge and form plaques and the large centers of defeat. Most often the hairy part of the head, area of elbow and knee joints is surprised. Rash can be followed by a moderate itch. At a scraped of a surface of papules there are phenomena of a stearin spot, a varnish film, dot bleeding. From the moment of allocation in 1801 by R. Whelan of psoriasis as an independent disease for his treatment the record number of methods and medicines was offered. Apply various groups of preparations to treatment of psoriasis: general drug treatment and detoxification therapy.

Aim. The analysis of the range of medicines for treatment of psoriasis in the pharmaceutical market of Ukraine has shown that today in the world about 300 medicines which are issued various foreign and domestic producers of Russia, the USA, Spain, Slovenia, etc. Among this rang eabout 30% make preparations of a vegetable and mineral origin. It has also caused interest in development of ex-temporal medicine for treatment of psoriasis.

Materials and methods. The raw materials of a phytogenesis, for example, laurels leaves, a grass of a train three-separate, nettle leaves by a two-blast furnace, leaves and flowers of black elder, sowing campaign garlic, a St. John's Wort grass, a root of an Acorus ordinary, a root of a Inula helenium , leaves of cowberry ordinary are most widely used, the grass Chelidonium , flowers of a Violet three-colored, sea-buckthorn oil.

Results and Conclusions. We have conducted researches on studying of technical characteristics on separate types of raw materials.

The conducted researches are the basis for creation various ex-temporal medicinal forms for treatment of psoriasis.

DEVELOPMENT OF EXTEMPORANEOUS OINTMENT WHICH BASED ON MEDICINAL PLANTS

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Introduction. The population of the entire planet began to feel the effect of environmental devastating factors, and especially, of the use of synthetic drugs, biologically active additives, preservatives and other substances to which people are not evolutionarily adapted. It is becoming more and more people with chronic diseases and those who can not tolerate drugs. Relevance, in this case, is the use of drugs based on natural medicinal plants. To date, there is a large amount of drugs (about 400 titles) with plastic-visco-elastic medium, which have a generic name - "Ointments" in the Ukrainian pharmaceutical market. Among them, 76% are representatives of foreign and 24% of domestic production.

Aim of our research was to develop a new compound of the combined extemporaneous based ointment which based on calendula extract and to study of its quality indicators.

Materials and methods. We prepared Calendula extract by aqueous extract of calendula flowers, followed by evaporation to a dense mass. The resulting mass is subjected to analysis for the presence of active substances and basic quality indicators. Then, researches on the choice of basics were made bie us. When we choose a basis we take into account the nature of the interaction of all ointment ingredients and the degree of release of main active substances from studied basis.

Results and discussion. According to the results of biopharmaceutical, physical and chemical research as the basis was selected hydrophilic polyethylene oxide basis - alloy of PEO 1500 and PEO-400. This basis provides a high osmotic effect, shows resorptive effect and dries inflamed mucosa. Benefits of the basis are a pharmacologically indifferent, ease to apply on the wound surface, and it is distributed evenly across the wound surface, improving contact with the of the ointment with tissues and the contents of the wound, it is mixed well, and at the same time it is saved its homogeneity. Conducted research on the study of the quality indicators of ointment showed that the ointment is a thermo and colloid stable and has good organoleptic properties and has a pH in the range of 5.27 – 5.79, which has a positive effect on the course of the healing process.

Conclusions. Thus, on the basis of conducted and generalized experimental data, we have proposed the composition of extemporaneous ointment, based on extracts of calendula, which meet the requirements of a given dosage form for it’s the main indicators.

STUDY OF STRUCTURAL-MECHANICAL PROPERTIES OF CARMELLOSE GELS

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Introduction. Gels, as a dosage form have become widely used due to their advantages, which include simplicity of technological process, stability, indifference and superb consumer properties. And sometimes gels are virtually the only appropriate dosage form. For today there is a large amount of gelling agents of synthetic and natural origin. Natural gelling agents include cellulose and its derivatives. Introduction of active substances in the composition of the gel base is done with their pre-dissolution in non-aqueous hydrophilic solvents (propylene glycol, macrogol-400, glycerol) the amount of which may vary in wide llimits. Therefore, study of capacity abilities of sodium carmellose gels is a prerequisite for creation of medicated gel for thrombophlebitis treatment.

The aim of the study. The study of changes in structural and mechanical properties of 2% sodium carmellose gels depending on the concentration of propylene glycol, macrogol 400 and glycerol.

Materials and methods. The objects of research were 2% sodium carmellose gels which differed by content of propylene glycol, macrogol 400 and glycerol. Concentrations of non-aqueous solvents ranged from 5% to 30% in increments of 5%. The study of structural and mechanical properties performed on a rotary viscometer "Reotest 2" (Germany) at 25 °C. According to the research built sample flow rheograms and structural viscosity dependence on shear rate gradient.

Results. As a result of studies it has been found that separate introduction of hydrophilic non-aqueous solvents in concentrations up to 20% results in increased structural viscosity. Increasing the quantitative content of propylene glycol, macrogol -400 and glycerol more than 20% reduces the structural and mechanical properties. At this all samples meet consumer requirements. It has also been found that propylene glycol reveals greater ability to influence the structural and mechanical properties.

Conclusions. The properties of the croscarmellose sodium gels with various content of non-aqueous solvents have been studied. It has been found that their amount may vary within 5 - 30%. The introduction of such concentrations in 2% sodium croscarmellose gel does not lead to the destruction of coagulation structure.

DEVELOPMENT OF THE COMPOSITION OF THE GEL WITH GLUCOSAMINE HYDROCHLORIDE AND NANOSILVER

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Introduction. Traditionally, in clinical surgery on the second phase of wound healing process continue apply different of composition and properties drugs on hydrophobic (mainly vaseline-lanolin) or synthetic unbalanced poliethilenoksid-based. Their use must be considered hyperosmotic and drying effects the components of substrate, and the possibility of creating a "greenhouse effect" in the wound.

Therefore, we have proposed a composition of drug in gel form on hydrophylic-based, namely on the basis of carbomer, which will be reliably protect the granulation tissue from mechanical damage and will exhibit a moderate drying effect.

The desired therapeutic effect in a soft dosage form can be achieved only in case the correct choice of active and auxiliary substances.

The main active ingredients in the gel are glucosamine hydrochloride and silver nanoparticles.

Glucosamine hydrochloride is a basic natural metabolite, which takes part in the formation of tissues, and also has hydrating properties, stimulates the production of collagen. Due to the fact that glucosamine stimulates the production of hyaluronic acid, it has a pronounced reparative, anti-inflammatory and antimicrobial activities.

Substance of nanosilver in gel composition was incorporated as an antimicrobial component, which, in contradistinction to antibiotics, does not cause the dysbiosis, contribute to the normalization of microbiocenosis, exhibits antioxidant properties and stimulate the healing processes in the wound. Substance of nanosilver (Ag) was introduced in dispersed form in a solution of polyvinylpyrrolidone(PVP).

The basic excipient is a gel carrier. Based on the analysis of literature data for researches as gelling agents carbopol (BF Goodrich, USA) was selected.

Aim. The aim of our work is to develop the optimum composition of the gel with glucosamine hydrochloride and substance of nanosilver for effective wound healing in the second stage of wound healing.

Materials and methods. Objects of the study is the model based on the samples of the gels of Carbopol Ultrez 10 with various neutralizers: triethanolamine (TEA) and sodium hydroxide.

We have conducted the investigation on the solubility of the main active ingredients and also the study about choice of neutraliser for the base of carbopol.

The gels we of obtained was monitored characteristic appearance and organoleptic properties (color, smell, texture, etc.) investigated the structural and mechanical properties. Also we monitored for signs of physical instability (aggregation of particles, coalescence, coagulation, separation), controlled the homogeneity of the samples and their osmotic activity.

In research and color appearance viewed smears samples layer 2-4 mm, which were deposited on a glass slide.

Measuring rheological parameters was carried out on a rotary viscometer "Myr 3000 V2R" (Viscotech, Spain) in a system of coaxial cylinders by the method of SPhU (ed., P. 2.2.10, p. 24) in a wide range of shear rates. Research was carried out at a temperature (25±0.1) ^{o}C.

Osmotic activity was determined using the method of dialysis through a semipermeable membrane.

Uniformity gel samples were obtained by the method of SPhU 1.0, p. 511.

Results and discussion. The results on the solubility of the basic active substances showed that glucosamine hydrochloride and a complex of PVP/Ag well soluble in water and glycerol mixture (1: 1), so that in the dosage form was included the unhydric hydrophilic solvent – glycerol, in the amount of 5%. Furthermore, glycerol prevents drying of gels and facilitates the penetration of the active ingredient.

Selection of neutraliser was carried out on the basis of organoleptic properties of the gels. At storage the received samples the gels we observed a change a color in gel, in which manufacturing process was used sodium hydroxide as neutraliser. Therefore, as a neutraliser for in the dosage form was chosen triethanolamine, because during storage we did not observe visible changes in gel.

Subsequent studies, including the structural and mechanical conducted for gel sample for neutralization which triethanolamine was used.

The results of these studies indicate that the sample is a thixotropic gel system, which is a rapid full restoration of the structure. Due to these characteristics of the gel, it is sufficient plasticity, easy to spread on the skin and squeezed out of the tube; that is why it has a good consumer properties.

As a result of osmotic investigation revealed that gel sample has an insignificant osmotic activity that will not obstruct the wound repair processes.

For a given sample was carried out the microscopic analysis, which allows to make a conclusion about the homogeneous structure of the gel.

Conclusions. The proposed composition of the gel corresponds all requirements that apply to drugs for the treatment of wounds in the second phase of wound healing process; and the obtained gel sample has a homogeneous structure and good consumer properties; which are caused by the rheological properties of the gel.

PRINCIPLES OF CORRECTION SKIN XEROSIS

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Introduction. Dry skin - constant symptom of various skin diseases such as atopic dermatitis, psoriasis, eczema and so on. Etc .. Now it is proved that the constant use of combined moisturizing skin lipid composition tools are an essential component in the treatment of many skin diseases. Restore damaged epidermal barrier becomes a priority for dry skin. The higher the permeability of the skin to water, the deeper it penetrates surface-active agents (surfactants) detergents, germs and toxins that cause inflammation and the formation of free radicals in the skin. Dry skin is cyclical in nature with a tendency to age deterioration, so it is very important rational beauty care, adapted to the structure and physiology of the skin. Moisturizers reduce the subjective feeling of tightness, dryness, discomfort, improve elasticity and skin tolerance, level micro and color, strengthen water-lipid mantle.

Principles care of dry skin include several stages:

• adequate, but not aggressive treatment - cream or lotion and shower and washing;

• toning (with skin care) - lotions and tonics;

• moisturizing and softening the skin, protect it - creams, masks sunscreen.

The choice of medical cosmetic form is essential to achieve maximum results when used in cosmetics. Depending on the form of cosmetic changes retention time and exposure to cosmetics (epidermal, transepidermalni). Inadequately selected medical cosmetic form can reduce the positive effect of active substances included in the cosmetic product.

In the first place are the cosmetic creams - a means for body care in a mazeobraznuyu mass with the addition of active substances as directed. Their share in percentage for cosmetic products is 86%, which indicates their advantages over other forms of medical cosmetics, namely:

- Creams relating to cosmetics is not washed off, so have a prolonged effect;

- Have a fatty or emulsion based, which contributes to the high degree of penetration of active substances in the epidermis and dermis;

- Does not require the use of additional materials for applying and rinsing.

Conclusions. Therefore, this cosmetic drug most rational form to create a new cosmetic product for care of dry skin. Whereas consider the information we can conclude the necessity of development of technology and the use of special cosmetic products for the care of dry skin.

INFLUENCE OF EXCIPIENTS ON DRUG RELEASE FROM THE MEDICAL FORMS

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Introduction. Excipients applied when creating new and improving existing drugs in technology of drugs. In the last decade range of auxiliary substances have been increased. Natural and synthetic compound are widely are used in the manufacture of medicines in deferens dosage forms with appropriate physical, chemical and therapeutic properties. Especially, excipients have a significant impact on the pharmacological effect of drugs by released them from soft dosage forms. Particularly influence of auxiliary substance significantly on pharmacodynamics and pharmacokinetics of drugs in such dosage forms as ointment. Variety of ointment bases contributes to the need to study their impact on the pharmacological effects of drugs.

Aim. The aim of this work was to study the effect of different ointment bases on the release of sulfonamides from ointments with concentration of 10% which were made in various ointment bases.

Materials and methods. Experienced ointments samples were produced in the laboratory by the general rules of suspension ointments technologies. Most of sulfonamides are poorly soluble in water, so they are introduced in dermatological ointments according to the type of suspensions. The drug substance was triturated in a mortar by Derjaguin rule with half the amount of molten basis, as its amount was> 5%. Total 5 ointments samples were manufactured with vaseline, petrolatum, lanolin, petrolatum with dimethylsulfoxide, emulsion bases and also with the hydrophilic bases (methylcellulose and polyethylene oxide). Degree of release of active substance from the test samples of ointments was determined by «in vitro» method. For this purpose, the method of «agar plates» and the method «dialysis» was used. The amount of released active substance was adjusted by rapid method for the diazotization reaction.

Results and discussion. They showed that the used excipients have a significant impact on the rate and extent of release of the sulfonamides from ointments. The data obtained at various ointment bases differ.

Conclusions. A variety of properties of auxiliaries and their wide range obliges their conversion attempts into universal which used with any drug substance. Apathetic substances do not exist. Excipients are essential variable pharmaceutical factor, the study of which is a binding in the development of composition and technology of various medicinal preparations. Carrying of biopharmaceutical research is mandatory requirements, while creating soft medicinal forms. The results of this work used in conducting of the educational process in Biopharmaceutics.

EFFECTS OF QUALITATIVE AND QUANTITATIVE COMPOSITION OF EXCIPIENTS, RESIDUAL MOISTURE AND PRODUCTION TECHNOLOGY ON THE MECHANICAL (CRASING) STRENGTH OF MAGNESIUM LACTATE DIHYDRATE TABLETS

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Introduction. Magnesium commonly used in pharmacy. It appears to be a cofactor for more than 325 enzymes of body. Nowadays 15 pharmacological effects of the Magnesium are known, and one of them is stress-protective action.

We have established that in pharmaceutical market of Ukraine are registered 93 drugs containing magnesium with different pharmacological profile. Magnicum, Magne-B_6 and Magvit which have stress-protective effect were chosen for our research as a comparator drugs that contains magnesium lactate dihydrate as an active ingredient, and a variety of binder excipients such as polyvinyl alcohol, gums, carboxypolymethylene.

However, the above-mentioned drugs have been produced by the technology by the end of the 20th and the beginning of the 21th century.

Aim. To develop a technology to produce tablets using binders that can interact more effectively with active ingredient in order to increase mechanical strength of tablets.

Materials and methods. To achieve this goal were used different modifications of polyvinylpyrrolidone (PVP): Kollidon K-25, Kollidon K-90, Plasdon S-630. Also we experimented with different PVP content in tablet from 0,0175 g to 0,03 g, and residual moisture content between 3.20% and 8.96% after drying. Finally, technologies of wet and dry granulations were compared.

The residual moisture content was determined by heating at 105 °C (Sartorius MA150), the mechanical properties were analyzed using a tablet hardness machine (PTB 311E).

Results and discussions. Best results were obtained with Plasdon S-630. We found that mechanical strength of tablets is proportional to PVP content, and inversely proportional to residual moisture. The use of wet or dry granulations showed no significant difference between them.

These parameters are important for a tablet coating process.

Conclusions. According to the results of the experimental work we have optimized the composition and technology parameters for magnesium lactate dihydrate tablets: quality of binders, their amount and the residual moisture of tablet mass.

STUDY OF NIMESULIDE MICROSCOPY AND TECHNOLOGICAL PROPERTIES

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Introduction. Nowadays drugs with a substance Nimesulide (nonsteroidal anti-inflammatory drug that belongs to sulfonanilides) are very popular. Nimesulide has anti-inflammatory, analgesic and antipyretic effect. Furthermore anti-inflammatory, antipyretic and analgesic effects, it also reduces the adhesion of platelets to each other, thereby diluting and lowering the blood clot. Analgesic effect is achieved in 15-20 minutes after taking the drug, which is particularly important in acute pain syndrome. Appointed by the drug most often to relieve symptoms in rheumatic diseases, degenerative lesions of the joints, inflammation of the muscle tissue. Also it is used in fevers of various origins, toothache, headache, menstrual and other types of pain.

Ukrainian doctors advise to use it at a high temperature, when other drugs do not work. However, one of the advantages of Nimesulide is well tolerated and relatively low incidence of complications from the gastrointestinal tract. Nimesulide is often compared to meloxicam (a drug that is mainly recommended for the treatment of pain in rheumatic diseases and other pathologies of the musculoskeletal system). It comes in the form of suppositories, it has more duration of analgesic effect than Nimesulide, but Nimesulide acts faster.

This substance is available as a tablet, gel, suspension and granules for suspension. But there are no drugs with Nimesulide in suppository. To develop a composition and technology of suppositories with Nimesulide it is necessary to study its technological properties.

Aim. The aim is to study of nimesulide microscopy and it technological properties to justify composition and technology of suppositories with Nimesulide.

Materials and methods. It was conducted a study of technological parameters of nimesulide: moisture content, flowability, particle size distribution and study of shape, size and surface properties of a powder.

Determination of moisture content. Moisture content of raw material is the loss in weight of hygroscopic moisture and volatile substances, which determine in the raw material by drying it to constant weight. Determination of the moisture content of the powder was carried out by auto express moisture analyzer Sartorius MA-150.

Determination of flowability. Into a dry funnel, the bottom opening of which has been blocked by suitable means, introduce without compacting 20.0 g of Nimesulide weigt with 0.5% accuracy. Unblock the bottom opening of the funnel and

measure the time needed for the entire sample to flow out of the funnel. The flowability is expressed in grams of powder related to 1 second. We used the apparatus VP-12A.

Determination of particle size distribution. Weigh 20.0 g of a Nimesulide, screen through a set of standard sieves (No. 355; 250; 180; 90). An assay is placed on the top sieve (No. 355) and the whole set is shaken up manually within 5 min. Then dismount a set and weigh the separated fractions of the powder on each sieve. The content of fractions are expressed in percentage of the initial weight.

Study of shape, size and surface properties of a powder. Shape, size and surface characteristics of powder particles are determined by means of microscope supplied with a digital camera DCM 300. Onto a surface of a microscope slide place the sample of powder, then eliminate the excess powder by slightly shaking glass. Examine crystals and measure their maximal and minimum length and width by using a computer program ScopePhoto.

Results and discussion. Moisture content of Nimesulide was 0.40%. So this substance is not a hygroscopic and does not need to be dried before using in technological process.

Nimesulide does not have a flowability. It means that when the bottom of the funnel is opened sample do not flow out of the funnel. It is a critical parameter in tablets technology. But in suppositories technology we can use substances without flowability. It requires only a certain raw material loading techniques in equipment.

The particle size distribution of Nimesulide was: >0.355 mm – 73.4%; 0.25-0.355 mm – 12.3%; 0.18-0.25 mm – 6.1%; 0.09-0.18 mm – 5.1%; <0.09 mm – 0.07%. So the main fraction size was >0.355 mm – 73.4%.

The powder of Nimesulide was examined in dry form by using transmitted light. The maximal and minimum length and width was measured. The surface properties of a powder was examined in dry form by using reflected light. The next step of investigation was to study microscopy of Nimesulide powder suspended in silicone oil. In dry form particle agglomerates more then 300 micron were observed. In the dry form in reflected light crystals were looked transparent and its surface was rough. The particles in silicone oil suspension were separated individually. The average particles size were about 35 microns, the smallest particles size were 17 microns, while the biggest particles size were 96 microns.

Conclusions. Thus Nimesulide does not need to be dried before using in technological process, but it requires a certain raw material loading techniques in equipment due to poor flowavailiability. The particle size distribution of Nimesulide showed that the main fraction size was >0.355 mm – 73.4%, but in suspension the partical size were from 17 to 96 microns, average size were about 35 microns. This occurs because the dry powder particles tend to form agglomerates.

JUSTIFICATION OF THE MOISTENING AGENT CHOICE FOR EFFERVESCENT TABLETS WITH THICK BIRCH LEAVES EXTRACT

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Introduction. Recently remain relevant researches on creation of solid dosage forms (powders, granules, tablets, solid dispersion systems) with controlled release. Instant (effervescent) dosage forms can be considered as drugs with a given improved bioavailability.

However, the production of effervescent dosage forms has a number of unsolved issues. Despite the apparent proximity of the form effervescent tablets and granules are significantly different from the traditional ones in composition and nature of technology as their main components are gas-forming agents. Given this, the most important trend is the theoretical substantiation and development of practical recommendations on the optimal choice of excipients composition.

As the active pharmaceutical ingredient is proposed to use thick birch leaf extract, which, together with the absence of side effects has a pronounced anti-inflammatory, hypoazotemic activity and promotes the dissolution of urinary concretions.

Aim. To determine the optimal composition of the humidifier for tablets with thick birch leaf extract.

Materials and methods. The objects of the study were granules and tablets with thick birch leaf extract; thick birch leaf extract. As humidifier for obtaining granules used purified water, 3%, 5%, 7% aqueous starch paste, 3%, 5%, 7% aqueous solutions of Kollidon 25. For tablets and granules obtained have been determined pharmaco-technological characteristics.

Results and discussion. In the analysis of pharmaco-technological characteristics of granules obtained using as a humidifier aqueous solution of Kollidon 25 it was determined that they perform better than the granules obtained using starch paste. Analyzing quality indicators of obtained tablets it can be seen that tablets produced using as a humidifier aqueous solution of Kollidon 25, including 5% have better indicators in friability and strength of tablets to crushing.

Conclusions. It has been established that the granules obtained using an aqueous solution of Kollidon 25 have better pharmaco-technological characteristics than using starch paste.

According to the research as a a humidifier for obtaining tablets with thick birch leaf extract was chosen aqueous solution of Kollidon 25 at a concentration of 5%.

IMPROVEMENT OF COMPOSITION AND TECHNOLOGY OF ANTITUMOR ACTION TABLETS

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Introduction. According to opinion polls, one of the greatest fears of modern man is the fear of cancer. Because oncological diseases - one of the most common causes of death.

Mammary gland cancer – one of the most common neoplastic processes in women around the world. In Ukraine, it ranks first among cancers of women. Mortality from cancer in women of working age in the time is ahead of death rates from heart and vascular diseases.

Every woman that got sick with breast cancer, on average, loses 17-18 years of life, and this is 53% of total losses of the female population of our country. Over the past 10 years, the incidence of breast cancer increased almost twice and amounts today 52 people per 100 thousand population. It makes anticancer therapy one of priority directions of modern medicine.

Over the years, has repeatedly been shown that the drug «Tamoxifen-Health» is an effective treatment for breast cancer. The current technology for drug «Tamoxifen-Health», which is based on the method of wet granulation lasts long enough, and the physical and chemical properties (friability, disintegration, crushing) are at the maximum permissible norms.

Aim. The aim of this work is development of composition and production technology of tablets «Tamoxifen-Health» that will allow refusing the use of wet granulation method in the production and obtain the drug of satisfactory pharmaco-technological properties by direct compression.

Materials and methods. As objects of study used the tablet masses and tablets «Tamoxifen-Health» obtained using various excipients. For these tablets and masses carried out determination of flowability, friability, disintegration, crushing.

Results and discussion. As a result of pharmaco-technological research it has been found that the optimal values of flowability, friability, disintegration, crushing have tablet masses and tablets where used as filler tabletose 80.

Conclusions. The composition and technology of tablets «Tamoxifen-Health» production by direct pressing has been developed, which will reduce power inputs, technological process time, improve pharmaco-technological properties of the drug and preserve the quality and compliance with all GMP requirements and international quality standards.

THE DEVELOPMENT OF THE SYRUP COMPOSITION WITH CHOLERETIC AND ANTHELMINTIC ACTION BASED ON HERBAL INGREDIENTS FOR PEDIATRIC USE.

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Introduction. Today the lack of medicines for children is one of the important problems of modern pharmacy. Among the arsenal of existing drugs on the Ukrainian market herbal products becomie increasingly popular, due to factors such as the small number of side effects, low toxicity, successful experience using many of them in traditional medicine, and so on. A significant proportion of compound herbal remedies constitute the herbal products, often presented in the form of syrups, teas and capsules. Currently, there is a "window" on market of herbal multicomponent pediatric medicines of domestic production that would combine the choleretic and anti-inflammatory action, given that the disease of the gastrointestinal tract is one of the most common problems among children 3 to 12 years.

Aim. It is the development of a syrup combined with plant extracts for use in pediatric as choleretic and anthelmintic remedy.

Materials and methods. The object of the study was inflorescences of tansy (Tanacetum vulgare) and fruits of rowan (Sorbus aucuparia) as raw materials for reception of extracts, fructose, sucrose, sorbitol, preservatives and flavoring agents of taste and smell. First, we conducted research on development methods of producing liquid extracts of tansy and rowan, providing optimal output extractives. Then we develop the rational drug composition as a syrup, and conducted tests of its taste properties and microbial stability.

Results and discussion. For extracts have been studied and selected the degree of grinding of raw materials – tansy inflorescences and fruits of rowan, concentration of the extractant – 70% ethanol, substantiated the extraction method – percolation. Multicomponent herbal medication consists of alcohol extracts of the aforementioned plant material dissolved in sugar syrup and combined with flavoring composition "Grapefruit". Microbiological stability of the product during storage is provided by the addition of sorbic acid, the amount of which is substantiated reduced by its presence in the composition of the extract of rowan.

Conclusions. We have proposed the composition of the multicomponent syrup for use in paediatrics as choleretic and anthelmintic remedy. The presence of rowan extract in syrup also serves a dual function as the active ingredient and preservative of plant origin. The further step in our work is to study the basic indicators of the quality of the plant syrup proposed composition according to the requirements of the State Pharmacopoeia.

DETERMINATION OF PHYSICAL AND CHEMICAL PROPERTIES OF THE SOLID DOSAGE FORM COMPONENTS WITH ANTICONVULSANT ACTIVITY

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Introduction. Development of tablets always starts with the study of the properties of the basic drugs, which largely determine a rational way of tableting and selection of assortment and quantity of auxiliary substances.

For the substantiation composition of the developed tablets at the first stage was necessary to conduct study the properties of the obtained substance samples. We studied the following parameters: organoleptic - appearance, color and odor; physical and chemical - form of particles, solubility, residual moisture; technological - microscopic and sieve analysis, fractional composition, bulk density and bulk volume, flowability, pressing, ability to shrinkage, strength of tablet model.

Objects and research methods. The objects of research were chosen 1. MCC-101, 2. Magnesium hydroxide, 3. Sodium starch glycolate 4. Carbamazepine, 5. Gelatin. Technological research conducted according to methodology of SPU 1 edition.

Results and their discussion. At the first stage of work was conducted research of the physico-chemical and technological properties of active ingredients. We have been studied solubility for predicting biopharmaceutical characteristics tablets developed. Was studied solubility of the samples in these solvents a) water, b) sodium hydroxide NaOH 0.1 M and in hydrochloric acid 0.1 M HCl. It was determined that all samples are soluble in all taken solvents and increase in volume, ie slightly swell.

The nature of the surface of the particles also essentially influences technological properties: the more complex surface of powder particles, the more connectivity and less flowability and vice versa. Therefore, we have studied the microscopic indicators of the substances. In the analysis of the photographs detected heterogeneous by size mixture of particles that requires study of the fractional composition and predicts the using wet granulation.

The next step was to study the properties of the auxiliary substances. Organoleptic properties of auxiliary substances that are proposed for introduction in composition of tablets are studied visually. Results of the study of organoleptic properties of the studied samples are presented in Table 1.

Table 1

Organoleptic properties of the studied powders

№, Substance	Characteristic
1. MCC-101	The white crystalline powder, tasteless and odorless.
2. Magnesium hydroxide	Finely dispersed white odorless powder, crystals of which have a cubic crystal lattice
3. Sodium starch glycolate	White, free flowing powder tasteless and odorless
4. Carbamazepine	White or almost white crystalline powder, practically insoluble in water, soluble in methylenechloride, sparingly soluble in acetone and alcohol
5. Gelatin	Dry gelatin - amorphous, fragile, colorless or pale yellow substance tasteless and odorless.

For tableting are also important the chemical properties as the presence of crystallization water, wetting and water absorption, the residual moisture.

From the table data seen that the value of residual moisture allows to tablet the researched mixtures (samples 5 – 4.0% and 6 – 3.70%) without pre-drying and stored without special conditions. The value of residual moisture of samples 2 (4.80%) and 3 (5.00%) is at the upper limit of the optimum value and requires correlation.

Conclusion. Were identified physicochemical properties of the components of solid dosage forms with anti seizure activity. Established that all samples have good solubility, gelatin has the ability to swell. According to microscopic research has established that the mixture for tableting requires study of the fractional composition. Established, that for conducting rational technological process is appropriate to use a wet granulation.

DEVELOPMENT OF FORMULATION AND TECHNOLOGY OF MEDICINAL PREPARATION IN THE CAPSULES FORM WITH ANTIINFLAMMATORY ACTIVITY

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Introduction. Pain, fever and inflammation occupy one of the first places among reasons of population disability. Nonsteroidal anti-inflammatory drugs (NSAIDs) are highly effective in the alleviation of these adverse conditions. Such effective NSAID as diclofenac sodium is commonly indicated in the treatment of rheumatoid arthritis and osteoarthritis, relief of mild-to-moderate acute and chronic pain. Diclofenac is widely used around the world. There is a lack of domestic diclofenac medicines in Iraq. Therefore creation of new medicinal preparations with diclofenac for pharmaceutical market of Iraq is topical.

Aim. The purpose of our work was a development of the composition and technology of hard gelatin capsules for oral administration with diclofenac sodium.

Materials and methods. The substance, auxiliaries, mixtures for encapsulation and prepared capsules on their basis were research subject. The research methods were used according United States Pharmacopeia (USP).

Results and discussion. The composition of capsules with diclofenac sodium was formulated under the supervision of Associate Professor Sichkar A.A. The dose of active pharmaceutical ingredient was 50 mg/capsule. The pharmacotechnological properties analysis of the test substance diclofenac sodium had shown that the substance had poor flowability, hence it was concluded that direct filling of powder into capsules was not possible. It is predetermined application of special inactive ingredients for improvement pharmacotechnological characteristics. Capsule mixtures on the basis of substance were investigated with combinations of lactose monohydrate, potato starch, croscarmellose sodium, aerosil, talc, magnesium stearate in different correlations. Since diclofenac sodium is poorly soluble in water, starch and croscarmellose sodium were used to increase penetration of the stomach liquid into encapsulated mass in capsules. Aerosil and magnesium stearate reduces the friction between particles of the composition and the surface friction between particles of the composition and the equipment surface. It was established that lactose monohydrate and aerosil have more influence on flowability of the active substance. The capsules samples were stored in plastic containers.

Conclusions. Auxiliary ingredients and technology of capsules with diclofenac sodium for manufacture in Iraq were chosen as a result of research. The received capsules correspond to all indexes of the USP (39th edition) for capsules.

CONCERNING THE CREATION OF AN OINTMENT FOR THE TREATMENT OF ALLERGIC DERMATITIS WITH SECONDARY FUNGAL INFECTION

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Introduction. Over the past decade especially increased proportion of the total incidence of human allergy primarily by skin lesions of allergic nature. The modern assortment of ointments enables use for the treatment of allergic dermatoses with secondary fungal infection anti-inflammatory and antifungal medicines of synthetic origin. As for medicines of natural origin with complex specified pharmacological activity only ointment "Fladeks" is available, containing polyphenols of Canadian desmodium grass.

Aim is creation of a new ointment for the treatment of allergic dermatitis with secondary fungal infection.

Results and discussion. As active ingredients in the composition of the new ointment with anti-inflammatory, anti-allergic and antifungal action proposed to use dry extract of licorice root, terbinafine hydrochloride and lavender oil. The process of the medicine's sample preparation was carried out in accordance with the generally accepted rules of ointments preparation. Dry extract of licorice root were introduced in the ointment as an aqueous solution. Terbinafine hydrochloride was dissolved in propylene glycol at a temperature of (40.0 ± 2.0) °C. Lavender essential oil was pre-dissolved in the calculated amount of soybean oil.

Because allergic dermatitis with secondary fungal infection occurring with fairly severe dry skin and need of constant moisture, as ointment's bases were examined emulsion systems.

After processing technology of the medicine was conducted studying of its organoleptic, physical, chemical properties and stability. The resulting ointment has a light brown color, pleasant odor, pH = 5.0-6.0, homogeneous and stable. The results of the rheological studies suggest that the said product is dispersed system with the coagulation type structure, characterized by elastic-viscous-plastic properties.

Study of osmotic activity showed that the model composition of the ointment provides "soft" and short dehydrating action that avoids damaging effect on the skin tissue and their repairing processes.

Conclusions. Proposed ointment with licorice root extract, terbinafine hydrochloride and essential oil of lavender is promising for use as a medicine for the treatment of allergic dermatitis with fungal complications.

CONCERNING THE ROLE OF PLASTIC STRENGTH IN GRANULATION

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Introduction. Wet granulation method is widely used in industrial technology of solid dosage forms, especially at creation drugs with a different range of technical and physicochemical properties. To substantiate the choice of the humidifier is applied such an important rheological characterization of binders mass like plastic strength.

Aim. Study plastic strength of the drug substances of Valaciclovir, Ornidazole and Nifuroxazide which belong to a group of antiviral and antimicrobial drugs.

Materials and methods. Plastic strength of powder is express "resistance" of the granular medium to the effect of mechanical load and measured by the depth of immersion of the standard cone in the test medium under effect of constant load. Plastic strength value depends on the humidity. The main characteristic of the cone method is the value of limiting shear stress by P. A. Rebinder.

Results and discussion. At the beginning, at the humidification of the powder occurs hydration and structuring process, the plastic strength increases and reaches its maximum value (0.076 kg / cm^2) due to adsorption and capillary moisture. Further increase of moisture leads to the appearance so-called "free moisture", resulting in reduced plastic strength. As a result of research as a humidifier when obtaining tablet mass of Ornidazole substance, which not soluble in water and by natural consistency has tight plasticity, justified the use of "moderately binder system" 5% solution plasdone S-630. Application of this humidifier improves pharmaco-technological characteristics of tablet mass with Ornidazole, increasing its plasticity and solubility. As a humidifier for the tablet mass with the easily soluble substance of Valaciclovir, which by nature consistency has the soft plasticity, justified the use of a 1% solution of HPMC with plasdone S630, the combination of which helps to delay the so-called "local dissolution of the substance. Maximum plastic strength for Nifuroxazide powder reaches a maximum in different ways, depending on the nature, moisture and humidifier concentration. Results of experimental research showed that the maximum strength of the plastic is reached when used as a humidifier solution of PVP K-29/32 at 10% concentration and minimum humidity of 17%. For other humectants (34% sugar syrup, 2% solution of HPMC (50 cP), a 10% starch paste, mortar plasdone S-630 10%) this value is higher and make up 18-25%.

Conclusion. The value of the plastic strength used in the development of composition and technology of tablets with Valaciclovir of antiviral action "Gerpeval 500" tablets with Ornidazole of antimicrobial action "Meradazol" and Nifuroxazide capsules for the treatment of acute intestinal infections "Diaplant".

FUTURE OF THE DRUG BASED BEE TO TREAT FUNGAL SKIN DISEASES

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Introduction. Mycosis of skin - this is a common disease of an infectious nature, caused by parasitic, pathogenic and opportunistic microorganisms. Superficial fungal infections of the skin is a group of diseases, including ringworm, keratomikozy, candidiasis. Fungal lesions can disfigure the skin of the sick, cause severe allergic reactions including mikidy.

athlete's foot treatment is based on the following principles:

• Eliminate and reduce inflammation

• The fight against fungal infection using antifungal agents

• Restoration of a healthy blood circulation in the affected areas (to prevent recurrence)

Antifungals available in the form of system (tablets, syrups, solutions, etc.) and local (gel, ointment, cream, etc.) formulations. Currently, for the systemic treatment of mycosis widely used tools such as: Griseofulvin, Terbinafil (trade name - Lamisil), ketoconazole (brand name - Nizoral), Itrokonazol, fluconazole. The choice of drug is performed after determining the type of fungus causing the skin disease.

Our studies of this problem have shown that in the treatment of fungal infections requires prolonged use of antifungal drugs, which can lead to the development of side effects.

To reduce side effects of the use of drugs for the treatment of fungal infections we set out to explore other substances with antiinflammatory and antifungal activity, as well as their possible combinations to increase the pharmacological effect. Given the high antimicrobial, anti-inflammatory, reparative and other pharmacological characteristics of bee products, - the creation of a new drug based on them, meets all modern requirements for the topical treatment of fungal infections is important.

The **aim** of our work is to develop science-based composition, preparation technology and analysis methods for the treatment of skin mycosis.

CONFECTIONERY DOSAGE FORMS – TASTY OR HEALTHY?

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Introduction: Many of us think about the problem of our health, how to safe it and strengthen. Sometimes we can solve this problem only with medication.

Confectionery dosage forms became quite popular recently. They are solid dosage forms with a large amount of sugar intended for domestic use, different in geometric form and consistency, containing the medicinal substance and slowly soluble base.

The question arises: whether the consumption of confectionery dosage forms has a benefit or we only get some pleasure?

The name of this group – confectionery – is not a pharmaceutical term, it is imaginary. Since the range of medicines in these forms is small, the quantity of such products on the pharmaceutical market is insignificant. But there is some need, especially in pediatric and geriatric practice. This is because you can combine some drugs in one dosage form, masking unpleasant taste and odor, adjust the pH of the oral cavity. As a rule, the prices of such products in the pharmacies are high.

The purpose of the study is to prepare lozenges, similar to vitaminised lozenges of industrial production in the laboratory, replacing artificial ingredients with natural, inexpensive, without using preservatives.

At club lessons, based on the study of confectionery dosage forms production materials, the following main ingredients for the preparation of the experimental lozenges were chosen: food gelatin, ascorbic acid, glycerin, menthol, as well as additional components: honey, ginger, orange essential oil (in small amounts). The essential requirements were rational choice formulations, no residual aftertaste of sweets, and a minimum of side effects.

The active substance is ascorbic acid. It has significant regenerative properties, participates in redox reactions, the regulation of carbohydrate metabolism, synthesis of collagen, improves capillary permeability, participates in the synthesis of hemoglobin.

Materials and methods. Gelatin was filled with the necessary amount of mineral water, adhere to the time for its swelling. Then the glycerine was added and it was put in a water bath until gelatin dissolved. After that ascorbic acid, menthol, honey, dried ginger was added to the half cold mass and the finished mixture was poured in molds. After keeping in the fridge, ready lozenges were taken and covered with the corn starch to remove excess moisture and to give them an aesthetic look.

Results and discussions: The prepared lozenges were studied by the members of inorganic and organic chemistry club "Vitalis". Since the active substance is ascorbic acid, quantitative and qualitative analysis was carried out. After having done some work the club students came to the conclusion that the lozenges are ready for use. Our College staff and students had the opportunity to taste the products.

According to the survey: the lozenges are not bright in color (which indicates the absence of the dye), have some pleasant sour - sweet orange taste. After consumption there was no allergic and other side effects. It is advisable to use them for adults, if children, it is possible to exclude the essential oil and reduce the dose of ascorbic acid to 0.75 on the whole mass of lozenges.

Conclusions: while working on this topic the material from scientific articles and books were used, and orange-ginger vitaminised lozenges formulation was developed in experimental way. As a result of the research we came to the conclusion that lozenges have advantages and disadvantages.

Advantages:

1. Tasty and healthy
2. Have a pleasant texture
3. Composed of most natural ingredients
4. If desired, you can always make adjustments to the recipe
5. The lozenges have an aesthetic look
6. Inexpensive at cost
7. Do not leave an unpleasant aftertaste in the mouth.

Disadvantages:

1. Not recommended for children under 6 years
2. Store preferably in a cool place
3. Contraindicated for people with diabetes
4. Short shelf life

So prepare experiment and be healthy!

HYDROPHILIC OINTMENT BASE JUSTIFICATION FOR WOUNDS TREATMENT

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Introduction. In order to expand the range of Ukrainian ointments which contains substances of natural origin, samples of hydrophilic ointment bases rheological studies was carried out. Base components has high impact on consumer properties of semisolid medicines. The effectiveness of wound treatment highly dependent on the quality of used medicinal forms. In this respect, ointments play an important role as a complex medicinal form.

Aim. The aim of our research was to choose an ointment base for use on the first and second phases of wound healing, which along with moderate dehydration antimicrobial action, helps to accelerate repair processes of wounds that are important precisely for the second phase of wound healing progress.

Materials and methods. There were studied literature data of PEO-400 (macrogol type 400) and PEO-1500 (macrogol type 1500) alloys properties which are the products of ethylene oxide polymerization with water or ethylene glycol polycondensation.

Results and discussion. For the first and second phases of wound healing well established emulsion and hydrophilic ointment bases, which shows a high osmotic effect, dried wounds, helps to reduce the quantity of fluid. Among hydrophilic bases today widely used polymers and copolymers of ethylene oxide. Polyethyleneoxide ointment bases has weak antibacterial properties, low sensitivity to pH and electrolyte administration. In the wound PEO-1500 linking inflammatory exudate. Smaller PEO-400 molecules can penetrate deep into the tissue forming of complex with AFI, PEO-400 delivers it to the localization of the infection.

In addition, PEO bases can increase the bioavailability of AFI, and increase therapeutic effect at relatively low concentrations of active substances. They are pharmacologically indifferent easily applied to the wound surface, evenly smears well mixed with exudate. The most commonly used PEO-400 and PEO-1500 in the ratio 6:4, 7:3, 8:2.

Conclusions. Taking into account its properties using of polyethyleneoxide ointment bases helps to improve ointments quality by increasing its stability, osmotic properties, opportunities to improve the bioavailability of AFI etc.

IMPROVEMENT OF COMPOSITION AND TECHNOLOGY OF BILE ACTION CAPSULES

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Introduction. In recent years, the Ukrainian pharmaceutical market there is a tendency to expand the range of medicines based on natural raw materials of vegetable origin . This is due to the fact that these drugs in the treatment of sparing effect on the human body and do not have side effects and complications. Such formulations have a lower cost as compared to synthetic analogues.

Aim. The main purpose of research is the best justification for the drug - artichoke extract Zdorovye capsules , 100 mg and improve industrial technology of its production. The company LLC " FC " Zdorovye" produced capsules with extracts of artichoke , the contents of which are prepared by wet granulation of powders . The use of this technology does not allow for a lot of high-quality encapsulation with optimal processing properties . These circumstances led to research on the improvement of the composition and preparation technology Artichoke extract Zdorovye - capsules of 100 mg.

Materials and methods. The active substance in the composition of the drug is a dry extract of artichoke , which contains a set of biologically active substances specific carbohydrates, hydroxycinnamic acids, phenolic compounds , ascorbic acid, carotene, B vitamins, minerals. This drug has choleretic and hepatoprotective effect. In the study of dry extract of artichoke established that it has small particle size and a very poor turnover that led to the use of various excipients in different proportions. Dry components of formulations , mixed to a homogeneous state and studied basic technological properties obtained masses for encapsulation and qualitative characteristics of capsules that were derived from them.

Results.The research showed that the best technological indicators has a pattern composed of, in addition to the dry extract of artichoke include: lactose monohydrate, aerosil, calcium stearate, crospovidone. These excipients provide mass for encapsulation necessary fluidity, precision dosing, mixing uniformity and reproducibility of quantitative composition.

Conclusions The composition led to the change of technology of capsules with dry extract of artichoke. The results of studying technological properties masses for encapsulation allow to receive it by direct mixing. The optimum composition of artichoke extract capsules, Zdorovye Capsules 100 mg based on dry extract provides a stable drug that meets all the requirements of regulatory documents and can be implemented in production by LLC "FC" Zdorovye".

RESEARCH ON THE DEVELOPMENT OF TECHNOLOGY TABLETS "IBUASKTAMOL"

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Introduction. Novadays anti-inflammatory pills are usually subdivided into steroids and non-steroidal drugs. Non-steroidal anti-inflammatory type tablet - a substance having a different chemical structure. They have an additional analgesic and antipyretic properties. Inflammation – is a universal reaction to the damaging effects of environmental factors: infectious, chemical, physical, etc. In many cases, inflammation plays a protective role, helps to limit the focus of the damage and destruction of the infectious agent.

All drugs of this group possess analgesic effect, lower the body temperature in fever and suppress inflammation. The need for a dosage form and range of medicines for the treatment of inflammatory etiology has a number of theoretical and social prerequisites.

In connection with the above, the development of formulations for the prevention and treatment of patients with this pathology is one of the most pressing scientific and practical problems.

Objective: The aim of this research was the study of technological parameters and creating user-friendly use of tablets "Ibuasktamol".

Materials and Methods: The study appeared substance ibuprofen, acetaminophen, ascorbic acid and auxiliaries. To study the composition and "Ibuasktamol" tablet technology have been studied technological characteristics of tablet mass. Determination of technological parameters were according to techniques GF XI and the relevant specification. The flowability of the test mass was studied in the EP-12A device according to the known method for literature. To determine the residual moisture content in the powder and granulate using hydrometer firm "Kett", as well as determined by the method of drying to constant mass at the GF XI. Determination of bulk density of the powder was carried out on the device model 545 P-AC-3 Mariupol. Moisture sorption properties of the substance have been investigated by the method of S.A. Nosovitskoy at different relative humidity values of the environment. Experimental samples "Ibuasktamol" pellets were prepared by adding various proportions and combinations of adjuvants. Used for humidification purified water, sugar syrup, ethanol and various concentrations of starch solutions.

Results: When humidifying varying strength ethanol, sugar syrup, granulated powder did not yield a result and decided that the use of sugar syrup and ethanol as a binder - not appropriate. Further hydration water carried, as it provides good tabletting granulation mass. When wetting the substance with water formed lumpy, doughy mass. When moistening the mass with water treated pellets after drying, it is not strong, resulting tablets had no quality appearance, durability was unsatisfactory. Therefore, in subsequent experiments, starch paste made moisturizing various concentrations.

Subsequently, the following processing characteristics were studied tablet weight: fractional composition, bulk density, flowability, angle of repose, porosity, residual moisture properties moisture sorption tablet weight. The study of the kinetics of the mass of drying the residual moisture of 3.96%.

Used auxiliaries some improved technological properties - flowability, bulk density. Also, according to the data obtained, it can be noted that with the addition of excipients tablet blend flowability of the masses increased twice increased bulk density.

The studies found that the studied mass is the mass of white. The results of the study of the fractional composition suggests that the bulk of the particles have a size of less than 250 microns (28.97%), characterized by unsatisfactory flowability values (0.501 10^{-3} kg / s), low bulk density (222.86 kg / m^3), an angle of repose (54.7 degrees), values residual moisture (up to 5.90%) and porosity (80.01%).

Conclusion: Thus, comprehensive technology research, based on indicators of physical, chemical and technological properties of the optimal composition of the tablets "Ibuasktamol".

STUDY OF STORAGE AND STABILITY TABLETS “NIME-S”

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Introduction. Stability – one of the most important characteristics of the drug. The company medical industry has ensured the content of a therapeutic dose of drugs in dosage forms for a specified period. Thus, reflect the regulatory technical documents. The criterion for the stability of the drug substance is the preservation of its quality, etc, appearance, solubility, authenticity and purity of the quantitative content. Reduction of the quantitative content of the pharmacologically active substance in the drug confirms its instability.

One of the major challenges of modern pharmaceutical technology is to develop a convenient dosage forms in the application, stable during storage. The stability of formulations greatly influences the physical state of a substance, the storage temperature, the ambient air, light, packing, cooking method, the selection of the auxiliary substances, etc. Various processes occur during storage of dosage forms which result in a chemical change of structure, which naturally leads to either pharmacological activity reduction or complete loss of its. The study dosage forms expiration dates is one of the main and final stages of drug development technologies.

Purpose: to study the effect of different conditions on the stability of the tablets "Nime-S» and determine their expiration dates.

Materials and Methods: the study was content pills “Nime-S” received the recommended contact the composition and technology. Experiments were carried out by a conventional method of storage and "accelerated aging" according to the manual and time-42-2-82 at 40 °C. The study examines such physical factors that have the greatest impact on the stability of drugs - temperature, light and humidity. "Nime-S» The initial stage of the experiment was to study the physical and chemical, qualitative and quantitative indicators of the initial samples of tablets. The following qualitative indicators were evaluated in the study: the appearance, average weight and deviation from average weight, solubility, disintegration, friability, moisture, microbial purity, quantitative content of active substances. The above figures were determined according to the GF XI. In the second phase of the experiment, these tablets were packaged in the following permitted for use in medicine are 4 types of packaging: clear glass jars (TU-64-228-84) with plastic screw caps and seal (TU-64-2-250-75); amber glass jars (OST 64-2-71-8) with plastic screw caps and seal (TU 64-2-250-75)

contour - no cellular packaging made of laminated paper coated with polyethylene on TU13-7308001-477-85 , contour-cell package of PVC film grade VC-73 and lacquered aluminum foil (TU 48-21-270-78).

Results: As known as, stability of the drugs depends on the chemical composition and properties of the packaging material. Particularly high requirements for packaging materials intended for the storage of medicines. Important is not only the stability of the packaging material, but also its ability to protect the drugs from the effects of temperature, light and humidity. Therefore, after the packaging material stability study investigated the stability of samples of drugs or dosage forms placed in the same package. Based on this set expiration dates of drugs in suitable packaging. Packed into different types of packaging pill "Nime-S» after the experiment meet the requirements set for a tablet formulation.

For example, the appearance of the tablets did not change over the entire period of the study - a cream-colored pills, odorless, round-shaped, biconcave, with Valium on one hand, the ratio of height to diameter of the tablet 39% deviation from the mean weight was up to 4.03% , disintegrate ranged from 9 to 12 minutes, the abrasion resistance of 98.9 - 99.1%, breaking strength of 65-70N and quantitative content of active substance is in the range 98.5-100.3%.

Conclusions. Thus, as in the studies by "accelerated aging", and when stored under ordinary conditions recommended us the composition and technology of production of tablets, as well as the types of packaging used provided the stability of tablets “Nimes-S” within 3 years.

IMPROVEMENT OF TECHNOLOGY OF EXTEMPORE SUSPENSIONS

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Introduction. The analysis of a pharmaceutical market of Ukraine showed that for treatment of dermatological diseases the prepared medications are widely used as ointments, creams, gels.

Among plenty of the prepared preparations found out by us only 3 facilities in form suspensions (Zinc Olive, Cindol, Maksideks), which are produced foreign producers. From our point of view for upgrading medical service of population expedient is the uses as ready so extemporal of medications.

Aim. As suspensions have higher bioavailability by comparison to ointments, consider after actual to recommend their use in therapy of dermatological diseases.

The analysis of composition of extempore suspensions showed a presence the row of difficulties in their technology.

Found out by us the laboured samples of writing of suspensions subject physical and chemical and to technological research with the purpose of improvement of their technology.

Materials and methods. By us it was collected and analysed extempore compounding from 8 pharmacies of Ukraine.

All samples of writing were classified after the types of medical forms. It is set that suspensions on water and non-aqueous solvents make swingeing majority among liquid extempore of medical forms.

Results and discussion. One of the laboured cases there is introduction of two-bit of hydrophobic matters in a suspension water-based. By us were the conducted researches in relation to possibility of previous formation of eutecticum mixture of these matters.

The conducted researches on the change of solvent set that offered technical receptions allow to get more stable suspension which guarantees homogeneity of dosage of medications.

Conclusion. For the high-quality providing of patients of extempore medications necessary are permanent researches in relation to perfection of composition and technology of different medical forms. Researches are conducted by us allow to recommend application of such technological receptions, as a receipt of eutecticum mixtures of hydrophobic matters and replacement of solvents on non-aqueous or mixed. Application of such technological receptions is instrumental in the increase of stability of suspensions and improvement of them biological availability.

INVESTIGATION OF PHYSICAL AND CHEMICAL PROPERTIES OF "ALOE-DENTAL" GEL

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Introduction. Because of the present busy life of humans these days, dental diseases are most common diseases in children and adults. Today dental caries remain one of the most common diseases throughout the world. It's also known as tooth decay, periodontitis, mouth cancer, bad breath, and many other.

Due to the side effects and the resistance that pathogenic microorganisms build against the common antibiotics, much recent attention has been paid to extracts and biologically active compounds isolated from plants used in herbal medicine.

Earlier Composition and technology of gel based on plant extracts (Aloe and oak bark) was developed at the Department of Drug Technology.

In order to ensure the pharmacotherapeutic effect of the drug, biologically active substances of natural origin: thick oak bark extract, which is a complex of plant polyphenols and exhibits anti-inflammatory, antimicrobial, membrane stabilizing, hemostatic activity and aloe extract, which has a pronounced antimicrobial properties and accelerates regeneration were entered in gel.

Aim. the aim of our work was physico-chemical and pharmaco-technological research of new dental "Aloe-dental"gel.

Material and methods Due to the experimental data, we have prepared samples of gel "Aloe-dental" by different technological process. According to the first technology, the introduction of active ingredients was conducted into the finished gel and by another technology was introduction active ingredients into the dispersion medium before thickening of gel.

Results and discussion. Gels, derived by both technologies, have gel-like uniform consistency with a specific pleasant smell and brown colour, pH 6,0-7,0. However, the study of colloidal and thermal stability proved the stability system, prepared only by the first technology.

Conclusion. On the basis of thermographic investigations gel, active substances and excipients, it was found that thermal effects studied samples are similar in nature, which may indicate no chemical interaction between the components of the gel, prepared on the proposed technology.

PLANNING AND IMPLEMENTATION OF THE EXPERIMENTAL PART OF THE 5TH YEAR STUDENTS OF THE FACULTY FOR FOREIGN CITIZENS MASTER THESIS

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Introduction. Preparation of master thesis of a student is carried out in order to study the latest theoretical, methodological and technological achievements of domestic and foreign science and securing of practical skills, the use of modern methods of scientific research, processing and interpretation of experimental data in the thesis research.

Purpose of the study. During planning and implementation of experiment magisters faced with problems associated with insufficient precision planning of the experimental work. Therefore, the aim of our study was to study the methodology of planning and preparation of master's thesis of 5 course students specialty Pharmacy training foreign students.

Objects and methods of research. During graduate magisters have the opportunity in accordance with the approved topic conduct research work according to the individual plan, as well as actively participate in the scientific and educational work of the department: attending lectures, practical classes and seminars leading experts have access to all scientific methodological developments Department of getting expert advice. In addition, graduate students participate in public and social life of the department.

The results. During the preparation of the master's thesis students had theoretical training (work with the scientific and technical documentation, patent search, work with electronic databases), based on the results of which was planned the experimental part of the research. The experiment consists of the following steps: the selection of developed drug compounds. study of pharmaco-technological and biopharmaceutical properties of the samples, selection of optimum compose of the drug corresponding to the requirements of RND, development of the technology. After finishing of experimental part studies prepare master thesis according to given requirements.

STUDY OF THE STABILITY AND STORAGE CONDITIONS CAPSULES "COAST-30"

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Introduction. Imbalances of nutrient metals is developing a number of diseases, including anemia of different etiology. Literature data confirm the efficiency of application of complex compounds of biogenic metal ions, including cobalt and iron with pharmaco-physiologically active ligands in the treatment of diseases of the blood. The development and introduction of new dosage forms of domestic drugs for the treatment of diseases of the hematopoietic system is relevant and appropriate. In the previous article we studied the possibility of obtaining capsules coast-30 with the use of different excipients.

Research objective. This work is devoted to scientific substantiation of the shelf life and storage conditions of the finished product is developed.

Materials and methods. One of the significant indicators in the development of new dosage forms is the stability of the drug during storage. The shelf life of the dosage form of capsules coast-30 was determined by the method of natural storage.

To study the storage conditions and establishing a shelf life, capsules packaged in 40 pieces. Before the start of the experiment and during the period of its physico-mechanical properties of the capsules were standardized according to the requirements of article "Tablets" ГФ XI., vol.2. p. 154 and the industry standard TST 42-01 2002 "Standards of quality of medicines". The study was conducted on five series of laboratory (experimental) samples. To assess the quality of capsules were selected following the criteria: description, authenticity, average weight and deviation from average weight, disintegration, dissolution, uniformity of batching, quantitative determination of active substances and microbiological purity. On the serves description was used organoleptic method, i.e. a method based on the evaluation of the appearance of the capsules to the naked eye.

The authenticity of the drug was determined by chemical reactions at its active substance: ions cobalt (II), methionine and ascorbic acid. Determining uniformity of dosing "coast-30" in the capsules was conducted according to the requirements of each capsules "coast-30" was selected 10 capsules, which determined the content of the cobalt-30 spectrophotometric method with nitroso-R-salt. The determination is based on formation of coloured chelation of cobalt (II) with nitroso-R-salt (1-nitroso-2-hydroxy-naphthalene-3,6-disulfonate sodium). The complexation of complete within 5 minutes at room temperature and 3 minutes at the boiling point of acetate in the environment. Alkali and alkaline earth metals, chloride-, sulfate-, nitrate-, acetate

- and citrate ions do not interfere with the determination. Determination of disintegration capsules "coast-30" was carried out on a laboratory identifier (device 545-AK-1), when the solution temperature is 37±2 °C. Samples of all batches of capsules "coast-30" fully disintegrated within 30 minutes. Definition of dissolution of capsules "coast-30" used-type device "rotating basket" (the device 545-AK -7). As the environment dissolution used 0.1 mol/l hydrochloric acid solution in amount of 1 liter at a temperature of 37±1 °C With and the speed of rotation of the basket 100 rpm in 45 minutes was sampled from the solution in an amount of 50 ml, which was filtered through a filter "Millipore" or "Vladipor" with a pore diameter of 0.45 μm (brand МФА-2А-2, ТУ 6-05-221-483-79) discarding the first 10 ml. Further determined the content of active substances. Cobalt -30 (30) were determined on spectrophotometer “Beckman” DU 65 at a wavelength of 420 nm in a cuvette with layer thickness of 10 mm. For the determination of ascorbic acid using iodometric titration method. The quantitative content of cobalt was 30 determined complexometrically method indicator xylens orange in acetate buffer medium, and ascorbic acid were used pharmacopoeial method statmetrics titration in an acidic environment.

Results. The findings of one study received the following data: the capsules do not change their appearance during storage, the authenticity, the deviation from the average weight ±2.86%, the disintegration of capsules ranged from 6 to 8 minutes, dissolution (75%), quantitative content of active substance cobalt-30 and ascorbic acid varied 0.0150 (±2.94%) and 0.030 g (±1.82%), respectively. In conducted researches it was established that all the drugs during the storage period were not changed physico-mechanical properties of capsules Coast-30. The content of active substances was within the norm.

Conclusions. Our data indicate that the capsules are stable. Capsules, is made on the optimal composition and rational technology ensure the stability of quality indicators within 3 years.

DEVELOPMENT OF TECHNOLOGY FOR PRODUCING COMPOUND THICK EXTRACT OBTAINED BY COMMON EXTRACTION OF THYME, YARROW, CHAMOMILE AND EUCALYPTUS

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Introduction. Medicinal herbs have invaluable treasures that were used yet in ancient times and their potential is not completely studied. Synthetic active pharmaceutical ingredients have powerful therapeutic activity, but they are inherent also side effects. In recent years, has accumulated a lot of data on the negative impact of substances that were previously considered safe. So important is the development of drugs based on plant material. On the basis of literary analysis has been selected herbs composition of thyme, yarrow, chamomile and eucalyptus, used to treat respiratory diseases. Inflammation of the airways is the most common disease among people of all ages. The development of drugs based on standardized complex dense extract will expand the range of pharmaceutical market and reduce its import-dependence.

The aim of the study. The aim of the scientific research was to determine the concentration of water-alcohol solution for carrying out bioactive substances extraction process from medicinal plant raw material.

Materials and methods. The objects of research were thyme herb, yarrow herb, chamomile flowers and leaves of eucalyptus. Were used 30%, 40%, 50%, 60%, 70%, 80% water-alcohol solutions. Medicinal herbs took in equal proportions. Definition of extractive properties of water-alcohol solutions was performed by determining the amount of extractives. Research performed by the method described in the USSR SP XI, Ed. 1. Determination of the amount of dry residue was performed using express thermogravimetric moisture analyzer MA 150 of the company «Sartorius», Germany.

Results. As a result of studies it has been found that the maximum extraction properties has 70% water-alcohol solution, providing a yield of extractives in an amount of 17%.

Conclusions. Based on the results obtained for the joint extraction process by percolation experimentally proved the use of 70% aqueous-alcohol solution.

THE STUDY OF THE RHEOLOGICAL PROPERTIES OF PASTE WITH NATURAL ZEOLITE

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Introduction. In the development of modern medicine major role plays the study a possibility of natural substances be using as active pharmaceutical ingredients in new medicines. One component which is very promising from this point of view is natural zeolite. Zeolite - a natural mineral of alumosilicate nature, which has a number of useful properties. In experimental work carried out at the Department of Industrial Technology of Drugs, were demonstrated the successful use of natural zeolite in solid dosage forms as filler, disintegrant and active substance (enterosorbent).

Currently we are developing technology and composition of oral paste containing the natural zeolite. This dosage form was chosen due to its several advantages: adsorption capacity is higher than for tablets; act faster than solid dosage forms; have good organoleptic properties; diluted forms of stable suspensions can be administered in unconsciousness states by using special catheters.

However, the disadvantage of water paste is an oral microbiological instability. They must be sterile or contain preservatives.

An important requirement for soft medicinal forms is studying their rheological properties. Compliance of these properties to modern requirements provides not only high consumer properties of dosage form but also its storage stability, ease of packaging and dosing.

Aim. The aim of this part of our researches is to study the rheological properties of paste.

Materials and methods. To determine the rheological properties viscometer REOTEST-2 was used.

Results and discussion. On the base of rheological investigations we experimentally selected the optimum type and concentration of the thickener (apple pectin 5%) and plasticiser (glycerine 7%) allowing obtaining paste with good rheological properties. Also we determined rational concentrations of natural zeolite which can be added to soft dosage. The range of zeolite concentration is 25-35%

Conclusions. In conclusion of the work, should be noted, that the natural zeolite is suitable ingredient for creating oral pastes on its base. The rheological properties of resulting composition correspond to all national pharmacopoeia requirements for pastes.

COMPLEX USE OF SAPROPEL IN MEDICINE AND COSMETIC

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Introduction. Sapropel – substance of biological origin, that is formed under water, on the bottom of freshwaters from residues of planktons and bentons organisms, involving bacterial processes that occur in the surface layers of sediments at low oxygen access. Sapropel consist of silt solution, skeleton and colloidal complex. Silt solution consist from water and substances dissolved in it – mineral salts, low molecular weight organic compounds, vitamins, ferments.

Aim. The aim is to focus in studing of sapropel identify promising set of biologically active substances and the creation on its basis of a medicament for the treatment of certain diseases.

Material and methods. Sapropel unique naturally occurring substance that finds its use as a source of organic minerals in traditional mud therapy, cosmetology and agriculture.

Given the wide range of pharmacological properties of sapropel – antimicrobial, anti-inflammatory, antioxidant, detoxic effects there is creation of medical and cosmetic products based on native raw materials and extractions from sapropel.

We was investigated chemical composition of sapropel from Pribich lake Shatsky district of Volyn region. Was indicated the presence of a wide range of amino acids, fatty and organic acids, microelements. Was getting aqueous, spirituous and oily extracts of sapropel. Was defined anti-inflammatory, reparative and antimicrobial activity of developed extracts. Was defined humidity, fractional composition, technological properties of native materials (bulk, volume, specific weight, porosity), was investigated dependent technological properties from humidity. Was soundly expediency of using native sapropel in cosmetics.

Results and discussion. For the results of physico-chemical, structure-mechanical and microbiology researches was developed the composition of cosmetics masks for different types of skin. The using of the gelling agent was soundly for increasing adhesion to skin surface. Conducted market analysis of the pharmaceutical market of drugs and cosmetics, which include derivatives sapropel and concluded that the ukrainian pharmaceutical and cosmetics market is almost no state producers, making them promising for development of new medications and cosmetics.

Conclusions. In the course of the thesis was achieved the main goal - to focused study of sapropel identify promising set of biologically active substances and the creation on its basis of a medicament for the treatment of certain diseases.

INTENSIFYING A CULTIVATION PROCESS OF PARENT CULTURE IN MANUFACTURE OF THE ALIVE VACCINE FOR THE PROPHYLACTIC IMMUNITY DRUGS

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Introduction. Creation of new medicine for protection of pets and livestock against virus infections does not remove from the agenda of a problem of improvement of known technologies of manufacture of alive vaccines.

The basic direction here is the increase of an output of sporous bacterial mass. It is known, that mixing at cultivation of parent cultures raises an output of sporous mass. Under production conditions mixing is often carried out manually, containers are taken from thermostat and stirred up manually. The aspiration to provide mechanical mixing of contents of containers is natural. The serial equipment for similar low-tonnage production has a narrow area of expertise and is not fully automated.

It is possible to intensify process by making containers move oscillatory. The technical decision of the given problem is imposing low-frequency fluctuations on content of containers.

Aim. Aim of research is development of device's design, that allows to accelerate process of cultivation of bacterial mass.

The device is electric thermostat with dry air, established on the vibrating basis, consisting of a platform on four elastic elements (springs) and the inertial vibrator. The device turns on automatically few times in day for a few minutes. It is enough for cells to be better washed by a nutrient environment, take components for growth and duplication.

Materials and methods. In the developed design thermostat is the standard equipment and additional calculations does not require. Therefore it is necessary to calculate parameters of vibrating installation.

The experimental researches demonstrate, that intensive mix of a liquid nutrient environment occurs at frequencies $15 \div 25$ Hz and amplitudes $0.002 \div 0.0045$ m. For work on such frequencies and amplitudes it is expedient to use the inertial self-balancing vibrator, that creates a constant on a direction and a variable on value disturbing force, that changes itself according to the harmonious law. In a format of theoretical research we have constructed mechanical model of installation, fluctuations of which are described by the heterogeneous differential equation of the second order:

$$m\ddot{x} + \mu\dot{x} + cx = 2m_0\omega^2 r sin(\omega t),$$

where x – movement of the center mass of installation;

m – the reduced mass of installation;

m_0–mass of disbalance;

ω– angular speed of rotation disbalances;

r– distance from the center of disbalances mass up to axis of their rotation;

μ – friction coefficient in system;

c– total rigidity of springs.

The partial decision of this equation conforms to the compelled fluctuations of system:

$$x = Asin(\omega t - \varepsilon),$$

where A – amplitude of the compelled fluctuations;

ε – shift of phases between the compelled fluctuations and disturbing force.

Frequency of disturbing force got out of a range 15÷25 Hz. Based on that installation with the specified drive work on resonant modes, own frequency of fluctuations of elastic system admitted to five times less resonant. Then on known ratio rigidity of springs, factor of friction in system, parameters of the vibrator, working and resonant amplitudes of fluctuations was defined.

Parameters of springs were defined from a condition of strength on normal tension, thus the maximal deflection of springs equal to resonant amplitude of fluctuations.

Power consumed by installation is calculated while it reaches the maximum at transition through a resonance. Based on calculated power was chosen drive motor.

Results and discussion. Dynamic calculation vibrating installation has allowed to define working and resonant amplitudes of the compelled fluctuations (accordingly 0.0023 m and 0.022 m), to design not balancing the vibrator, to calculate parameters of springs and to select drive motor with the most economic characteristics.

Conclusions. Carried out experimental and theoretical researches have allowed to develop a design of the vibrating installation that mix effectively parent culture and provide an increase of output of sporous mass on 25%.

THE PERSPECTIVE OF USE OF CLATHRATE COMPOUNDS COMBINED WITH MEDICAL SUBSTANCES

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Introduction. Much attention has been payed to creation of clathrate compounds of active pharmaceutical ingredients (API).

Clathrate complexes are supramolecular structures. These structures are formed by inclusion of APIs ("guest") into the hollows in the crystal frame of molecules of the supplementary substance ("host"). The compounds do not form any kind of specific link between molecules of the "guest" and the "host".

Aim. Thus, the aim of this research is reviewing the perspectives of use of clathrate compounds combined with medical substances.

Results. At the present time the process of clathration has a number of advantages. Production of clathrate compounds improves the process of API transportation through mucosae to the target organs, widens the therapeutic potential of substances.

The technology of transportation of clathrate compounds with API can radically change the idea of existing substances, improving their bio-availability and lessening the therapeutic dose. The analysis of written data shows that there are way of obtaining water-soluble medicinal compounds for such substances as Sibasone, Mesapam, Indometacyne. The results of research suggest lowering of therapeutic dose of medicinal substances several times. The use of clathrate compounds allows lessening the dosage of the substance, thus lowering its toxicity.

As the basis of clathrate compounds high-molecular supplementary substances are used, such as β-cyclodextrin, propylene glycol, non-organic polymers, etc. Compositions with NSAIDs (paracetamol, ibuprofen, ketoprofen, flufenamic and mefenamic acid, etc.), steroids, prostaglandins and prostacyclins, barbiturates, sulfonamides, heart glycosides might be examples of compounds with β-cyclodextrin.

Conclusion. The results of research have shown that the perspective of use of clathrate compounds with API is developing rapidly. Clathrate compounds are suitable for most forms of medicines and entering ways. The acquired data suggests superiority of physical-chemical properties of clathrate compounds, which boosts the absorbability of medicinal substances with low bio-availability, allows lessening of therapeutic dose and the substance's toxicity, boosts the dissolution of the substance in water.

COMPARATIVE ANALYSIS OF PHYSICAL-CHEMICAL, MICROBIOLOGICAL PARAMETERS AND THE ELEMENTAL COMPOSITION OF BEE POLLEN AND PERGA

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Introduction. Physico-chemical and microbiological parameters, as well as the elemental composition of bee pollen and bee bread, in the process of maturation. Table. Research shows the results of 2013 and 2014, the results of 2015 and 2016. were similar.

The pollen load and Perge concentration of crude protein, flavones-idnyh compounds, crude fat are almost identical. Humidity pollen is significantly lower humidity pollen. The content of free amino acids (amino nitrogen) in Perge and pollen same. This suggests that during pollen maturation occurs hydrolysis of proteins. The concentration of vitamin B12 in Perge was significantly lower compared with the pollen. This is probably due to the activity of certain microorganisms, during pollen maturation. The pH of the 2% aqueous solution of bee pollen and pollen significantly different.

Results and discussion. Number mesophyllic aerobic and facultative anaerobic microorganisms (KMAiFAM) in pollen taken from pyltseulovitelya more than 20 times higher than in Perge, stored in a cell. The content of molds in pollen 47 times more than the pollen.

Pollen maturation studies have shown that a decrease in humidity, a decrease in pH and an increase in the microbiological purity perge occur mainly in the first 9 days after putting it in a cell bees. So reduction in moisture beebread first 9 days of its maturation in 2003 amounted to 100.0% in 2004 g - 96.2% of its total reduction during the entire maturation (15 days). Reduction of pH 2 on average per year during the first 9 days of ripening was 80.4% of the level reduction of this index and the number of molds and KMAiFAM was 75.7% and 89.3% respectively in the first 9 days fermentalization beebread .

Conducted in 2013-2014. study content perge and pollen-ing obnozhka macronutrients (K, Na, Ca, Mg), essential trace elements (Cu, Zn, Ag, Fe, Cr) and toxic elements (Cd, Pb, Sn, As, Hg) showed times -lichy between products according to their composition.

Also found no significant changes in concentrations of cations (K^+, Na^+, Ca^{2+}, Mg^{2+}) and anions (Br, Cl^-, SO_4^{2-}, NO_2^-, NO_3^-, F^-, PO_4^{3-}) in perge during its ripening. Among the investigated cations not detected the presence of ammonium cation being

an elementary decomposition product of amino acids and proteins, ie. E. During pollen fermentalizatsii no decomposition of its protein components.

Table

Physico-chemical and microbiological parameters of bee pollen and pollen

Indicators	Bee products	The values of indicators	% of pollen	Credibility with pollen difference
Water,%	pollen	20.80 ± 0.361	100.0	-
	ambrosia	17.93 ± 0.780	86.2	p<0.05
Crude protein, %	pollen	24.33 ± 1.220	100.0	-
	ambrosia	23.13 ± 1.968	95.1	p<0.05
The amine nitrogen,	pollen	1.840 ± 0.0865	100.0	-
	ambrosia	1.903 ± 0.0551	103.4	p<0.05
Flavonoid compounds, %	pollen	3.567 ± 0.2333	100.0	-
	ambrosia	3.327 ± 0.2949	93.3	p<0.05
Vitamine B6, мг/100 г	pollen	0.258 ± 0.1774	100.0	-
	ambrosia	0.784 ± 0.4920	303.9	p<0.05
Vitamine B12, мг/100 г	pollen	3.148 ± 0.3908	100.0	-
	ambrosia	1.758 ± 0.2679	55.8	p<0.05
Crude fat, %	pollen	2.927 ± 0.3950	100.0	-
	ambrosia	3.410 ± 0.1997	116.5	p<0.05
pH	pollen	5.397 ± 0.0353	100.0	-
	ambrosia	4.087 ± 0.2576	75.7	p<0.05
KMAiFAM	pollen	$433.3x10^3$ ±$433.3x10^3$	100.0	-
	ambrosia	$20.0x10^3$ ± $20.0x10^3$	4.6	p<0.05
Mould	pollen	233.3 ± 98.88	100.0	-
	ambrosia	5.0 ± 3.42	2.1	p<0.05

Conclusions. In connection with the studies it can be concluded that pollen is not only identical in physical-chemical, microbiological parameters and elemental composition of bee pollen, but also surpasses it in some database.

DEFINING THE OPTIMAL MOISTURE CONTENT FOR GRANULATING MICROCRYSTALLINE CELLULOSE

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Introduction. In this article is considered the problem of determining the moisture content of microcrystalline cellulose for granulation. Microcrystalline cellulose is wide used in a pharmaceutical industry as auxiliary substance at creation of medicine. To consider all the factors defining optimal values of moistening for the big variety of multi-component powder mixtures, their interrelation and interoperability is very problematic. We offer the following approach to solving this problem.

The formation of a granule from the moment when a drop of the liquid binder falls into the powder layer. Under the influence of capillary forces is going on distribution of the liquid binder on volume and pore volume filling between individual powder particles.

From the literature it is known, that powder moistening passes through 4 successive states which are named a pendulum, a rope, a capillary and a drip. Rope state is an intermediate stage between the pendulum and the capillary when the amount of fluid increases and the liquid bridges, formed earlier, can bind more particles through voids in the powder layer. In the capillary stage voids are filled with liquid. It is believed that the capillary stage gives the highest strength of a granule. From the surface of agglomerate the liquid is pulled in pores by capillary action, until emptinesses of agglomerate will not be completely filled with a liquid. The drip stage corresponds, so-called in granulation, overwetting. Wetted mass becomes firmest and turns into a paste.

Aim. The purpose of work is to determine experimentally by achieve the capillary state in a powder MCC volume when wet.

Materials and methods. In this work were carried out experimental study on the wettability of powder MCC 101 by distilled water. It is necessary to note high wettability of a powder (work on adhesion – 98.1), satisfactory compactibility (parity Haysnera – 1.5) and not so good flowability (index Carra – 32.4). Moistening spent discreetely by means of laboratory pipette. Water was added in an amount from 1 to 3 drops. Weighing of powder samples before and after moistening spent on analytical weights. Moisture content of microcrystalline cellulose defined by means of the laboratory hydrometer. Have been carried out microscopic researches of moistening samples.

Results and discussion. The experimental researches demonstrate, the increase the amount of moisture content up to a certain value leads to expansion of wetting area and moisture content formed damp agglomerate one step at the time raises. Then process of propagation of a moisture stops, that testifies to filling emptiness between particles and about the beginning of formation of a capillary condition. The maximum value moisture content (80%) that correspond, in our opinion, that the beginning of transition in a drop condition is reached. Because the area of wetting is on surface, the excessive moisture falls outside the limits the moistened space and moisture of formed agglomerate greater volume, naturally, decreases. Decrease in moisture of agglomerate is limited by value of 48%, which, apparently, is border between pendulum and rope a condition of system. In process of addition of a moisture new emptiness are filled, and the capillary condition agglomerate once again is reached.

In laboratory conditions powder has been granulated. The researches demonstrate, that the operating range of moisture for granulation is 80–90%. And at 90 % moisture content of granules are the most durable.

Microscopic researches demonstrate, that when moisture content of powder is 80 %, we can observe growth and sealing of granules. Excess of this value up to 90% leads to the beginning conglutination of granules. And at 80% moisture content of microcrystalline cellulose granules are homogeneous.

Conclusions. In this work, process of wet granulation of microcrystalline cellulose 101 has been studied.

We offer an approach to optimize search of a range of moisture of microcrystalline cellulose for granulation.

It is found that the range of moisture content of microcrystalline cellulose 101 for granulation is from 48 to 90%. Optimal moisture content is from 80 to 90%. This range conforms to transition of the moist microcrystalline cellulose from a capillary state to drop state.

IFLUENCE OF AUXILIARY AGENTS ON THE TECHNOLOGICAL PROPERTIES OF CAPSULE MASS

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Introduction. Development of domestic generic drugs of major pharmaceutical groups which have effective, safe and high quality, meet the objectives of the strategic import substitution program of Ukraine Government. Dispite increased production in Ukraine , the major volume of pharmaceutical drug groups still needs of domestic health seervise in drugs with high quality and appropriate bioavailability, which is not satisfied fully yet.

Aim. Study of the effect of excipients on the quality of the capsule mass in solid dosage forms.

Materials and methods. Determination of physical and chemical parameters of the granulates in accordance with the requirements of the State Pharmacopoeia of Ukraine. The solution to this problem involves the use of an integrated approach to the creation of solid dosage forms by use of modern technological methods which based on systematic study of the properties, processing characteristics of substances and auxiliaries and their rational choice

Results and discussion. In the development of drugs the important role played by excipients, which are selected for each dosage form should be a reasonable estimate of the physical ,chemical and technological characteristics, the study of their impact on the efficacy, safety and stability of drugs. It has been studied all characteristics of excipients for science-based selection of the composition and technology of encapsulated dosage forms; The choice of the proportion of auxiliaries was carried out taking into account the requirements to the quality of the mass for filling of capsules. In this case it was necessary to fulfill the following conditions: auxiliaries were mixed with the active substance with the greatest possible uniformity; the mass of granulation capsule should have sufficient fluidity to ensure the accuracy of the dosing process. As humectants solutions used alcohol plasdona K-29, polyvinylpyrrolidone (PVP), S-630 plasdona. The quality of resulting granules after moistening of the powder mass plasdona alcoholic solution of K-29 is significantly different from the latter, namely the granulate flowability sufficient for dispensing the formulation of an industrial production, which contributes to the homogeneity of dosing.

Conclusions. The results of these studies have shown the influence of excipients on the pharmaco-technological parameters of quality granulates. To ensure the homogeneity of dosing granulated mass is necessary to use a wet granulation method, and K-29 use as the humectant alcoholic solution ofplasdone.

DEVELOPMENT OF COMPOSITION CAPSULES FOR TREATMENT OF VARICOSE VEINS

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Introduction. Treatment of varicose veins, at this time, is in the first place and has a great socio-economic importance. According to various sources, in varying degrees, varicose veins suffer up to 35% of women and 15% men. Varicosities, however, are frequently the cause of discomfort, pain, loss of working days, disability, and deterioration of health-related quality of life.

The leading symptom of varicose veins is the expansion of the saphenous veins, because of which the disease got its name. One of the common symptoms that appear at the very beginning of the disease, there are transient swelling and pain along the veins (often not yet expanded) so-called "heavy legs syndrome", symptoms are usually more pronounced in the evening, after work, or during prolonged standing, especially in hot weather. Severe form may also lead to loss of limb or loss of life.

The complexity of the etiology and pathogenesis of venous diseases, the complexity of their currents, as well as a high probability of complications explain the need for a comprehensive drug therapy of this disease with the use of safe and effective herbal remedies. Development and production of medicines in capsule form is among the most dynamically developing areas of the pharmaceutical industry, due to a number of advantages of this formulation: ease of use, precision dosing, high bioavailability.

Aim. Therefore, the aim of our work was to study the physical, chemical and pharmaco-technological properties of active substances and excipients for the formulation and development of technology-based capsules hazel and horse chestnut extracts.

Materials and methods. Development of the drug was carried out using a thick hazel extract and dry extract of horse chestnut.

Determined pharmaco-technological properties of the extracts and their mixtures with auxiliaries, then the quality of the capsules was evaluated by the procedures of State Pharmacopoeia of Ukraine (SPU).

Results and discussion. Studied pharmaco-technological properties of thick hazel extract, obtained on the Department of Pharmacognosy NUPh and dry extract of horse chestnut. As a result of investigations, developed the optimal composition of capsules, which in terms of quality meet the requirements of SPU and suggested the technology of their production.

Conclusions. Thus, as a result of the research developed the composition and technology of production of capsules with thick hazel extract and dry extract of horse chestnut, which fully comply with the requirements of SPU.

STUDIES IN DEVELOPING DRUGS FOR THE TREATMENT OF GENITAL HERPES

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Introduction. Nowadays, there are many methods of therapy for genital herpes (GH), but none of them provides the elimination of herpes simplex virus (HSV) from the body. The cells of the nervous system remains a reservoir of HSV, which leads to outbreaks. Modern methods of treatment are aimed primarily at preventing the development or restoration of disturbances caused by its activation in body.

The most commonly used treatments for Herpes simplex virus type I and II are antiviral mono-drugs by synthetic origin, which often leads to both local and systemic allergic reactions. The antiviral therapy has as a rule short-term effect. Therefore the treatment of genital herpes treatment requires an integrated approach. Combined using of antiviral drugs with different chemical structure and fundamentally different mechanism of action leads to increased antiviral effect of additive or synergistic nature and helps reduce the toxic effects of essential drugs by adequate antiviral activity of combinations of lower concentrations compared with using every compound separately. Moreover, the combined using of antivirals with different mechanisms of action could prevent or reduce the probability of appearance of mutant viruses with resistant inhibitors. In Ukraine, most of antiherpetic drugs are mono synthetic drugs with high therapeutic efficacy, which usually have a wide range of toxicological properties. List of drugs of plant origin is very limited, and for the local treatment of herpetic disease - completely missing. But the number of domestic antivirals of combined compound is insufficient, that determines the need for a similar drugs.

Conclusions. That's why the creation of new combined drugs with plant components for the local treatment of herpetic infections and expanding the list of plants that can be used for this purpose is very reasonable. A combination of two or more substances in a single dosage form allows creating a closely new and more effective and harmless drugs of local action on an existing range of pharmacological aids.

INVESTIGATION OF THE EFFECT OF SURFACTANTS ON THE FLAVONOIDS EXTRACTION

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Introduction. Medicinal plants are a popular source of raw materials for pharmaceuticals. Our attention was attracted by Vitis vinifera as the source of flavonoids. Grape (lat Vitis Vinifera.) - the kind of perennial bush vines of the Grapes genus of the Grape family. Vitis vinifera grows in temperate and subtropical regions, it is widely cultivated in many countries all over the world. Grapes grow on a trellis normally. The fruit is juicy berries with different colors and shapes. Berries are gathered in clusters, ripen in late August – September. Wine takes foremost among the grapes products. The consumption of ripe berries increases metabolism and tones the body. Folk medicine advises to use decoction of dried grapes with a small amount of impurities onions to treat cough and hoarse singers and lecturers. Grape leaves are used to treat hypertension. Powder of dried leaves is good to stop bleeding. Prom in boiling water, winepress fresh grape leaves is applied to purulent wounds, venous ulcers and bedsores. With grape marc are also taken grape seed oil, which has proved to be an effective antioxidant due to its high content of vitamin E.

Grape leaves are used less, but contain a lot of biologically active substances. Vitis vinifera leaves are a rich source of vitamins A, B_6 and C, manganese, magnesium, iron, calcium, fiber, niacin, riboflavin, flavonoids and other substances.

To get the flavonoids from the grape leaves the extraction methods must be applied. Maceration and percolation are often used methods as the most simple. They do not require complex technological equipment. Maceration can be used in small pharmaceutical enterprises or pharmacies. For extraction of flavonoids alcohol at a concentration of 40-70% is used as extractant.

To intensify the process of extraction different methods are used. Advanced equipment, grinding materials, new extractants, the effect of pulsation, vibration, hydrodynamic conditions, the addition of surfactant are used. Among these methods the addition of surfactants is interesting because this method does not require replacement of existing equipment and technology. Surfactants increase the solubility of substances and reduce the surface tension and thus accelerate the process of extraction. Widely known surfactants is sodium lauryl sulfate, Tween-20, Tween-80. Sodium lauryl sulfate is an anionic surfactant, Tween-20, Tween-80 are a non-ionic surfactant.

Aim. The aim of this study is to investigate the effect of surfactants on the flavonoids extraction from vitis vinifera leaves.

Materials and methods. The first step was to prepare a sample extract from the vitis vinifera leaves. Sample of 10 g of crushed grape leaves was extracted with 100 ml of 40% ethanol by appropriate method (maceration). For other samples 40% ethanol with the addition of surfactants were used as extractant. We used 0.1% of sodium lauryl sulfate, 0.01% sodium lauryl sulfate, 0.1% Tween-20, 0.01% Tween-20, 0.1% Tween-80%, 0.01% Tween-80. Ready extract was poured into measuring flask 100 ml and the volume was adjusted to the mark. That was the solution A.

1 ml of solution A, 1 ml of aluminum chloride were transferred in measuring flask 25 ml. Amount of solution was adjusted to mark by 5% solution of acetic acid in 95% alcohol. After 30 minutes, the optical density of the solution in a spectrophotometer at a wavelength from of 390 to 430 nm in the cell with a layer thickness of 10 mm was measured . As the reference solution using a solution consisting of 1 ml of extract, 5% solution of acetic acid in 95% alcohol brought to the mark in a volumetric flask 25 ml.

Parallel optical density of state standard sample routine was measured, which was prepared as follows. In the volumetric flask 25 ml 0.25 ml of state standard sample routine solution was transferred. Amount of solution was adjusted to mark by 5% solution of acetic acid in 95% alcohol. As the reference solution using a solution consisting of 0.25 ml of extract, 5% solution of acetic acid in 95% alcohol brought to the mark in a volumetric flask 25 ml.

The content of the amount of flavonoids in terms of routine and absolutely dry raw material as a percentage calculated by the general formula.

Results and discussion. Solution extract using 40% ethanol has a maximum absorption at a wavelength of 404-405 nm. Solutions extracst using 40% ethanol and surfactants have a maximum absorption at a wavelength of 406-408 nm. So spectrometric method can be used to quantify flavonoids in alcohol extracts and alcohol extracts containing surfactants.

The results determine the quantitative content of flavonoids in extracts show that using surfactants solution amount of flavonoids in extracts increased. The solution of 0.1% sodium lauryl sulfate and 0.1% Tween-20 showed the best results. The number of flavonoids increased in 1.68 times. The use of other samples increases amounts of flavonoids in 1.41-1.48 times.

Conclusions. Thus found that the use of surfactants does not prevent spectrophotometric determination of flavonoids. So spectrometric method can be used to quantify flavonoids in alcohol extracts and alcohol extracts containing surfactants. By using vitis vinifera leaves as example it was shown that surfactants increased amounts of flavonoids extracted from medicinal plants. 0.1% sodium lauryl sulfate and 0.1% Tween-20 in 40% ethanol can be used as extractants to increase yield of flavonoids.

GEL AND POLYMER FILM CONTAINING LINCOMYCIN HYDROCHLORIDE FOR INFLAMMATORY PERIODONTITIS DISEASES TREATMENT

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Introduction. The actual problem of contemporary pharmacy and therapeutic dentistry is the development and implementation of new effective drugs for periodontitis diseases treatment into medical practice, the signs of periodontitis diseases are characteristic for 95% of adult and 80% of children of the Ukrainian population. At present moment in spite of the presence of great number of finished drugs that are proposed for prophylaxis and treatment of periodontitis diseases, the dentists use local application of antibiotic drugs more and more frequently.

Aim. Development of the gel and polymer lincomicid hydrochloride coating film for inflammatory periodontitis diseases treatment.

Materials and methods. Lincomycin hydrochloride in the form of 30% solution manufactured by private stock corporation "PhF "Darnitsya" located Kiev has been used as the active pharmaceutical ingredient (API) in the composition of the gel and polymer coating film. Carbomer 934P, sodium carboxymethyl cellulose, propylene glycol, benzoic acid, hydroxide solution (10%) and calcium chloride (1%) were used as additional materials in the process of work. Polymer coating films were prepared by the method of flow resist coating. The gel pH was determined potentiometrically, the polymer film solubility was determined by the State Pharmacopeia of Ukraine method.

Pesults and discussion. In the process the gel developing, carbomer 934P was used as the gel formation substance (1%), the concentration of which was grounded under structural-mechanical properties, 10% sodium hydroxide solution was used as the neutralizing substance till pH 7.2 obtaining. Other additional substances that were used in the gel composition are propylene glycol (20%), benzoic acid (0.2%) as the preservative and water purified to 100.0. The lincomicin hydrochloride concentration was 30 mg/g.

The composition of the gel and its technology:

Lincomicin hydrochloride 30% solution	10.0 g
Carbomer 934P	1.0 g
Benzoic acid	0.2 g
Sodium hydroxide 10% solution	to pH 7.2
Purified water	to 100.0 g

The process of the gel production is the following: lincomicin hydrochloride solution, are added to benzoic acid solution and carbopol in the purified water under

the pH control and during sodium hydroxide mixing and then it is homogenized at the 0,9 c^{-1} rate during 10 minutes. The gel deaeration is performed if necessary. The gel standardization must take into consideration the following indicators: description, identification, pH, microbiological purity, and assay.

The term of the drug action on the site of application is usually 15-20 minutes, consequently, the frequency of its application must be 5-6 times a day, what is not very convenient for the patient. Unlike the gel, which is washed with the saliva and needs repeated application, the polymer film is the most rational form, as depending on its composition, the polymer coating film can stay on the site of application 3-6 hours and longer, and API concentration, contained in the gel concentration is almost fully absorbed on the site of application. Another advantageous peculiarity of this medicinal form is the accuracy of API dosing, decreasing of the drug intake quantity, superficial protection of the medicinal tissues, side reactions minimization.

The composition of the dental polymer film produced by the flow resist coating method applied on the dish horizontal surface (Petri dish) or special iron sets includes anionic polyelectrolyte solution (sodium carboxymethyl cellulose), the concentration of which depends on the trade mark, API solution (30% lincomicin hydrochloride), propylene glycol (plasticizer), coupling agent ($CaCl_2$ solution in which cations Ca^{++} are present) thanks to what between carboxylic groups of different macromolecules of anionic polymer cross bridges ($-\overset{o}{\overset{||}{C}}\text{-O-}Ca-O-\overset{o}{\overset{||}{C}}-$) are formed, the presence of these cross bridges delays the process of swelling and solubility of the obtained polymer film. In the process of polymer film preparation, the obtained solution is poured out on the smooth horizontal surface and dried (water eliminating) to the residual 5,0 ± 0,5% moisture (it should be taken into consideration that plasticizer is not evaporated), the final stage of the obtained film cutting is carried out by the use of acute tube of a cylindrical form with 10 mm diameter. The thickness and mass of the coating film, and also API concentration are chosen experimentally, and the term of swelling and coating film solubility at the site of application depend on the "coupling agent" (Ca^{++} concentration is also regulated).

The standardization of the obtained polymer coating film is carried out in accordance with the following requirements: description, identification and quantitative API analysis, film adhesion to hydrophilic surface, stability and elasticity of the coating film, microbiological purity.

Conclusions. The composition and gel technology and dental polymer coating film containing hydrochloride for inflammatory periodontitis diseases treatment have been developed. It has been demonstrated that polymer coating films prepared on the basis of anionic polyelectrolyte – sodium carboxymethylcellulose is a prolonged form, the solubility of which is regulated and depends on concentration of divalent cation Ca^{++}.

QUALITY STANDARDS OF DICLOFENAC SODIUM AND BENZKETOZONE COMBINED CAPSULES

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Introduction. Preconditions for creation of medicinal preparations of combined composition are the possibilities for improving pharmacotherapeutic effect on the account of intensification of curing and decreasing adverse effect, optimal combination of doses of active substances, convenience of use and reasonability from economic point of view.

Aim of research. Taking into consideration the above-stated facts, the aim of our present research was the quality evaluation of capsules with combined composition, worked out in the Tashkent pharmaceutical institute and possessing non-steroidal anti-inflammatory action.

Materials and methods: quality control of the analyzed capsules of combined composition containing as active substances by 25 mg of diclofenac sodium and benzketozone, was conducted in accordance with the requirements of the general pharmacopoeia article "Capsules" and corresponding normative documentation. Moreover was conducted the determination of such qualitative characteristics as appearance of capsules, authenticity, average mass of capsules and content, and also deviations from these parameters, disintegration, dissolution, other admixtures, microbiological purity. Quantitative determination of active substances was identified by spectrophotometric method at wave length of 276±2 nm for diclofenac sodium and 305±2 nm for benzketozone. Results are given in the table.

Table

Results of determination qualitative characteristics of diclofenac sodium and benzketozone capsules

Determined characteristic	Requirements according to ND	Analysis results
Description	Capsules of yellow colour with orange colour cover №4, contents of white colour	corresponds
Authenticity	Diclofenac sodium. UV- spectrum 0.0025% of preparation's solution in the interval of 220-300 nm must have absorption maximum at λ=276±2 nm	corresponds
	Benzketozone. UV- spectrum 0.001% of preparation's solution in the interval of 220-350 nm must have absorption maximum at λ=305±2 nm	corresponds
Average mass of capsule and deviations from it	0.1363-0.1700 g ±10.0%	0.1585 g ±0.71%

Average mass of capsule's content and deviations from it	0.0918-0.1122 g ±10.0%	0.1060 g ±0.83%
Disintegration	Must not be disintegrated during 60 min. in hydrochloric acid solution (0.1 mole/l)	corresponds
	Must be disintegrated in phosphate buffer solution (pH 7.4) during not more than 20 min.	8 min. 20 sec.
Dissolution	Must sustain the test on gastro-resistance during 60 min. in 0.1 M of hydrochloric acid solution	corresponds
	Not less than 75% during 45 min at rotation speed of basket 100 rot/min in phosphate buffer solution with pH 7.4	94.6% (diclof. sodium) 92.4% (benzketozone)
Other admixtures	Diclofenac sodium: except the basic stain on chromatogram it is permitted the presence of additional stains, which on the sum total of the size and colour intensity don't exceed the stain on chromatogram of SSTS. Content of admixtures must not exceed 1%	corresponds
	Benzketozone: on chromatogram of the tested solution any stain except the basic must not exceed on intensity the stain, obtained on chromatograms of SSTS solutions of phenylglioxilic acid (not more than 0.25%) and thiosemicarbaside (0.25%). The sum of all admixtures must not exceed 0.5%	corresponds
Microbiological purity	In 1 g of preparation it is permitted the presence of general amount of aerobic bacteria not more than 10^3, general amount of fungi not more than 10^2, in absence of Escherichia coli	corresponds
Quantitative content of active substances	Diclofenac sodium: 0.0231-0.0269 g (±7.5%) in 1 capsule	0.0248 g (99.37%)
	Benzketozone: 0.0231-0.0269 g (±7.5%) In 1 capsule	0.0246 g (98.23%)

Obtained results: the studied capsules №4 have the content of white colour. Deviations from average mass of capsules and content didn't exceed the regulated 10% and were ±0.71% and ±0.83%, correspondingly. The analyzed capsules on such characteristics as authenticity, microbiological purity and other admixtures corresponded to the maintained requirements. Disintegration was 8 min. 20 sec., and the amount of the released active substances in 45 min was equal to 94.6% (diclofenac sodium) and 92.4% (benzketozone). Quantitative content of diclofenac sodium and benzketozone was 0.0248 g (99.37%) and 0.0246 g (98.23%), correspondingly.

Conclusion: According to the results of conducted research the capsules of combined composition on the analyzed qualitative and quantitative characteristics correspond to the requirements of SP XI and NTD.

STUDYING THE PROPERTIES OF EMULSION BASE FOR COSMETIC DRY SKIN`S CREAM

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Introduction. In our days, invention the new agents for the treatment and correction problems of dry skin is an important issue in the development of native medical and prophylactic agents. Dry skin - is not just a problem of cosmetic nature, dry skin often is a clinical symptom of a variety dermatological conditions, if it wasn't payed attention to that, it can worsen the disease. Many people of different age groups have this problem.

Aim of our work is the theoretical rationale of composition and technology of the emulsion cream base for the treatment and prevention on dry skin problems.

Materials and methods. The objects of this study is a oily and gelling agent Aristoflex AVC, emollients Lanol 99, Lanol 2681, and specimens of their base.

Results. As the cream base was chosen emulsion of first kind direct oil in water. As emulsifier was selected Aristoflex AVC, which has gelling properties but has the ability to form stable emulsions without the addition of further emulsifiers too. During the study of experimental samples with concentrations Aristoflex AVC from 0.5 to 2.5%, the optimum value allowing to obtain a stable emulsion at 20% of the oil phase concentration was 2% emulsifier.

A separate level of creating the cream was to improving the quality of the oil phase. Were selected Lanol 99 and Lanol 2681, emollients, due to which cream is better absorbed and distributed in the skin. During the experiment, it was found that the introduction of the foundation, even in small quantities (2%), these substances improve the basic consumer properties of the cream (foundation is easy to apply, leaves no residue and stickiness, the foundation acquires softening properties). However, the introduction of emollients in more than half the amount (75%) of the mass fraction of the oil phase, or its complete replacement were not possible due to violations of emulsion stability and the deterioration of the sensory properties.

Conclusions. The emulsion base of cream for dry skin was developmented. The optimal concentration of emulsifier Aristoflex AVC was 2%, the optimal composition oil phase was plant`s oil – 15%, a mixture of Lanol 2681 and Lanol 99 (1:1) – 5%. The physicochemical, structural and mechanical properties of the developed base was explored.

CROMATO-MASS-SPECTROMETRY RESEARCHING OF VOLATILE COMPAUNDS IN THE COMBINED INTRAVAGINAL GEL WICH BASES ON LIQUID EXTRACT OF HOP`S CONES.

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Introduction. Quite common in gynecology pathology is infectious-inflammatory disease., as the treatment was used antibiotic and hormone-replacement therapy, depending on the etiology and pathogenesis. Recently, the range of this group of medicines has increased significantly. However, herbal preparations given nosology group hardly represented. For next research and development of the drug was elected Humulus lupulus. In the cones are a large groups of biologically active substances common being bitter, polyphenolic compounds, essential oil, organic and oily acids. Interest in the use of hops caused by the use, availability prenil flavonoids, including 8-prenilnaringenine, as powerful phytoestrogen.

Aim. Using the chromatography-mass spectrophotometry method to determine the composition of volatile compounds in intravaginal gels, wich based on liquid extract of hop cones (1: 2).

Materials and methods. The method of chromatography-mass spectrometry were investigated volatile compounds in intravaginal gels. For identification use vuvaly-chromatograph Agilent Technologies, co-equipped chromatographic column was from the 6890 series mass spectrometer series 5973. The study was identified composition and the total content of volatile compounds combined and intravaginal gels.

Results and discussion. Surveys were identified on gels volatile compounds.

Terpenoids with another compounds:

α-copayene,

squalene allo-aromadendrene,

β-selinene,

tridecane-2

and *organic acids:* caprinic acid, laurinolic acid, myristic acid, pentadekanic acid, palmitoleinolic acid, palmitic acid, heptadekanic acid, linolenic acid, linoleic acid, oleic acid, stearinic.

Conclusions. Was investigating, by chromato-mass-spectrometry volatile substances in combined intravaginal gels wich based on liquid extract of hop`s cones.

RHEOLOGICAL STYDY OF CARBOPOL ULTREZ 10 NF HYDRO-GEL

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Introduction. For medical applications, some properties of soft medicinal forms are great importance, namely: good flexibility, controlled disposal, dosage and etc. Qualitative description of these properties are based on measurement of rheological parameters, including viscosity, which plays an important role.

Aim. In this study we examined the physical properties of cross-linking polymer gels, by rheological investigations.

Materials and methods. The investigate sample was polyacrylic acid Carbopol Ultrez 10 NF (Lubrizol, Belgium). This polymeric gel was obtained with concentrations 1% by mixing them with distilled water and deacidifying by solution of 10% sodium hydroxide. The pH value of the preparation containing Carbopol Ultrez 10 NF was 7.5-8.0.

Viscosity of this sample was measured at different shear rates between 0 and 200 rpm with rotational viscometer. Measurements were performed in the temperature range 20-25 °C. The following rheological parameters have been determined:

$$\eta = K \times N \times \alpha,$$

where: η – dynamic viscosity,

K – cylinder constant,

N – shear rate constant,

α – value well-road on apparatus scale.

Results and discussion. Viscosity measurements enabled to determine the dependence of shear stress on shear rate of the systems. From the analysis of the results on samples of Carbopol Ultrez 10 NF noted that this sample shows a decrease in viscosity after increase of shear rate. This behavior reveals a non-Newtonian flow type shear-thinning

All the tested systems are viscoelastic liquids have determining yield stress. It is the value of shear stress below which the system behaves like an elastic solid body. Having reached a certain threshold shear stress, the structure of the system is rapidly and totally destroyed and it starts to flow like viscous liquid. This law is typical for Carbopol.

Conclusion. Tests with Carbopol Ultrez 10 NF sample showed decrease in viscosity with increasing shear rate and restructuration after force reduction. This behavior reveals about non-Newtonian flow type shear-thinning and thixotropic properties.

PERFORMANCE-BASED SUPPOSITORIES LOCAL RAW MATERIALS IN MEDICAL PRACTICE

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Introduction. Based on Maternal and Child Health, the State program "Healthy Generation" provides a highly empowering health and medical care of the younger generation. One method of achieving the objectives defined by this priority is the development of the pharmaceutical industry capable of on the basis of local raw materials to create high-performance native broad-spectrum drugs, which not only allow the release of the republic on the import of foreign drugs, but will be subject to export. At the present time is the actual creation of highly effective antibiotics, antivirals for treatment and prevention of diseases related etiology.

Results and discussion. Priori analysis of published data showed that at present there is a tendency of growth of bacterial and viral diseases in the population, in particular diseases chlamydia and herpes. Since the infection from mother to child infected with these types of viruses, there antennal or during birth, depending on the location and severity of infectious process. Perinatal infection of infants impact on the child in the early neonatal period and first year of life. Planning for an integrated treatment and prevention of these diseases is undoubtedly requires urgent attention to maintain health as a newborn and mothers. Scientists from the Institute of Bioorganic Chemistry. Named after Acad. A. S. Sadykov AS RU proposed the creation of the dosage form using drugs and gozalidona megosina synthesized on the basis of gossypol obtained from cotton in the laboratory of polyphenolic compounds. Clinical study of these drugs indicates antihlamidiynoy and antiherpetic activity gozalidona megosina property. Currently approved and successfully used in medical practice gozalidona tablets of 0.1 g and 3% ointment megosina. These drugs are unique in that apart from antibacterial, antiviral action of interferon inducers are. This property makes it possible to use them not only for treatment but also prevention of chlamydia and herpes the same time it should be noted that these dosage forms as tablets and ointments are considerably inferior in efficiency rectal dosage forms. Especially when it comes to newborns and infants, from birth, infected with the herpes virus and chlamydia from infected mothers through amniotic fluid. All this confirms the relevance of the research and development activities antiinfectious suppositories containing gozalidon and megosin for children and adults. At the present stage of development of pharmaceutical technology, scientific research in this area is aimed at

getting the dosage form, minimally traumatic child's mind, easy to use for children and adults at the same time providing an optimal therapeutic effect. In modern medicine, the most interesting use of the rectal route of administration of drugs. Rectal formulations combine the favorable features inherent in both oral and injectable dosage forms: the intensity of absorption and rapid onset of therapeutic effect, the accuracy of dosing.

Conclusions. Selection of compositions of suppositories and gozalidona megosina, conducted according to the results of pharmacological studies, as well as their cooking done on the fundamentals of pharmaceutical technology. It is planned to conduct clinical trials for children suppositories gozalidona in II- Tashkent Medical Academy clinic Republic of Uzbekistan. Suppositories for adults gozalidona TMMCDQME (The main management control of drug quality medical equipment) at Ministry of Health Republic of Uzbekistan approved TPA(Temporary Pharmacopoeia article) 42-Uzb 0804-2005 authorizing their use as an effective means antihlamidiynoe. Also developed Temporary Pharmacopoeia article on antiherpetic agent megosina suppositories for adults is under consideration in TMMCDQME Ministry of Health of Republic of Uzbekistan. At the same time drugs are tested in the II- Tashkent Medical Academy clinic Republic of Uzbekistan. A preliminary feasibility study showed a weighty advantage of local resources in creating and implementing suppository into production.

DEVELOPMENT OF GRANULES WITH NATURAL ZEOLITE AND EXTRACT OF CHAMOMILE

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Introduction. Today, one of the most actual problems of modern medicine is increasing of quantity of digestive system diseases, among which the first place is occupied by gastritis. Gastritis belongi to a "diseases of civilization" group and their wide prevalence can be explained by increasing of urbanization, unhealthy diet, harmful habits, by the decreasing in the share of physical labor in modern life, by the influence of adverse social factors and by numerous stressful situations. In the course of treatment, anti-inflammatory drugs are being used for a long time, and it is often the cause of side effects. That is why the development of natural medicines (herbal anti-inflammatory drugs), which allow to treat the patient for long courses with minimal risk, is still topical.

Among the plants that have anti-inflammatory effect, special attention should be paid to chamomile, extracts from which flowers are widely used in folk and officinal medicine. Hamazulene is the main active ingredient of chamomile extract. It has antispasmodic, anti-inflammatory, choleretic, antiseptic action; reduces the incidence of allergies, improves regeneration processes, increases the secretory activity of digestive glands, improves appetite and more.

The second component, which we believe to be included in a composition with chamomile extract, is natural zeolite.

Aim. The aim of our study is the development of composition and technology of combined granules, based on powder of natural zeolite and liquid extract of chamomile flowers.

Materials and methods. We used methods of pharmacopoeia for determination of the technological properties of experimental compositions.

Results and discussion. We experimentally selected the optimum ratio of the components. It is the ratio of natural zeolite and extract of chamomile about 1.0 to 0.5. As a binder, starch paste 7% has been chosen, which is allowing getting granules of high quality. The basic technological properties of granules were studied (flowability – 6.5 g/sec; bulk density – 1.3 g/cm$^{3)}$, and also the technology of wet granulation was developed.

Conclusions. In conclusion of our work, it is should be noted, that the natural zeolite is optimal filler for getting granules containing liquid extracts. All technological qualities of the resulting composition meet national pharmacopoeia requirements.

DESIGN OF TABLETS, DISPERSIBLE IN ORAL CAVITY WITH ECHINACEA EXTRACT

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Introduction. Pharmaceutical Technology is one of the fastest growing areas of pharmaceuticals, main important issues which in modern conditions is the choice of a rational dosage form, the optimal ingredients, the search for new substances and rational technological methods to ensure proper quality of the finished drugs with maximum terapeutic efficacy with minimal adverse effect. In he area of the development of tablet dosage forms the main task of the research is scientific and experimental justification of the excipients (physico-chemical and technological properties of excipients their nature and number of excipients, the order of the technological processes and optimal methods of preparing a dosage form).

The bioavailability of medications in the form of tablets, dispersible oral cavity absorption of drugs is enhanced by the absorption drugs in oral cavity and absorption of saliva containing drug, before reaching the stomach. Among other things, the amount of drug exposed to presystemic metabolism, or first pass effect (reduction in the amount of drug in blood as a result of presystemic metabolism - inactivation in the liver before reaching the systemic circulation) is reduced in comparison with the standard tablet.

Aim. Design of the the optimal ingredients of the tablets, dispersible oral cavity with echinacea extract according to the requirements of the State Pharmacopoeia of the Republic of Kazakhstan. **Materials and methods.** Object of study - orally disintegrating tablet with echinacea extract. Research Methods: standard, pharmacopian (physico-chemical, pharmaco-technological).

Results and discussion. The extract of Echinacea has immune stimulating properties, antibacterial, antiviral and fungicidal properties. Echinacea inhibits the growth of Streptococcus, Staphylococcus, E. coli, influenza and herpes, is also effective in the treatment of diseases of the oral mucosa, periodontal and and of external integuments providing anti-inflammatory, hemostatic, and regenerative effects. The Echinacea grass contains two main groups of biologically active compounds - phenylpropanoids (cichoric acid, echinacoside and polysaccharides which have antimicrobial, antiblastomic and immunomodulatory effects, and therefore the choice of excipients was due to their overall compatibility, and the degree of release active substances from tablets. In the above components were designed tablet models, dispersible oral cavity with Echinacea extract.

Conclusions. As a result, will be developed a new dosage form: orally disintegrating tablet with echinacea extract. Based on the research designed an optimal composition of the tablet (active pharmaceutical ingredient, excipients), to produce new highly effective dosage form for Kazakhstan, extending the range of dosage forms, the introduction of which in medical practice will ensure the high availability of medicines.

THE STUDY OF THE RHEOLOGICAL CHARACTERISTICS OF EMULGEL FOR THE TREATMENT OF ATOPIC DERMATITIS

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Introduction. Atopic dermatitis (AD) is a chronic inflammatory disease of the skin of the allergic nature, which is characterized by dryness, reddening, rash and itch. AD is considered to be a children's disease – 65% of little patients with such diagnosis symptoms develop before the age of 1 year, 90% – before the age of 5 years, in rare cases, AD remains for the rest of all life. Local treatment of atopic dermatitis consists in applying of various soft drugs.

Due to the wide range of functional qualities inherent emulsion and gel, as a dosage form the emulgel was chosen. As gel it is well distributed on the surface of the skin, releasing the active ingredients and providing high bioavailability and prolonged effect. The oil phase of emulgel prevents rapid drying of the skin that is an important factor in the treatment of atopic dermatitis.

The desired therapeutic effect in a soft dosage form can be achieved only in case the correct choice of active and auxiliary substances.

In emulgel composition for the treatment of atopic dermatitis, we have decided to introduce as active pharmaceutical ingredients dry green tea extract and *dexpanthenol (*D-panthenol). Due to the complex effect of polyphenols, catechins and antioxidants green tea extract has good penetrating ability that allows the bioactive substances to influence the deeper layers of the epidermis, thus providing antibacterial, antiseptic, antifungal, anti-inflammatory, calming and antipruritic actions. In addition, green tea extract improves oxygen and water-salt metabolism, skin hydration, reduces redness and irritation, stimulates regeneration.

In the process of metabolism in the body D-panthenol (provitamin B5) is oxidized to pantothenic acid, which has regenerating, anti-inflammatory and skin protective action. By entering in cells of the skin D-panthenol increases the number of fibroblasts, collagen, frequency of mitosis, thus accelerating the regeneration of the skin and promoting healing. It also affects the resilience and elasticity of the skin.

The main excipient of emulgel is a carrier. Based on the analysis of literature data for researches as gelling agents carbopol (BF Goodrich, USA), Aristoflex AVS (Clariant, Switzerland), Amigel (Savitri, France) and Sepimax ZEN (Seppic, France) were elected.

The objective characteristic of quality of medicinal product with plastic-viscosity medium is structural-mechanical properties such as rheological parameters modeling samples of emulgels.

Aim. The aim of our work is studying of rheological characteristics of emulgel for the treatment of atopic dermatitis.

Materials and methods. The objects of research are the modeling samples of emulgels on the base of different gelling agents (carbopol, Aristoflex AVC, Sepimax ZEN, Amigel).

Measuring rheological parameters was carried out on a rotary viscometer "Myr 3000 V2R" (Viscotech, Spain) in a system of coaxial cylinders by the method of SPhU (ed., P. 2.2.10, p. 24) in a wide range of shear rates. Research was carried out at a temperature (25±0.1) ^{o}C. The viscosity was measured using spindle R6 and R7 at a rotation speed from 0.3 rpm to 20 rpm, units mPa*s. For the study took a weight of experimental sample (20 g) and placed in a container, in which immersed the spindle. Indicators of viscometer were fixed at each speed after reaching stable results. Determination was performed by increasing the rotational speed of the spindle and in the opposite direction. By curve of fluidity the type of flow system, the presence of thixotropic properties, lower, upper and extrapolated the yield strength, viscosity were determined.

Results and discussion. Based on materials of research rheograms were built, showing the dependence of the tangent shear stress τ_r from gradient of velocity D_r. The results showed that the obtained dependencies are nonlinear that indicate about non-Newtonian type of flow of emulgel systems.

In rheograms descending and ascending curves are formed a hysteresis loop, confirming thixotropic character of samples.

Should be noted that the highest viscosity have emulgels based on carbopol and Aristoflex AVC. Emulgels on Sepimax ZEN and Amigel have approximately identical values of structural viscosity.

Conclusions. All experimental samples have similar stable behavior, good plasticity, so will be easily applied on the skin and squeezed out from tube that speaks about good consumer characteristics. Further objective of our research is to study the osmotic activity of emulgels to select the optimal gelling agent.

JUSTIFICATION OF THE COMPOSITION OF COMBINED DERMATOLOGICAL OINTMENTS

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Introduction. The issue of treatment of skin diseases remains an important problem of modern medicine. Since the majority of pathogens fungal infections, infectious and parasitic skin diseases have sensitizing properties, they often cause the development of various secondary rashes or allergic transformation of certain clinical forms of skin infections in eczema. During the treatment process of skin diseases, there are frequently observed relapses, which are often accompanied by itching, as well as complications caused by secondary infection.

Aim. Before developing a new drug we analyzed the studying of needs of modern medical practices of local anti-inflammatory agents, antimicrobial and antiparasitic action.

In order to designate dermatological formulations containing antihistamines, anti-inflammatory, antiparasitic, drying, antimicrobial, and antibacterial, antifungal and hormonal drugs.

Materials and methods. According to it, the composition of a multicomponent ointment has been developed for the treatment of skin diseases (acne, rosacea, demodekoz) which contains: permethrin, metronidazole, zinc oxide, sulfur, salicylic acid, vitamins A and E, Suprastinum, vaseline and lanolin.

Results and discussion. As the dried ingredients ointments we offered to enter in its composition zinc oxide and salicylic acid. To extend the range of antimicrobial and antiinflammatory action of the ointment was introduced metronidazole. Also, composition of the ointment were included sulfur which has an antiparasitic effect, and permethrin - acaricidal formulation for topical application. Suprastin was introduced as a component of an antihistamine to suppress allergic reactions, which are quite often observed in the development of secondary infection.

Conclusions. An important characteristic of preparations for the local treatment are opportunities of vector which should be chemically and pharmacologically indifferent, must be compatible with the active ingredients sufficient to provide release of drug components from the dosage form. Taking into account the compatibility of the components of ointment and direction of action, as such a framework, we choose a mixture of vaseline and lanolin in a specific ratio.

COMPOSITION IMPROVEMENT OF "BRONHOMAX" SYRUP

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Introduction. Respiratory infections occupy an important place in the structure of human diseases and up to 80% of diseases diagnosed with children. The treatment problem of acute inflammatory diseases of the upper and lower respiratory tract with children remains urgent for modern medicine. Among the numerous assortment of pharmaceutical substances fenspiride hydrochloride deserves special attention, as it has a complex mechanism of influence on a respiratory tract inflammatory process – the histamine effect blocking H_1-receptors, that provides antihistamine, spasmolytic actions of fenspiride on smooth muscles of the bronchi and prevents the development of swelling, reduces passage of nasal mucus and bronchial secretions amount; - anti-inflammatory action, which is the result of inhibition of the formation and secretion of inflammatory factors; - inhibits a_1-adrenergic receptors which stimulate the secretion of viscous mucus. Medicines for the treatment of inflammatory diseases of ENT-organs are manufactured in various officinal forms, but the most common and appropriate for use in pediatric practice are syrups. The problem of treatment of inflammatory respiratory diseases among children and adolescents is complicated by the anamnesis of diabetes. Physicians should choose thoroughly and carefully the medicine for the treatment, which must not contain substances affecting blood glucose levels. Therefore, the improvement of "BronhoMax" syrup (Pharmaceutical company «Zdorovie») by means of removal sugar from the composition is a topical area of the research and will expand the range of application of "BronhoMax" syrup.

Aim. The aim of the research was the replacement of sugar by sweeteners that do not affect blood glucose levels in the composition of "BronhoMax" syrup.

Materials and methods. Fenspirid hydrochloride is a dry white substance with a strong bitter taste. As the taste and scent flavors the following have been used: sorbitol, sucrose, fructose, mannitol, sodium saccharin, stevia, glycyram, glycerol, citric acid, flavors (banana, strawberry, lemon, caramel) and their different combinations. Flavor qualities of the test samples were determined according to the methods by Tentsova A.I. and Egorova I.A. We have performed the research of the sample viscosity, pH and stability.

The results and discussion. Fenspirid hydrochloride has a strong bitter taste, its masking is achieved by using a combination of taste and scent flavors. As a result of the research we have offered a sample of fenspiride hydrochloride syrup based on 70% sorbitol with the addition of stevia, glycyram and glycerol.

Conclusions. Implementation of the improved "BronhoMax" syrup (Pharmaceutical company «Zdorovie») would expand the range of its application and reduce the import dependence of Ukrainian pharmaceutical market.

MICROBIOLOGICAL RESEARCH OF SUPPOSITORIES WITH FLUCONAZOLE FOR THE TREATMENT OF VAGINAL CANDIDOSIS

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Introduction. Today the problem of creation effective drugs for the treatment of vaginal candidosis is actual for modern pharmacy.

According the research of vaginal drugs on the pharmaceutical market of Ukraine the quantity of national drugs, especially combined is not enough.

Aim. The study of microbiological activity models of vaginal pessaries with fluconazole and amaranth oil developed on the basis of macrogols in ratio of 9:1.

Materials and methods. Samples were prepared by pouring pessaries based macrogols 400 and 1500, taken in the ratio 1:9. Content fluconazole and amaranth oil is defined in the literature. Pessaries contains 5.0% fluconazole and 14.5% amaranth oil. Invastigation of antibakterial activity pessaries performed on base at the institute I.I. Mechnikov under the direction of Candidate of Sciences Biology T.P. Osolodchenko.

Results and discussion. Study of antibacterial activity showed that samples pessaries of fluconazole and amaranth oil on based macrogols have activity against these microorganisms strains: Bacillus subtilis ATCC 6633, Candida albicans ATCC 885/653, Peptococcus niger, Peptostreptococcus anaerobius, Fusobacterium necrophorum.

The results of antibacterial activity established that the sample pessaries of fluconazole and amaranth oil was significantly higher than the effect of the medicinal product ("Futsys") against strains of S. aureus (to 17.4%), B. subtilis (17%), C. albicans (to 32.1%), P. niger (to 22.2%), P. anaerobius (24%) and F. Necrophorum (21.4%).

Pessaries which are entered substance of natural origin, namely, amaranth oil, exhibit a pronounced antimicrobial properties than those which contain only fluconazole substance - synthetic substance.

Conclusions. The research allowed to develop a rational composition pessaries based synthetic (fluconazole) and natural substances (amaranth oil) and concluded that the claimed means has pronounced antifungal properties and are perspective for use as a medicament for the treatment of the female genital organs.

COMPARATIVE ASSESSMENT OF IMMUNOLOGICAL REACTIVITY OF GLIKORAZMULIN AND ITS STARTING MATERIAL

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Introduction. The immune system is one of the main structures, which ensures the integrity of the body in contact with alien biologically aggressive factors. When there are violations of the immune system due to various diseases, stress, impact of unfavorable climatic, environmental, physical, chemical and other factors form the secondary immunodeficiency states (IDS).

Nowadays in order to restore the disorders of the immune system in immune conditions scientists use substances of different chemical structure and origin. One of the important sources of biologically active substances are different kinds of plants. It is known that the plants are the source of a wide variety of biologically active substances, which are widely used in medical practice in the treatment of diseases of different etiology. Among the plants allocated substances belonging to different groups of chemical compounds with a broad spectrum of biological effects. Thus, for example, flavonoids and phytoecdysteroids allocated into different groups were extracted from different species of plants. These groups of compounds exhibit pronounced activity in the various processes of vital activity and their effects are manifested in the different systems of the microorganism.

Goal: study the effect of glikorazmulin and its initial components in the immune reactivity in normal and secondary immunodeficiency states.

Materials and research methods: There were used 60 white outbred mice, 24 mice BALB / c and 32 white mongrel rats in experiments. The animals were kept on a standard diet of the vivarium.

It is known that among a large repertoire of immune stem cells have a special place, as the progenitors of all corpuscular elements of the hematopoietic and immune systems. Acting on this population of cells can modulate the direction of their differentiation in one direction or another.

We have carried out studies to assess the impact of glikorazmulin and its components in the proliferative properties of hematopoietic stem cells.

Two series of experiments were conducted. In the first series of albino mice with the age of 2-3 months, weighing 20-22 g were exposed to sub lethal totally (6.5 g) dose. After irradiation, the mice were injected intraperitoneally once test substances

(glikorazmulin and its original components - mummy and dry extract of the roots and rhizomes of Rhodiola Semenova, Rhodiola Hetrodonta) at a dose of 50 and 100 mg / kg. The activeness of substances with immunomodulatory properties were compared with immunal preparation (brand "Lek"), which was administered at a dose of 0.02 and 0.04 ml / kg intragastrically once. Then, on the 9th day after irradiation, and the drug injection the mice were killed and spleen were counted on the surface of the number of nodules (endogenous colonies), each of which is formed of a stem cell.

In a second embodiment, mice BALB / c were irradiated at a lethal (8 g) dose of intravenously injected after syngeneic bone marrow cells 5×10^4 and tested substances. The result was evaluated by the number of colonies growing on the surface of the spleen on the 8th day after irradiation (exogenous colony). In this model, colonies are formed from stem cells of bone marrow transplant.

Results and discussions: It is found that the studied substances have the property of stimulating proliferation of hematopoietic stem cells. The number of endogenous spleen colonies on the surface of the introduction of Rhodiola Semenova increases 2,18-2,60 times, Rhodiola Hetrodonta - at 1,97-2,5, mummy - to 1.73-1.82 times glikorazmulin - 1, 60-2,0 times immunal - in 1,91-2,40 times. Consequently, the study of matter have the ability to influence the proliferative activity of endogenous hematopoietic stem cells. The next step was to study the effect of substances on the level of Iroko immunized rats. Studies have shown that five of all studied substances have the ability to raise the level of iroko in the central and peripheral organs of immunity in rats. Iroko studies in the thymus gave the following results: under the influence of Rhodiola Semenova at doses of 50 and 100 mg / kg increased the number of thymocytes, respectively, 1.55 and 1.43 times; Rhodiola Hetrodonta, 1.47 and 1.41 times; mummy - 1.3 and 1.35 times; glikorazmulin - 1.58 and 1.41 times immunal - 1.62 and 1.53 times. Under the influence of these substances in the spleen population iroki rats increased to a greater extent than in the thymus. Thus, the introduction of the studied dose of Rhodiola Semenova Iroko increases the amount of respectively 1.61 and 1.65 times, Rhodiola Hetrodonta -1.58 and 1.61, mummy - 1.52 and 1.58 times, glikorazmulin - 1, and 65 times immunal 1.81 - 1.91 and 1.71 times.

Conclusions: It found that Rhodiola Semenova, Rhodiola Hat Rodonta, mummy, glikorazmulin are capable of exhibiting immunological reactivity in normal and secondary immunodeficiency states.

THE DEVELOPMENT OF VAGINAL GEL

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Introduction. Menopause in a woman's life is an actual problem of medicine and pharmacy due to a large proportion of its impact on overall health. After the menopause malfunctions of many systems appear in woman's body. First of all there is a deterioration in functioning of the reproductive system accompanied by many unpleasant symptoms such as significant acceleration of inflammatory diseases of the genital organs, painful urination, itching and vaginal dryness, itching vulva.

Aim. Thereby the aim of our work is the development of composition and technology of a drug in the form of emulgel with an extract of broccoli which is widely used in the treatment of menopausal symptom disorders.

Materials and methods. The composition of the gel with the extract of broccoli has been compounded by hyaluronic acid and vitamin E. The main active ingredient is an extract of broccoli indole-3-kabinol which has anti-inflammatory, regenerating activity, and prevents the development of proliferative processes. Hyaluronic acid and Vitamin E in menopause when applied locally have a protective, regenerating, and hydrating effect on the mucous membranes of the female genital organs preventing the appearance of atrophic changes which may appear due to insufficient quantity of estrogen in the body. The organoleptic, physical and physical-chemical analysis of the three samples of the gel has been carried out, the most optimal excipients have been chosen. Since broccoli extract and hyaluronic acid are water-soluble active ingredients and vitamin E is fatsoluble the dosage form of emulgel has been selected for optimal release of the substances.

Results and discussion. In the course of the research excipients composition of vaginal gel has been explained. Sepimax which has surface-active properties and allows you to introduce into the dosage form both hydrophilic and hydrophobic substances has been chosen to form the gel. To prevent microbial contamination of the drug preservative Suttocide has been introduced. An extemporaneous and industrial technologies of emulgel obtaining have been proposed. They consist of the following stages: dissolution of broccoli extract and hyaluronic acid in water, preparation of oil solution of vitamin E, dissolution of gel forming substance in water, emulsification, addition of the antimicrobial preservative.

Conclusions. According to the research the composition and technology for the treatment of menopausal symptoms with the help of vaginal emugel have been corroborated.

TECHNOLOGICAL RESEARCH OF CINNARIZINE

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Introduction. The half-life T1 \ 2 for Cinnarizine is equal to about 3-4 hours, depending on the quality of raw materials, age and condition of the patient. So important is the creation of prolonged dosage form

Purpose. For prolongation was decided to create a mixture of auxiliary substances that would help extend the half-life of Cinnarizine up to 12 hours and reduce the frequency of taking dosage form to once per day. The purpose was to study the properties of Cinnarizine for creating a solid dosage form of prolonged action.

Materials and methods of research. The obtained results. Was conducted microscopic analysis of cinnarizine powder, crystals have rod-shaped elongated shape. Form factor is 0.28. By type of crystalline system of Cinnarizine substance can be attributed to monoclinic system. The particle size is 0.5-3 micrometer, indicating about fine powder, opportunities for a good seal. The obtained data allow us to conclude about the possibility of using direct compression in case of rational choice of auxiliary substances.

One of the important characteristics of mass for tableting are the figures of bulk density that can be used to predict the rheological properties and compressibility. These are just two of the many parameters which are important in the overall process of tableting, which in turn requires powder compaction in hard solid form with the correct mechanical strength, porosity and dissolution characteristics. Together with an indicator of fluidity, we determined the natural angle of slope (α). The angle gives an idea about the nature of powders fluidity and characterizes the balance of all forces which are acting on the particles of powder. It is a comprehensive indicator that depends on the shape and particle size, density and moisture content of the material, the value of the total surface of the particles. Therefore, to reduce the error determination of these two indicators, the substance was dried to constant moisture content.

Conclusion. Thus based on conducted microscopic researches we can conclude about the expediency of application of direct compression. Defining technological parameters showed necessity of introducing the auxiliary substances to improve fluidity and indicators of bulk mass. Low value of hygroscopicity indicators allows to state about inexpediency of injection of wet regulators and coating tablet shell.

PHARMACEUTICAL DEVELOPMENT OF MEDICINE FOR UROLITHIASIS TREATMENT

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Introduction. Urolithic disease (nephrolithiasis or urolithiasis) is a common disease among urological diseases. This disease is characterized by the formation of stones in the urinary tract and kidneys. In most cases, the cause of urolithiasis is a small congenital metabolic disorder, through which appear insoluble salts, which then form a stone. Depending on the composition the stones are divided into several types: phosphates, urates, oxalates and so on. Treatment of patients about kidney and ureter stones can be conservative, instrumental and surgical. Conservative treatment is used in patients with crystalluria, and in the presence of calculus of small size that can depart by themselves. The main group of drugs for conservative treatment of urolithiasis make up phytopreparations. We have processed data of scientific literature on the use of medicinal plants in kidney diseases and proposed to use for the development of drug thick Rubia Tinctorum root extract and cornflower flowers.

Aim of the study. The aim of the research was the elaboration of tablets containing thick extract of Rubia Tinctorum and cornflowers.

Materials and methods. Thick Rubia Tinctorum and cornflower extracts were obtained at the Department of Industrial Pharmacy of the National University of Pharmacy. The composition of model samples differed by content in tablets of dry adhesives (microcrystalline cellulose, gum) and the humidifier (Plasdone K 25, Benecel). Tablets obtained using wet granulation. Made pharmaco-technological research of mass for tabletting (granulate) such as fractional composition, fluidity, bulk volume and the ability to shrink, angle of repose. Calculated Hausner and Corr coefficients.

Results. All model samples met the requirements of the test disintegration according to the State Pharmacopoeia of Ukraine and requirements for mechanical resistance (friability and resistance to crushing). Tablets disintegration time was 15 minutes. Friability – 0.3%.

Conclusions. As a result of experimental research has been substantiated composition of tablets codenamed "Nephrolith".

STUDY MOISTURE SORPTION CAPACITY CAPSULE MASS

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Introduction. The modern pharmaceutical science is constantly looking for new effective drugs, one source of which is the traditional medicine, there are numerous data on the use of natural objects in the treatment of diseases. Natural remedies, in most cases, have long established themselves as low-toxicity, usually gently acting on the human body. Therefore, along with synthetic drugs, microbial and animal origin, creating drugs based on vegetable components it is very urgent task.

Diuretic agents are among the most widely used in medical practice, medicaments. Drugs and medicines from plants - is the most promising and physiological means. In connection this research for ways to improve the prevention and treatment of patients with this pathology, as well as taking into account the coming of this complication it is one of the most pressing scientific and practical problems.

Purpose. The aim of our research developed optimum composition, and science-based technology encapsulated dosage form of dry extract "Meliflos". This report presents the results of research moisture sorption properties of encapsulated mass that is important for producing high-quality finished product.

Materials and methods. The material of the study was to obtain the recommended weight of the composition. moisture sorption properties of encapsulated masses known methods reported in the literature were reviewed.

To determine the residual moisture content in the powder and granulate using hydrometer firm "Kett".

Moisture sorption properties of the substance have been investigated by the method of S.A.Nosovitskoy different relative humidity values of the environment. Moisture sorption properties at different rates relative humidity environment:

I - 100% - Purified water, II - 90% - saturated with zinc sulfate solution, III - 78% - saturated solution of ammonium chloride, IV - 59% - saturated sodium bromide solution were carried out by determining the mass analyzes within 7 days. The next stage of research devoted to the study of the compositions according to the flowability of the dry extract with different adjuvants on their moisture content.

Results: The findings showed different dynamics of growth of moisture in the mixture, and a corresponding decrease in the flowability of the compositions.

Excipients as calcium carbonate, magnesium oxide, basic magnesium carbonate in the capsules with the dry extract yielded compositions that retain flowability wt moisture. Positive values of flowability was observed in combination with aerosil.

Also it determined that the composition has an increased moisture sorption capacity, which is a linear function of relative humidity environment, and to a lesser extent depends on quantities area of the sample surface.

High concentrations of residual moisture sorption properties, large bulk density, low friability weight expressed indicates the adhesive properties of the powders in the mixture.

The studies found that the studied mass (weight for capsules) is a hygroscopic mass of brown, with white patches. fractional composition results indicate that the majority of the particles have a size of less than 250 microns (31.34%), characterized poor flowability values (0.499 10-3 kg / s), low bulk density (212.45 kg / m3), an angle of repose naturally (55.2 degrees), increased values residual moisture content (up to 14.20%) and porosity (75.97%).

Conclusion.

1. Studied process ability encapsulated mass (depending on the excipients) obtained dry extract "Meliflos".

2. Experiment found that optimum moisture regulator is aerosil, filler - basic magnesium carbonate, allowing the mixture to obtain a homogeneous filling of capsules.

RESEARCH IN THE FIELD OF STANDARTIZATION CAPSULES "MELIFLOS"

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Introduction. The modern pharmaceutical science is constantly looking for new effective drugs, one source of which is the traditional medicine, there are numerous data on the use of natural objects in the treatment of diseases. Natural remedies, in most cases, have long established themselves as low-toxicity, usually gently acting on the human body. Therefore, along with synthetic drugs, microbial and animal origin, creating drugs based on vegetable components it is very urgent task.

At present, the development of new, easy-to-use, stable medicinal products of local medicinal plants is one of the main problems of modern pharmacy.

Given the properties of herbal preparations in the Department of Pharmacognosy at the Tashkent Pharmaceutical Institute carries out scientific research on the creation of "Meliflos" collection and on the basis of drugs. In view of the above, it has become urgent question of creating easy-to-use, standardized dosage form "Meliflos" different enough bioavailability and stability during storage.

Purpose. The aim of this study is to develop a method for the quantitative determination of major components (the amount of flavonoids and coumarin) in capsule dosage form "Meliflos".

Materials and methods. The main active ingredient with diuretic action of collecting "Meliflos" is the amount of flavonoids and coumarins, so the basis for the methods of analysis laid its definition more sensitive detection methods and GC spectrophotometric method. The development of this method for the quantitative determination began with the study of the spectral characteristics of the dry extract. Subsequently studied amount of flavonoids and coumarins and dry extract in capsules and experimental samples were evaluated by content of the basic substance in comparison with its content in the standard.

Results: the results of spectral data of the test solution has a maximum absorption at a wavelength of 416-417nm. Absorption at this wavelength has sufficient sensitivity and is used for quantification.

Research on the development of a method of quantitative definition of "Meliflos" capsule of active substances was started by studying the spectral characteristics of the drug. The results showed that the capsule "Meliflos" has an

absorption maximum at a wavelength of 417 nm, and the absorption of this wavelength has sufficient sensitivity and was used to quantify the recommended finished medicinal form. Further studies examined the amount of flavonoids in the extract and dry "Meliflos" capsules were evaluated on the content of the basic substance.

Methods of quantitative determination of components based capsules dry extract "Meliflos". Identification and quantification of the components of the "Meliflos" was performed by spectrophotometry and GC spectrofotometry. Flavonoids content in one capsule, based on the percentage of quercetin and calculated according to the formula. The content of flavonoid in one capsule, based on quercetin should be less than 0.5%.

Quantification of coumarin GC spectrophotometry method. The plate with deposited samples were dried in air for 5 minutes and the system was chromatographic petroleum ether-ethyl acetate (9: 1) (mixture of solvent poured into the chamber immediately before chromatography). When the solvent front reached the end of the plate was removed from the chamber, dried in a hood for 2 minutes, and again chromatographic on the same system. Then, the plate was dried again in a fume hood for 2 minutes and viewed under UV light at a wavelength of 278 nm. Coumarin marked spot test solution and a standard sample. Cut out the plate portions with spots and blank portion equal to the square of the same plate for the blank test, each cut into pieces the size of 0.3-0.5 cm, were placed in a flask with a thin section with 50 ml, was added to 10 ml of 95% alcohol , stopped and shaken for 1 hour. The optical density was determined Eleatic spectrophotometer in a cuvette with layer thickness of 10 mm at a wavelength of 278 nm. The solution was used as a comparison Eleatic control experiment.

The content of coumarin, based in one capsule per cent calculated on formule. Results obtained determine the methods of data error is small, the methods are different sensitive enough.

Conclusions: Thus, the developed spectrophotometric method for the quantitative determination of the amount of flavonoids and coumarins chromatographic spectrophotometric method is suitable for the analysis of the encapsulated dosage form "Meliflos".

RESEARCH SELECTION OF OPTIMAL COMPOSITION AND TECHNOLOGY BASED COMBINATION THERAPIES DRY EXTRACT "MELIFLOS"

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Introduction. Currently, development of new medicines, convenient for use and stable formulations of medicinal herbs is local one of the major challenges of modern pharmacy. Using medicines makes possible to broaden the range of pharmaceuticals, to strengthen certain aspects of the therapeutic effect, reduce toxicological manifestations.

This attitude particular interest is the creation of tablet dosage forms. A promising area is the development of new pharmaceutical dosage forms on the basis of complex herbal remedies, one of which may include the collection of "Meliflos" obtained on the basis of yarrow and clover, and the drug used in medical practice as a diuretic. Gathering "Meliflos" it was developed by employees of the Department of pharmacognosy by Professor Kh. M. Kamilova.

Currently arterial hypertension (AH) economically developed countries refers to the most common chronic non-communicable diseases among the adult population with a high risk of organ damage: Cerebral stroke or myocardial infarction, etc. In recent years, for the treatment of hypertonic cal disease abroad more widely used antihypertensive drugs combined, containing in its composition two, at least three drug substances with different mechanisms of action. The use of combinations of data increases the effectiveness of monitoring the level of blood pressure (BP) and improved tolerability associated with dose-related adverse events.

Therefore, development of new domestic combined antihypertensive drugs is relevant to pharmacy and medicine.

Purpose: The aim of this work was to develop a technology for the combined tablets of dry extract "Meliflos" and dihlozid.

Materials and Methods: The study devoted to the study of dry extract "Meliflos" as a substance for the development of tablets and dihlozid technology.

At the same time we studied the technological properties of the above mentioned methods of powders listed in the GPC! and in the literature.

Results: As a result of the research found that the investigated substance (dry extract) is a hygroscopic dry, fine powders from red to dark brown color with a specific smell. fractional composition results indicate that the majority of the particles

have a size of less than 250 microns (32.20%), characterized poor flowability values (0,601.10-3 kg / s), low bulk density (241.35 kg / m^3), high compression ratio, angle naturally slope (44 degrees), increased values residual moisture content (up to 10.23%) and porosity (81.74%). From these results it can be concluded that the dry extract "Meliflos" has poor flowability and at the same time quite satisfactory moldability. Study dizlozida technological properties of the powder showed that it has a poor bulk density and compressibility.

Initially, we studied the possibility of making tablets by direct compression, which, as is known, has a number of advantages. Analysis of the technological parameters showed the need for adjuvants additives that improve the flowability. glucose, lactose, potato starch, microcrystalline cellulose, calcium carbonate, magnesium oxide, calcium stearate: different adjuvants recommended SP XI, both individually and in combination, were used. Because of inappropriate technological properties of the tablets were of poor quality – stick to the tablet mass press – instrument, tablets did not meet the requirements of disintegration. The tablets obtained by direct compression, did not meet the requirements of the GF XI. Therefore, to achieve the goal of using a wet granulation method.

Given the chemical and physical-technological properties of a dry extract and dihlozida when developing composition and technology studied possibility of using such excipients as lactose, sucrose, starch, cellulose derivatives MCC, GMPTS calcium carbonate. As disintegrating agents, potato starch was used, and as an antifriction substance - calcium stearate. Pre-selection of the fillers were also carried out on the basis of their ability to reduce moisture absorption of moisture substances. For use purified water, sugar syrup, various concentrations of ethanol - 30, 40, 50, 70%, 90% and 10.2% starch solutions. After numerous experiments conducted humidification was performed 90% ethanol, as it provides good tabletting granulation mass. When moistened mass of purified alcohol obtained granulate, after drying, strong obtained tablets had a high quality appearance.

Conclusion.

Thus, unsatisfactory results investigated process parameters dihlozida dry extract and requires the use of auxiliary substances. Used Excipients improve some processing properties of the substance - flowability, bulk density and compressibility.

THE USE OF "DISSOLUTION" FOR EVALUATION OF TABLETS "PIRZIN"

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Introduction. Currently, adopted the concept of "Quality through development» (QbD), which implies thorough detailed drug development, including the most effective methods of test "Dissolution". As part of the concept is necessary to carefully examine the properties of the drug substance and formulations developed, critical production parameters; set risk impact on the effectiveness of medicines; perform the test under physiological conditions to determine the possible dissolution processes of change mechanisms; evaluate the significance of the impact of production changes on the clinical manifestation of drugs and so on.

One of the most important quality criteria for solid oral dosage forms (tablets, pills, capsules, granules) test "Dissolution". Its use in the analysis was an attempt to introduce a normative document test, which, along with the assessment of pharmaceutical equivalence, would be allowed to carry out a rough estimate of bioequivalence of drugs.

The test "dissolution" is intended to determine the amount of Pharmacopeian article, which conditions specified in the private pharmacopeia article for a certain period of time should be released in a dissolution medium of a solid dosage form.

Purpose. The objective of this work to develop methods of test "Dissolution", tablets containing as active ingredient Piracetam and cinnarizine.

Materials and methods: The study was cinnarizine and more commonly used adjuvants. Cinnarizine - drug derivative difenilpiperazina. Piracetam - nootropic drug pyrrolidone derivative. Tests on the development of "dissolution test" carried out by conventional methods given in SP XI, issue 2, p.159, the study underwent pills "Pirzin". Dissolution test for the development of such factors have been studied as the amount and type of solvent medium, the rotational speed of the basket and the pH. To evaluate the dissolution using USP apparatus 29 «ERWEKA» DT 6 (Germany), the unit "rotating basket", the volume of the dissolution medium 500-1000 ml. As the solvent, use purified water, hydrochloric acid solution, buffered media with different pH values. Basket rotational speed of 50-200 rev/min. In the study of the temperature held back 370^0C + 1. One tablet was placed in a basket, the basket rotation is enabled. Samples were taken after 5, 15, 25, 35, 45 minutes in amounts of 5 ml, and filtered through filter paper ("blue tape") ,. 5 ml of the filtrate is placed in a volumetric flask

of 50 ml, the volume is brought up to the mark with solvent, stirred and filtered through a membrane filter with a pore size 0.45 mkm. The amount of active ingredient passed into the dissolution medium was determined by spectrophotometry at 254 nm.

Results: studies have shown that the rate of release of active substance from the tablets is influenced by factors such as manufacturing operations, the type and amount of used excipients, a method for producing the tablets, as well as factors that occur during trials (amount and type of solvent medium, basket rotational speed, time). purified water, acid - - 0.1 N hydrochloric acid and alkaline - of 0.1N sodium hydroxide solution neutral: For selection of an optimal pH solvent medium dissolving the following medium was used. In the experiments, the amount of dissolution medium taking into account the sensitivity of the developed method of quantitative determination of the active substances has been selected - 1000 ml. In this set usefulness as dissolution medium - purified water in a volume of 1000 ml. It should be noted that the basket at a rotational speed of 100 rev/min the concentration of active substances passed into the solution for 45 minutes is over 75%, which meets the requirements of the GF XI.

Optimum basket rotation speed of 100 rev/min. In 48-55% of active substance is released within the first 15 minutes. In 80-85% of released active ingredients during 45 minutes.

Conclusions:

1. The results of the studies were used to determine conduct "dissolution test" conditions for determining the composition of tablets "Pirzin".

2. On the basis of the research developed "dissolution test" for the tablet "Pirzin" by rotating basket.

THE AFFECTING FACTORS FOR THE QUALITY OF TABLETS "PIRACETAM"

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Introduction. In recent years, around the world increase number of disorders of the central nervous system, including disorders of cognitive functions of the brain (note, memory the ability to analyze the situation, decision-making, spatial orientation). The range of conditions for which said pathology is very broad. It includes cognitive deficits with brain injury, stroke and chronic cerebrovascular disease, brain lesions neurodegenerative character, chronic alcoholism, developmental delay in children.

The prevalence of cognitive pathology and diversity its individual manifestations in humans dictate the need to expand the arsenal of substances which normalize impaired cognitive function. To date, the medical practice, used a number of drugs have psychotropic activity. However, most of these drugs, together with major pharmacological effects have a number of undesirable side effects. From a biopharmaceutical point of view, this fact requires a search for new drugs with high psychotropic activity or improve their technology, but with a low risk of side effects.

This time one of the most important tasks of pharmaceutical sciences improve the already known dosage forms. Such known drugs include piracetam. Among nootropics piracetam so far maintained its leadership. Piracetam - is practically harmless and effective drug which is used as a nootropic agent. It speeds up the metabolic processes in the brain, improves the conductivity of the nerves, improves the blood circulation (1).

In connection with the above have conducted research in providing improvement advanced-technology tablets of piracetam.

Purpose. The purpose of this research were studied influence of pressing conditions on the quality tablets of "Piracetam" studied pressing pressure effect on the quality tablets of piracetam obtained by the recommended composition and technology.

Material and methods. Materials of this research is Piracetam powder. According to sensory analysis, they are powders in white, odorless, crystalline structure of the particles is. Structurally-mechanical properties of the substances under study were examined by an optical microscope «LEITZ» company «Biomed» with an increase of 330 times.

For experiments tablet composition was prepared: 1. 0.2 g piracetam, starch 0.0475 g, 0.0025 g calcium stearate 0.4 g 2. Piracetam, 0.1445 g starch, calcium stearate 0.0055g tablets of piracetam by 0.2 g prepared with an average weight of 0.25 grams per manual hydraulic press with a diameter of 9 mm and piracetam on 0,4g with an average weight of 0.55 g per mold with a diameter of 12 mm, intended for the production of tablets flat cylindrical form. Tablet mass was compacted under pressures ranging from 50 to 300 MP.

Next we were studied such physico-chemical indicators such as disintegration, the ratio of height to diameter, breaking strength and friability of tablets. Physical and mechanical properties were studied by conventional methods given in SP XI, the published methods and relevant specification.

Results. The data obtained from the above studies have shown directly proportional to the strength properties of tablets from the pressing pressure. The study qualitative changes Piracetam tablets of 0.2 g and 0.4 g, depending on the compaction pressure noted that with increasing compression force of 50 MP to 300 MP in direct proportion. With an increase in compaction pressure increases the disintegration time of tablets from 6 to 20 minutes.

Fracture strength under these conditions increased from 20 N to 90 N, and the abrasion resistance was increased from 97% to 100%. Specific pressing pressure was 150-200 MP.

The resulting tablets was studied on the following parameters: appearance, breaking strength, disintegration time, friability.

Conclusions. Thus, on the basis of studies identified the optimal compression pressure for tablets "piracetam by 0.2 g 0.4 g and" recommended for advanced composition. The optimum compaction pressure is 150-200 MP. The dependence quality of the tablets from the pressing conditions.

THE ISSUE OF THE DEVELOPMENT AND TECHNOLOGY TABLETS "PIRZIN"

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Introduction. Medicines mechanisms influence on the central nervous system, probably a few: the change in velocity of propagation of excitation in the brain; enhancement of metabolic processes in nervous cells; improvement of microcirculation by influencing the rheological properties of blood without causing at the same time the vasodilating effect. It improves communication between the hemispheres of the brain and synaptic conductance in neocortical structures. After prolonged use of the drug in patients with brain marked decrease in functional improvement in cognitive function, attention.

The progress of modern pharmacy and clinical medicine is largely determined how discovery of new biologically active substances, and expansion of opportunities and prospects for the use of well-known and popular medicines. This is particularly relevant for neuro and psychotherapy, which is largely due to the steady growth of the importance of nervous and mental diseases as a leading cause of morbidity, especially in developed countries.

To date, the medical practice, used a number of drugs have psychotropic activity. These facts confirm the relevance of the development of new and improvement of existing neuroprotective drugs.

Given this fact, it was decided to develop the technology and structure of tablets based on piracetam and cinnarizine.

Purpose. The aim of the study was development of new dosage forms of the original domestic drug nootropic and neuroprotective action.

Materials and Methods: recommended tablet "Pirzin" – is a combined preparation. The active ingredients of the drug - piracetam (cyclic derivative GABA) and cinnarizine (selective calcium channel antagonist). Piracetam - nootropic drugs acting on the brain, improving cognitive (cognitive) function, such as learning ability, memory, attention, and mental ability to work. Cinnarizine - inhibits contraction of smooth vascular muscle cells by blocking calcium channels. -technological Physical properties of powders was carried out by the methods given in SP XI and NTD. In separate experiments we studied technological parameters of piracetam. As technological parameters studied - bulk density, flowability, angle of repose,

porosity, compressibility and compactibility coefficient, compressibility and residual humidity.

Results: In the process of obtaining tabletted dosage forms are powders processing different processing steps - screening, grinding, mixing, granulation, compression and humidification. The quality of granules and tabletting mass, and therefore also the quality of tablets, is influenced by many factors, including the dispersion of drug substance and the form of particles.

From the data obtained by the research of the physico-chemical and technological properties and piracetam cinnarizine, it implies that the drug (both) with respect to its tablettability is complex medicines. For they have plate-shaped crystals with an average size of 16-25 microns of length values of the length and width of 14 m. This form factor 1.4. fractional composition results do not coincide with those of microscopic examination. Thus, most of the substance piracetam - 45.15% is the fraction -500 + 250 microns, and the average particle size exceeds 35.7 times.

Especially noticeable effect of the shape and size of the particles of the substances on the technological characteristics of tablet mass, designed for direct compression. Tablet blends for direct compression, as is known, must have a number of optimal processing properties, such as good flowability (at least 5.6 g/s), high compressibility (not less than 70-100 N), the optimum value of bulk density (at least 0.4-0.5 g/ml, angle of repose low (less than 400). According to the study, samples were studied substance piracetam and cinnarizine characterized poor flowability values (from 0.290 to 1.070 * 10-3 kg/s), the bulk density (from 224.56 to 420.25 kg/m^3), the angle of repose (from 54.7 to 63.0 degrees), increased residual moisture value (from 4.4 to 6.3%) and porosity (from 67 53 to 86.14%).

Conclusions. Based on the foregoing, in the preparation of piracetam tableted dosage forms and cinnarizine use excipients and separate technological operations.

DEVELOPMENT OF THE SUPPOSITORY COMPOSITION BASED ON "SHUKUR MAY"

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Introduction. The main objectives of pharmaceutical technologies in modern conditions are the selection of the optimal type and composition of the dosage form, the search for new substances and rational technological methods to ensure proper quality of finished drugs with maximum therapeutic effectiveness at their minimal side effects. The main task of research in the development of suppository dosage forms is scientific and experimental validation of pharmaceutical factors (amount, physical and chemical and technological properties of the substance, the nature and amount of excipients, the order of the processes and the optimal conditions of preparing a formulation) that ultimately determines the result that produced by the dosage form.

Aim. Development of rational suppository composition with the original substance "Shukur May" according to the requirements of the State Pharmacopoeia of Republic of Kazakhstan.

Materials and methods. The object of study is suppositories with the active substance "Shukur May". Research methods are standard pharmacopoeia methods (physical and chemical, pharmacy-technological).

Results and discussion. "Shukur May" substance is a multi-component composition consisting of extracts of burdock roots, liquorices, Tangut rhubarb, leaves of nettle. The main biologically active substances of "Shukur May" are lipophilic. For this reason the choice of the base is based on overall compatibility with the substance, as well as on the degree of release of active substances from the base. Cocoa butter, hard confectionery fat, Witepsol, yellow wax, bentonite are substantiated as the components of the base. 5 suppository models with active "Shukur May" substance developed for the above-mentioned components. The selection criteria were mass homogeneity, melting point, while the total strain, tensile strength.

Conclusions. Selection of the suppository base and auxiliary substances for the development of rational suppository composition of "Shukur May" that possess anti-inflammatory, wound healing, improves intestinal motility effects was done.

PROBLEM ASPECTS OF THE NEW TECHNOLOGIES OPHTHALMIC DRUGS

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Introduction. The current level of production of ophthalmic drugs allows for the presence in their composition of certain biologically active substances directional, and in calibrated quantity.

They naturally included in the chemical processes occurring in the body. Thus, the immune system identifies them as "friendly" and passes in its area of responsibility, such as the respiratory tract mucous membranes allows them to stimulate phagocyte function, which are necessary to combat such as respiratory infection. In the aspect of the above, in our opinion, it is interesting raw materials bee products, their standardized biologically active substances and drugs based on them.

Results and discussion. Analyzing the foregoing we carried out a robot to create ophthalmic drugs to the application of new technologies on the basis of a new domestic natural resources - propolis - bee products.

In addressing this issue, we use environmentally friendly technology, it is very economical and easy to implement. The day of the propolis obtained 10 kg and 200 liters of an aqueous solution purified by ion resins and propolis mechanical impurities, which is stored under normal conditions at room temperature for 4-6 months. The solution can be lyophilized to a powder with the extension of shelf life of up to 1.5 years, which has a broad spectrum of biological activity (wound-healing, regenerative, capillary firming, antimicrobial, antiviral, anti-inflammatory, etc.) and in addition it can be widely applied as an antioxidant in pharmaceutical and a preservative in food technology.

Currently, the solution proposed propolis powder and used for preparation of eye drops "propolis" as a medicament for the treatment of conjunctivitis, herpes and other visual organ lesions.

Conclusions. We hope as well that the use of antimicrobial, antiviral, germicidal solution in the food industry to improve the quality and extend the shelf life of beverages and others food.

SOLUTION FOR INJECTION OF BEE VENOM - PROMISING DRUGS FOR CANCER TREATMENT

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Introduction. Over the past 100 years the level of morbidity and mortality oncopathology moved from 10th place to second, second only to diseases of the cardiovascular system. According to WHO annually recorded incidence of 10 million. People, and forecasts for 2016 indicate output probability of cancer pathology in the first place.

In Ukraine, for the past 10 years the number of patients increased by 25%, and the total number decreased by 4 million. man. Onko-patology incidence steadily increasing by 2.6 - 3% per year, and the cancer continues to "younger." At the same time, the average life expectancy of Ukrainians for 10 - 20 years lower compared to those of developed countries.

The main problem in Ukraine is timely diagnosis of cancer pathology. Most patients who have suspected this group of diseases, refuse treatment because of lack of funding, or oscillate, feeling fear, and even waiting for an invitation to be examined by a doctor. Thus, fixed annually more than 160 thousand new cases of malignant tumors, but almost 100 thousand patients -.. Dying of cancer.

It is well known that the main factor that affects the extent of cancer is smoking (50% of Ukrainians - smoking) and the quality of drinking water and food.

Results and discussion. The main areas of pharmacotherapy today consider surgical removal of the tumor, chemotherapy, radiotherapy, cryotherapy, photodynamic therapy, hormonal therapy, immunotherapy, combined treatment and TD Almost all of them in one way or in some way cause certain complications, which limits their use in certain categories of patients.

Therefore the search for new highly efficient, standardized natural substances, as well as development on their basis of drugs for use in therapy of cancer is an urgent task of modern pharmacy.

In this regard, special attention is attracted by a bee product bee poison. Currently poison preparations of bee found wide application in the treatment of asthma, joint diseases, nervous and cardiovascular system, for various skin diseases, eye, allergic diseases and the like. D. It is used not only in pure form but also in the complex with other drugs.

Introduction to bee venom human body occurs in different ways: bee stung, injection, rubbing, orally by means of aerosol and steam inhalations and electrophoresis and ultrasound. The most effective of all these methods is to introduce poison into the body by stinging bees.

The presence of high physiological activity, multi-faceted spectrum of therapeutic action, bioavailability allowed to consider bee venom as a promising raw material of natural origin from the point of view of the relevance of solving the problem of large-scale domestic production of finished drugs based on it.

As the physiological activity of bee venom is due to a collection of biological agents, with the purpose of prevention and treatment is advisable to use bee venom or drugs with their maximum content. However, it is known that the action of bee venom on the body is also dependent on the dose, route of administration, age and physiological state of the organism.

From literature it is known that bee venom in small doses, excites the activity of the body's defenses. Publications of foreign scientists testify about the possibility of using bee venom in radiation protection. Biological studies have established that a marked effect is the main Melitin venom component (peptide, which is about 50% of the dry residue of poison).

With the development of a new intact liquid medicament for use in cancer therapy has been used by us standardized, powdered, purified bee venom substance. The resulting model samples of bee venom solution on two technologies that are different conditions and stages of production, was investigated by the organoleptic, physico-chemical (physical stability under different temperature conditions) and chemical (identification of biologically active substances (colored and sedimentary response)) indicators.

Conclusion. Recent publications of scientists of the world and our research suggests the establishment of bee venom inhibitory effect on the proliferation of mouse melanoma, which proves once again the prospect of the use of this substance in the treatment of malignant neoplasms.

INVESTIGATION OF THE TECHNOLOGICAL PROPERTIES OF THE ACTIVE PHARMACEUTICAL INGREDIENTS AND EXCIPIENTS FOR CREATING ANTACID ACTION TABLETS

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Introduction. The current pharmaceutical market offers a number of drugs that have pharmacological action aimed at eliminating the discomfort of heartburn and epigastric body that can be raised in the area of the esophagus. Each pharmacy has a number of antacids to deal with this disease. According to opinion of people suffering from this problem, not all of antacid formulations available in the pharmacy range suitable for use.

Aim. The aim of this study is to investigate the technological properties of the active pharmaceutical ingredients and excipients for creating antacid action tablets.

Materials and methods. A study of antacid drugs that are on the pharmaceutical market of Ukraine was conducted and active substances and excipients of these drugs were compared. Based on this study active pharmaceutical ingredients and excipients were chosen to create antacid drug action. Next step of this study was to investigate the technological properties of the active pharmaceutical ingredients and excipients by commonly known metods: flowavailability, bulk density, tapped density, particle size distribution by sieve analyses, moisture content.

Results and discussion. There are a number of antacid drugs that are absorbed from the gastrointestinal tract on the pharmaceutical market of Ukraine such as Alumag (tablets), Rennie (tablets), Remmax-KV (tablets), Secrepat forte (oral suspension, tablets). These medicines contain aluminum hydroxide, magnesium hydroxide, calcium carbonate, magnesium carbonate, magnesium trysylikat as active pharmaceutical ingredients. Potato starch, gelatin, sorbitol, mannitol, magnesium stearate, milk powder, sucrose, lactose monohydrate, talc are the most commonly used excipients. Peppermint oil, vanilla flavor, lemon flavor, flavor “orange flavor”, saccharin sodium, flavor “raspberry taste”, flavor of anise, sodium cyclamate are used to improve the taste and smell.

There are a number of antacid drugs that are not absorbed from the gastrointestinal tract on the pharmaceutical market of Ukraine such as Agiflux (oral suspension, tablets), Almagel, Almagel-A, Almagel-Neo (oral suspension), Almagel-T (tablets), Gaviscon (oral suspension, tablets), Gastal (oral dispersed tablets), Manti (oral dispersed tablets), Phosphalugel (oral gel). These medicines contain magnesium hydroxide, aluminum hydroxide, benzocaine, simethicone emulsion, sodium alginate, sodium bicarbonate, calcium carbonate, aluminum hydroxide-magnesium carbonate

gel dried, the aluminum phosphate as active pharmaceutical ingredients. Carmellose sodium, sorbitol solution, sorbitol, hydroxyethyl, propylene glycol, macrogol 400, mannitol, microcrystalline cellulose, kopovidon, carbomer, lactose, pregelatinized starch, colloidal anhydrous silica, croscarmellose sodium, magnesium stearate, agar, pectin and others are the most commonly used excipients. Menthol, sodium citrate, sodium saccharin, oil of peppermint, oil of lemon, orange flavor, acesulfame, lemon flavor, aspartame, mint flavor are used to improve the taste and smell.

Among the existing dosage forms of antacid medications the most comfortable are tablets. Tablets provide stability of active ingredients for long term storage. They do not need introduction of preservatives unlike suspensions for oral use. Tablets are convenient to carry around. The composition of the tablets may allow to use them without of drinking water by using of chewable tablets or oral rapidly dispersed tablets in a small amount of saliva.

Sodium alginate has advantages over other active ingredients. In the acidic environment it turns into an insoluble film that protects the mucous membranes from damage acid. We also chose sodium bicarbonate to neutralize the acid, mannitol and sorbitol as excipients.

In the next step we have identified technological options of these substances. Flowavailability of sodium alginate – 1.8 g/s; sodium bicarbonate – 4.2 g/s; mannitol – 7.0 g/s; sorbitol – 6.8 g/s. Bulk density of sodium alginate – 0.98 g/ml; sodium bicarbonate – 0.71 g/ml; mannitol – 0.65 g/ml; sorbitol – 0.67 g/ml. Tapped density of sodium alginate – 1.2 g/ml; sodium bicarbonate – 0.95 g/ml; mannitol – 0.78 g/ml; sorbitol – 0.74 g/ml. Particle size distribution (<0.09 mm; 0.09-0.18 mm; 0.18-0.25 mm; 0.25-0,355 mm; >0.355 mm) is for sodium alginate – 14%; 69.1 %; 11.5 %; 0.8 %; 0.05 %; for sodium bicarbonate – 17 %; 69 %; 9.85 %; 1.25 %; 0.5 %; for mannitol – 0.5 %; 25 %; 30 %; 21.5 %; 22.5 %; for sorbitol – 2.25 %; 11.5 %; 15.5 %; 24.5 %; 45.5 %. Moisture content of substances is sodium alginate – 12.23%; sodium bicarbonate – 0.83%; mannitol – 0.33%; sorbitol – 1.19%.

Flowavailability of sodium bicarbonate, mannitol, sorbitol is excellent. Flowavailability of sodium alginate needs to be increased by adding glidants or will increase in mixture with excipients (mannitol, sorbitol). The bulk density of the substances is almost identical, which will facilitate their mixing and will prevent their segregation. Similar values of particle size distribution facilitate the formation of a stable mixture. The results indicate the potential for the production of the antacid action tablets by direct compression, if the substance will have a compressibility. High humidity value can affect the adhesion of tablets to the punches.

Conclusions. The obtained technological parameters will be used in the development of the formulation and technology of antacid tablets.

PROSPECTS FOR THE DEVELOPMENT OF MEDICINES FOR THE TREATMENT OF HELMINTH INFECTION BASED ON MEDICINAL PLANT RAW MATERIAL

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Introduction. The most susceptible to helminth infection are children aged 7-10 years. However, the existing range of the medicines for the treatment of helminth infection includes, in the main, substances of synthetic origin, while not all of them are suitable for pediatric practice.

Aim. The aim of this work is to investigate prospects of the development of new domestic medicines for helminthes treatment on the basis of medicinal plant raw material.

Materials and methods. Analysis of the proposed range of medicines for helminth infection treatment was carried out on the bases of compendium and the Reference book of medicines of Ukraine (04/01/2013).

Results and discussion. Pharmaceutical market of Ukraine includes the following medicines with anthelminthic activity: praziquantel (P02B A01), mebendazole (P02B A01), albendazole (P02B A03), piperazine (P02C B01), pyrantel (P02C C01), levamisole (P02C E01) and tansy flowers (P02C X10**).

Foreign experience in the treatment of helminthes provides two goals of pharmacotherapy: the destruction of helminthes and elimination of the illness complications. Therapy with medicines on the basis of mebendazole, albendazole, thiabendazole, niklozamina, praziquantel is recommended. Phytomedicines are not given in guidelines of the USA and the UK neither as adjuvant therapy nor during the rehabilitation period. Also, it is given that existing medicines cannot be used in pregnant women, nursing mothers and children under the age of 2 years.

Nevertheless, there are a lot of recipes to fight against the different types of helminthes in folk medicine. They are based on such plants as tansy flowers, Artemisia Cina flowers, pumpkin seeds, onion bulbs, male fern, aspen bark, cloves, elecampane, ginger, etc. The listed plants have been used for decades and still have not lost their popularity. The effectiveness of these traditional methods is quite high, indicating the prospects of scientific research to create anthelmintic medicines based on them. For example, it was clinically proven that aspen’s bark dry extract has a high anthelmintic action when opisthorchiasis.

Conclusions. Based on the above-mentioned, it can be concluded that work aimed at creating medicines based on this and other plant is relevant and meets the needs of the modern pharmaceutical market.

DEVELOPMENT OF THE TECHNOLOGY OF THE HYDROPHILIC COMPLEX OF BUPLEURIUM AUREUM

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Introduction. Widespread and aggressive advertising of drugs, their use without appropriate medical control are responsible for a significant increase in the incidence of the negative effects of drugs on the human health.

Side effects of drugs become one of the important problems of modern medicine, and it is topical to find ways to reduce the negative impact of side effects of drugs on our health. One of the first organs that are suffering from uncontrolled use of drugs is the liver. Drug damage of the liver is one of the main problems of hepatology.

It is possible to prevent the liver damage by drugs with creation of complex drugs, which composition includes hepatoprotectors contributing to preservation and restoration of the damaged liver tissue in addition to the main active component.

The pharmacological screening of some plant extracts has shown a high hepatoprotective activity of the aqueous extract of Bupleurum Aureum herb in prevention of the hepatotoxic effect of a number of sulfanilamides.

Aim. Development of the technology for the hydrophilic complex of Bupleurum Aureum herb with the purpose of its further inclusion in the complex antimicrobial sulfonamide drug and prevention of hepatotoxic side effects of the main active pharmaceutical ingredient.

Materials and methods. Extraction of Bupleurium Aureum herb with ethyl alcohol of different concentrations or with water by the method of fractional maceration when heating was conducted in a round-bottomed flask under reflux while heating on a boiling water bath.

Results and discussion. The extractin of Bupleurium Aureum herb with water on a boiling water bath the total yield of extractives calculated with reference to the dry raw material was 35.4%

The extraction of Bupleurium Aureum herb with ethyl alcohol of different concentrations when heating has been conducted. The yield of extractives was 18.26% when extracting with ethyl alcohol of the concentration of 40%; 49.13% – when extracting with ethyl alcohol of the concentration of 50%; and 40.00%, – when extracting with ethyl alcohol of the concentration of 70%.

Conclusions. The more appropriate method of removing the hydrophilic complex for the Bupleurium Aureum herb – is extraction with ethyl alcohol when heating to the boiling point, it provides extraction.

STUDY OF PHYSICO-CHEMICAL AND TECHNOLOGICAL PROPERTIES OF ACTIVE SUBSTANCES INTHE COMPOSITION OFMEDICATED CHEWING GUM

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Introduction. Medicated chewing gum (MCG) - one of the modern pharmaceutical forms, which is widely used to treat a wide range of diseases. This formulation is especially effective for the treatment of dental diseases, which involves a number of advantages compared with other oral dosage forms: the length and location of action, the consistency of concentration of active substance, the rapid action and fewer side effects. As active ingredients for inclusion in the squad of MCG were selected proteolytic enzymes - lysozyme and papain, due to their combined effect on the oral tissue and a wide use in dentistry.

Aim. The aim of our work was the study of the physico-chemical and technological properties of active pharmaceutical ingredients (APIs), and their mixtures for the development of rational technology and composition of MCG.

Materials and methods. The objects of research were lysozyme and papain - protease of animal and vegetable origin, and their mixture as well. Were carried out following physicochemical (moisture content, shape and size of the crystals) and pharmaco-technology (bulk density before and after shrinkage, flowability, angle of repose) researches of samples of substances. Microscopic analysis of powders was performed using laboratory microscope «Konus Academy», equipped with a video camera ScopeTek. Images were processed by the software ScopePhoto (version 3.0.12.498). Moisture content of samples was studied using rapid moisture analyzer «Sartorius MA-150» (Germany). Fluidity defined on the device VP-12A by measuring the time of leakage of sample powder (100.0 g). Bulk density installed on the device for determining bulk volume type PT-TD1 (PharmaTest, Germany) (100.0 g).

Results and discussion. Lysozyme - animal enzyme from the class of hydrolases, has immunomodulatory, anti-inflammatory, antitoxic and antibacterial effect, and stimulates regeneration processes and erythropoiesis. It affects gram-positive and gram-negative bacteria and cell walls by hydrolysis.

Papain - enzyme of plant origin, which is obtained from the papaya fruit juice. It has anti-inflammatory, antibacterial, wound healing and an antioxidant action. In addition, it provides local cleaning of dental hard tissue by destroying microbial plaque and preventing its formation, thereby providing prophylactic and therapeutic effect on the teeth.

During the researches, for papain and lysozyme were studied following physico-chemical parameters - crystal size, their shape, character of surface, and moisture content. From the technological characteristics was determined the bulk density before and after shrinkage, the angle of repose and flowability.

According to the microscopic analysis, lysozyme particles are crystals of isodiametric (nearly spherical) shape, the size of 1.0-0.1 microns, with the presence of debris. Papain - flat, sometimes three-dimensional crystals with polygonal and uneven edges of anisodiametric type with a particle size of 2.0-0.1 microns, and with the presence of debris. The magnitude of the thickness and length of crystals both substances can be classified as fine. A mixture of papain and lysozyme crystal is polydisperse systems with particles of different shape and size.

The results of physicochemical and pharmaco-technological properties of the main components of MCG and their mixtures are shown in Table. 1.

Table 1

Physico-chemical and pharmaco-technological properties of the API and their mixture.

№	Properties	Papain	Lysozyme	Mixture of APIs
1.	Moisture, %	0.68±0.01	7.82±0.01	5.50±0.01
2.	Flowability, c/100 г sample	15.33±0.6	27.17±2.5	21.84±1.0
3.	Angle of repose, degree	29±1	31±2	30±1
4.	Bulk density before shrinkage, $\frac{m}{V_o}$,g/ml	0.771±0.015	0.565±0.015	0.649±0.015
5.	Bulk density after shrinkage, $\frac{m}{V_{1250}}$, g/ml	0.834±0.015	0.735±0.015	0.769±0.015

Note: n = 5, P = 95%.

The obtained data indicate that the API and their mixture have a good flowability, but during tests powders hung in the funnel, which required the use of vibration.

Conclusions. During the studies were identified physicochemical and pharmaco-technological properties of papain, lysozyme, and their mixtures, that will allow us to predict the including of rational auxiliaries of relevant groups to develop MCG.

DEVELOPMENT OF EXTEMPORANEOUS DRUGS FOR TREATMENT OF MASTITIS

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Introduction. According to WHO "Mastopatia - is a fibrocystic disease, characterized by impaired relationships epithelial and connective tissue components, a wide spectrum of proliferative and regressive changes in breast tissue." As benign disease and breast cancer have a lot in common in etiological factors and pathogenetic mechanisms mastitis risk factors and breast cancer is largely identical.

Therefore, the actual problem, in terms of maintaining the women's health and improving demographic indicators of the country is searching for new methods of mastitis prevention and treatment, developing domestic preparations with a comprehensive action effective and economically affordable.

Aim. Make a detailed analysis of the domestic pharmaceutical market drugs used in the treatment of mastitis; develop and substantiate the structure and assembly technology medicinal plant to treat this pathology.

Materials and methods. To reach the goal of the study systematic, structural and logical analysis, comparative analysis and graphical methods of summarizing data were made. Analysis of the range of drugs that are used in the treatment of mastitis, were made with the help of marketing research methods based on materials of Drugs State Register of Ukraine.

Results and its discussion. According to the chemical structure and pharmacological influence of biologically active substances major groups that this herbs contains, number of benefits dosage form and efficiency technologies the medicinal plant assembly and the possibility of their use in the treatment of mastitis were proved. Medicinal herbs containing plant hormones were included (hops cones, stevia herb, parsley planting grass), substances that exert choleretic effect and normalize the metabolism of hormones in the liver (corn columns with stigmas, yarrow grass, barberry root), regulate the menstrual cycle (leaves of sage, nettle leaves).

Conclusion. Based on the chemical structure and pharmacological activity of active ingredients extemporaneous composition of medicinal plant substantiates for complex pharmacorrection recipe of mastitis were defined. Extemporaneous assembly will enrich the range of local pharmacies that cause positive results in the treatment of this pathology, saving women's health and reproductive function.

DEVELOPMENT OF EXTEMPORAL UNGUENT FOR TREATMENT URTYKARIYIV UNDER DISEASE IN CHRONIC HIVES

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Over the last years an importance allergy problems in pediatric has grown because during this period the prevalence of children's allergic diseases in has been steadily increasing. The spreading of the children's disease is associated with genetic predisposition, environment and lack of attention to his mother's body during pregnancy.

Nowadays allergic diseases include the six most common children's diseases in According to statistics, allergy suffers every third child. Allergic diseases – a group of diseases caused by increased sensitivity to exogenous and endogenous allergens. According to forecasts of WHO, XXI century will be the era of allergies because the prevalence of allergic diseases has been increasing 2-3 times every 10 years and has reached epidemic proportions.

The problem of creating children's medicines, launched by the World Health Organization (WHO), is relevant and timely, as the features of physiological and biochemical processes of the child indicate that half-dose of drugs designed for adults may not be adequate for the child.

Children's bodies have specific characteristics that determine its special sensitivity to drugs and the body's reaction to the kind of input, resulting in the development of toxic or unwanted side effects.

One of the most difficult problems in pediatric allergy was, is, and probably will long chronic hives. Most treat hives antihistamines have using a variety of dosage forms, including unguent. There are used some different dosage forms for the treatment of in children's allergic diseases: tablets (65%), injection (12.5%), syrup (11%), oral solutions (4%), drops (3%), pills (3%), gel for external use (1.5%). Among the 72 types of medicines registered in Ukraine for the treatment of children's allergies, domestic manufacturers produced 44.4%, foreign – 55.6%. Among the producing countries Ukraine provides 45% of medicines, India – 11%, Switzerland – 8%, the Czech Republic and Hungary 6%, Poland, Germany and Canada 4%, Slovenia and Turkey to 3%, and Bulgaria, Russia, Belgium UK and Austria by 1%. Manufacturers of drugs to treat allergies in Ukraine pharmaceutical company "Darnitsa", LLC " pharmaceutical company "Health", "LLC" Pilot Plant "HNTSLZ" and JSC "Farmak".

Ukrainian pharmaceutical market of allergic drugs was analyzed by country manufacturers. Analysis shows that the pharmaceutical market of Ukraine is almost equal to quantities of drugs of foreign production.

We conducted a study extemporal formulation for the treatment of allergic diseases in children, whose number is now being growing steadily. The study was conducted based on the “Pharmacy №9” in Kharkov and "Pharmacies Medical Academy" in Krivoy Rog and Dnepropetrovsk.

Mainly there are used powders and mixtures in extemporal compounding pharmacies to treat hives in children. Local treatment must remove and reduce the itching and inflammatory reaction and stimulate repair processes in the skin, prevent and eliminate secondary infection, moisturize and soften skin, restore its protective properties.

According to the modern ideas of any drugs that are used for topical application medications should have several pharmacological effects that can simultaneously and comprehensively affect different pathogenetic links of this disease.

The main objectives of the local treatment of chronic hives is the elimination of pain, eliminate itching, stop bleeding, inflammation of the withdrawal, it is necessary that a drug was combined and allowed to effectively address these challenges. That is to treat hives in children may use topikal form.

The analysis of prescriptions and consultations with doctors allergists allowed to develop extemporal combined ointment composition for the treatment urtykari, when the disease in chronic hives.

SECRETION OF A SNAIL SLIME AS THE FOUNDATION OF MODERN MEDICAL AND COSMETIC ANTI-AGING SKIN CARE PRODUCTS

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Introduction. The skin condition reflects the general physiological condition of the body.

Therefore, using medical and cosmetic products are for preventing biological aging processes, and combining their recipe classical cosmetic ingredients with vitamins, herbs, phytohormones, seaweed extracts, animal products, etc. The essence of the anti-age therapy is a combination of internal and external funds: Cream + lymph drainage massage + supplements with antioxidants.

The most common problem is age-related changes of the body lymphocytosis - It is a condition caused by a violation of lymphatic drainage and accumulation in the tissues of the interstitial fluid, which leads to increasing permeability and rupture of lymphatic capillaries. The stagnation of lymph causes chronic swelling, tissue hypoxia, disturbances of water and electrolyte balance and metabolic processes, dystrophic and sclerotic changes.

The most characteristic symptoms of lymphatic stagnation are:

- Swelling of the face and extremities;
- Bags under the eyes;
- Cellulite;
- The point of inflammation of the skin.

These processes are often accompanied by the expansion of vessels in the skin in the form of "veining" red - rosacea, dermatological -telangiectasia. The primary prevention of rosacea is the hydration and protection.

Aim. The subject of our research was the development of new therapeutic and cosmetic products for anti-aging care which basis on secret slime snail skin, avocado oil and essential oil of rosemary. Secret snail slime contains mucin, which protects the skin from UV radiation, slows down aging, reduces wrinkles, evens relief, accelerates healing, improves the condition of rosacea, rosacea and dermatitis. Avocado oil in its composition similar to human skin, comprising proteins, carbohydrates, saturated and unsaturated fatty acids, vitamins A, E, D, B_1, B_2, B_3, B_9, E, K, PP, F, lecithin, essential oils, amino acids, magnesium, copper, potassium, phosphorus, calcium. Antioxidant vitamin E possesses potent anti-aging and immunoprotective properties, avocado oil includes 5 times more than olive oil has. It contains powerful antioxidant – squalene, which is the main component of human

skin, subcutaneous fat and sebaceous glands. Rosemary essential oil restores elasticity, smoothes and refreshes the complexion.

Materials and methods. We have developed and processed on the method of preparation of an emulsion of the anti-age skin care products that contain snail slime extract, avocado oil and essential oil of rosemary. We used the snail (Achatina fulica standard).

Given the problem of preservation of natural resources, applied humane methods - to obtain secret snails were subjected to physical pressure (rotation and shaking) in the laboratory under strict control. The secret was produced, going through a large amount water and filtered. This process does not cause any harm to snails and does not affect the therapeutic properties of secretions.

Received extract was used for creating a moisturizing emulsion for mature skin care, with the manifestations of rosacea.

To purified water was added to the extract and glycerin mucus cochlea. The resulting solution in portions emulsify with lanolin. To molten wax added avocado oil and essential oil of rosemary. Water-glycerine extract of snail slime solution was introduced in portions in the resulting fat base. Emulsification was carried out until the disappearance of the foam.

Results and discussion. There was carried out 10 lymphatic drainage facial massage with an emulsion produced. In the zone of influence of an improvement in the trophic tissue, in turn intensified excretion of metabolic products of stagnant zones and destructive fibroblasts produce new structural fibers. Correction of facial contours is due to:

- Softening and reduction of destructive compacted tissue, fat, and fibrous and sclerosed fibrous connective tissue;

- Stimulation and restore the contractility of the facial muscles.

Conclusions. The positive changes observed and to determine the properties of the product will significantly expand the scope of its application in medical cosmetology.

THE STUDY OF THE CHEMICAL COMPOSITION OF PORTULACA OLEACERA L.

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Introduction. Portulaca oleacea L. is an annual herbaceous plant, widespread in South America, North Africa, all countries in Europe, Central Asia, Indochina, etc. According to who, this plant is widely used as a source of food and biologically active substances. In folk medicine, the aboveground part of the plant is used as antipyretic, antioxidant, wound-healing agent. The Portulaca oleacera is given the title "global panacea". In traditional Chinese medicine, the plant has been used for many thousands of years and is described as "vegetable for long life". Also, the plant is used to stop bleeding from wounds, to reduce high temperature, for reducing fever, dysentery, diarrhoea, carbuncle, eczema and bloody stools. We have begun the study of the aerial parts of the plants growing in the Republic of Uzbekistan, as according to many researchers, each plant and a separate organ of the plant depending on the growing place, time of collection, soil and climatic conditions is a separate object of study.

Materials and methods. The object of the research is a dry extract obtained from the aerial parts of plants harvested during flowering. Freshly collected aerial parts of the plants were crushed, passed through a meat grinder, fresh squeezed juice, were separated. Meal 3 times insisted in a 2 fold volume of purified water (12 hours), the aqueous extract was separated, combined with squeezed juice, pressed in a vacuum evaporation boats installation, was dried at room temperature. The remaining mass is crushed and subjected to analysis. For the study of biologically active substances used as classical methods (percolation, separation by solubility, acid-base titrations and other chemical analysis methods) and instrumental methods (HPLC, mass spectrometry, infrared spectrometry, absorption methods of analysis).

The results of the study. The amount nitrogen-containing substances in the extract has identified to the classical methods start with obtaining water-soluble salt of the grounds, with alkalinization of 25% it with aqueous ammonia and extracting the free bases with an organic solvent. In alkaloid the sum is dominated by norepinephrine, and dopamine. The amount of grounds in the dry extract is 0.52%.

The content of flavonoids was determined spectrophotometrically by complexation with an alcohol solution of $AlCl_3$. The content of the sum of flavonoids in terms of quercetin is 0.08%.

The HPLC method found apigenin, luteolin, and quercetin myricetin.

Macro – and microelement composition of dry extract was determined by the method of mass spectrometry, found 98 items, of which the predominant is magnesium, calcium, copper, zinc, selenium, manganese, iron and phosphorus.

Conclusions:

1. Developed by optimum technology of obtaining dry extract from fresh aerial parts of Portulaca oleacera.

2. Defined qualitative and quantitative composition of the nitrogenous bases, flavonoids, macro – and microelements.

3. Purslane vegetable can be used as pharmacologically active component in a medicine with antibacterial, antidiabetic, antioxidant, anti-inflammatory and other medicinal properties.

PHARMACEUTICAL DEVELOPMENT OF OINTMENT FOR COLD DISEASES TREATMENT

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Introduction. Upper respiratory tract diseases, especially in preschool children are the most common. In the complex treatment and prevention of such diseases are often used medications of local external application - different ointments. They exhibit symptomatic treatment that is aimed at eliminating individual symptoms and relief of cold and cough. The main action of these ointments - locally irritating and distracting. Pharmaceutical market in Ukraine is not saturated with such drugs and represented only by foreign products. Therefore, the development of domestic ointment containing menthol, methyl salicylate, terebinthine, eucalyptus oil based on fatty ointment is a topical area of research. Menthol, methyl salicylate and terebinthine oil have reflex vasodilator effect with analgesic effect, irritating and distracting action. Essential oils of eucalyptus and pine needles as part of ointment cold at evaporation penetrate the airways and reveal their inherent properties: antimicrobial, anti-inflammatory and expectorant (reduce the viscosity of mucus and improve expectoration). Therefore the base of this ointment should be fatty with melting temperature equal to the temperature of the human body. Melting at application ensures the release of vapors of essential oils that provides a therapeutic effect.

The aim of the study. Creation of ointment bases composition for use in catarrhal diseases.

Materials and methods. The objects of research were ointment bases manufactured on the basis of solid fat with added sunflower oil and beeswax. Samples were subjected to rheological studies at different temperatures and determined the structural and mechanical properties. Also measured drop point of samples. Rheological studies were performed on rheoviscometer "Rheotest 2" with a set of coaxial cylinders N.

Results. It has been found that ointment consistency with drop point 36 °C has a sample with solid fat content 40%, sunflower oil 40% and beeswax 20%.

Conclusions. Scientifically substantiated ointment base composition for treating colds containing menthol, methyl salicylate, terebinthine oil and essential oils.

DEVELOPMENT OF MAGNETIC SOFT MEDICINAL FORMS WITH $Ag@Fe_3O_4$ FOR THE CRYOTHERAPY

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Introduction. In the development of nanopharmacy ranks first plays magneto-containing medicines. As magnetic filler of the ointment compositions typically use a modified magnetite. One of the ways to optimize the existing methods for the removal of benign neoplasms of the skin is a search for fundamentally new approaches that, in turn, will give an undeniable effect.

Analysis of the literature sources shows that in practice, methods such treatment of neoplasms of the skin as surgical, cryotherapy, electrocoagulation or diathermocoagulation, chemical coagulation, laser method. Due to the positive aesthetic effect, virtually painless of manipulations, the simplicity of the procedure, the most common method is cryosurgery. This method of local action of low temperatures with a curative effect, in which the tissue to be removed, is subject to destruction (destruction) by freezing with liquid nitrogen.

In medical cryology have experience of using ointments and creams. The use of soft magnetic dosage forms is perspective in the cryology. Their advantage is determined by the fact that by using an external magnetic field can penetrate to a sufficient depth and due to the high thermal conductivity facilitate freezing of the entire thickness of the affected tissues.

Making of an ointment containing magnetite modified with silver provides the appearance of bactericidal, bacteriostatic and wound-healing properties of such a system, since silver ions help restore damaged skin tissue, destroying the old and the cancer cells, normalization of the inflammatory processes, etc.

Aim. Introduction of magnetite an ointment, consisting of a magnetic carrier with a silver-coated islet of the "core-shell"– $Ag@Fe_3O_4$, in the known method cryodestruction of skin neoplasms. The proposed ointment contains ingredients that provide anti-bacterial, analgesic, anti-inflammatory and wound-healing properties.

Materials and Methods. The object of research is the nanocomposite, which is part of an ointment intended for cryotherapy on skin neoplasms. Optimization of magnetite ointment includes the step of justification required properties of magnetically nanocomposite $Ag@Fe_3O_4$ by: microbiological, magnetic properties medical and biological properties. Performing the experiment was performed in liquid nitrogen using a special portable apparatus for cryosurgery CRY-AC (Brymill) and contact cryoprobe with nozzles that are used depending on the shape and location of skin lesions.

Results and Discussion. According to studies of the magnetic properties nanoparticles composites such as $Ag@Fe_3O_4$ selected sample, which has a strong performance of the specific saturation magnetization $\sigma = 62.5$ emu/g.

Size of magnetite nanoparticles coated silver sheath insula – 23 nm, specific surface area of the composite is 145 m^2/g thermal conductivity of magnetite $\chi \sim 5.3$ W/(m×K), silver ~ 420 W/(m×K). The presence of silver on the surface of magnetic nanoparticles making a significant additional contribution to the thermal conductivity of the composite, characterizing one of the valuable properties for use in cryosurgery. For all investigated indices sample corresponds to a mole ratio Ag/Fe_3O_4 1 : 0,5.

The screening of antimicrobial activity in terms of the impact on the composite strains of microorganisms and fungi has been carried out.

Biomedical researches are based on improving of the method of cryotherapy to pathological growths of the skin by the use of magnetically ointments with $Ag@Fe_3O_4$ to the increasing of cryotherapy. For this purpose, magneto controllable ointments: I (superimposed before handling removal) and II (applied to improve and promote healing without complications and relapses) have been used.

The results obtained show that the use of the improved method can significantly improve the results of cryosurgical intervention by:

- Creating of close thermal contact of the tool with the entire surface of the affected area due to ointments I and ability to penetrate to a certain depth of the disease outbreak.
- Decreasing the time of freezing by 50%, and increasing the depth of penetration of the devastating effect of cold, reducing the operation time to 30 - 60 seconds.
- Providing the complete removal of the structured fabric with exudate by an external magnet.
- Prevention of infection and inflammation of the operated area due to the analgesic, anti-inflammatory and regenerative effects ointments II, which is applied after cryointervention.
- Reduction of post-operative recovery of 55%.

Conclusions. The magnetic characteristics of the studied nanocomposite $Ag@Fe_3O_4$ are providing sufficient control of thermal conductivity and antibacterial activity of ointments due to the insula silver shell. Application of ointments based nanoparticles of $Ag@Fe_3O_4$ for microsurgical interventions has its advantages: the ointment I - provides a deep and complete freezing of the tissues without damaging healthy skin, ointment II - has a bactericidal, anti-inflammatory and wound-healing ability. Its use significantly reduces the time of cryoablation and subsequent rehabilitation.

SECTION № 5

MODERN BIOTECHNOLOGY

THE PROBLEM OF OPTIMIZATION OF SEED MATERIAL PREPARATION EREMOTHECIUM ASHBYII

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Introduction. Recently, there is an increased interest in aromatic and biotechnology products of their preparation. The quality of essential oil depends on environmental factors, culture conditions, the genetic characteristics of the producer. Currently, the promising bioobjects are the members of Eremothecium, synthesizing the essential oil, which is approximated by the component composition to a rosa oil. The purpose of the study is the research of the influence of strains specificity on the status of the seed, the accumulation level and quality of Eremotecium oil.

Materials and methods. Objects of the study are strains of Eremothecium ashbyi Guilliermond 1935 VKPM F-36, 36 Ob, VKM F-4565 (mutant derived from a population of VKPM strain F-36), VKM F-3009, sp-916 (made selective by means of strain VKM F -3009). Storage of micromycete culture was carried out on a slant potato dextrose agar. Seeds were grown in a deep way in glucose-peptone liquid medium with yeast extract by continuous shaking of 200 shak. / Min. for 20 hours at 28 ° C. Fermentation was performed in a deep way in soy sucrose medium for 48 hours at 28 ° C by continuous shaking of 240 shak ./ min. The relative content of riboflavin was evaluated by the intensity of the color in the score: 1 - light yellow, 2 - lemon, 3 - yellow 4 - orange 5 - bright orange. Producer biomass was separated by filtration from the culture medium, it was weighed before and after drying. Isolation of aroma substances from the culture liquid was performed by triple extraction followed by removal of solvent (hexane) using a vacuum rotary evaporator. The resulting lipid residue is weighed on an analytical balance.

Results. Intense accumulation of seed was occurred in the strain 36-Ob and the fungic mass in the fermentation process – in the strain VKM F-3009. Upon receipt of the inoculum the change of pH to the acid side was significant in the 36-Ob strain and the fermentation of alkalization was more signified in the strain VKM F-4565. By the number of extracted oil it was separated sp-916. The strain VKPM F-36 synthesized the smallest amount of essential oil. The maximum content of riboflavin in the culture liquid was seen in the VKPM F-36 and 36 Ob. The highest total number of monoterpene alcohols is in the oils sp-916 , 36 Ob and VKM F-3009. The lowest ratio of phenylethyl alcohol to monoterpene alcohols was observed in highly-active strains 36-Ob and sp-916, which indicates that they are most valuable.

Table 1

Comparative analysis of the 338noculums of strains and of variants of E. ashbyi

Strain	biomass, g/l		pH	B_2, points
	raw	dry		
36	38,56	2,40	5,08	5
36-Ob	37,21	2,62	5,04	5
4565	41,37	2,47	5,10	3
3009	31,64	2,14	5,33	2
sp-916	35,41	2,23	5,20	3

Table 2

Comparative analysis of the productivity of E. ashbyi

Strain	biomass, g/l		pH	B_2, points	extracted oil, mg/l
	raw	dry			
36	72,30	8,58	6,80	5	127,0
36-Ob	64,81	8,72	6,90	5	129,0
4565	68,43	8,44	7,11	3	150,0
3009	84,49	8,90	7,09	4	200,0
sp-916	78,98	8,95	7,05	4	240,0

Table 3

Comparative characteristics of the component composition of the essential oil, synthesized of E. ashbyi,%

Strain	phenyl ethanol	geraniol	citronellol	nerol	mono terpene alcohols	phenyl ethanol/ mono terpene alcohols
36	18,0	74,1	5,6	2,0	81,7	0,220
36-Ob	8,6	82,8	4,0	2,5	89,1	0,097
4565	8,9	73,7	7,4	4,9	86,1	0,103
3009	9,3	78,6	5,4	5,4	88,1	0,106
sp-916	4,3	80,9	11,4	3,4	95,7	0,045

Conclusion. The most productive is a new strain sp-916 by our team selected, featuring a high quality essential oil, approximate to the world standard - Bulgarian rose oil.

INDICATORS OF QUALITY OF PROBIOTIC PREPARATIONS

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Introduction. At the present time taking into account new concepts for prevention and therapy a healthy intestinal flora is given of special significance. The consumption of fermented dairy products and proceeds of probiotic strains of bacteria provides a number of useful properties for the human body, which is confirmed by the results of numerous medical researches. They include not only antagonistic activity against pathogenic microorganisms; probiotics are involved in the formulation of important vitamins, amino acids and some hormones, which indicate a positive effect on physiological, biochemical, immune response, and balance regulation of fat metabolism. Despite the fairly wide range of imported and domestic drugs, actual problem is the increase of production efficiency of probiotics, which is related to improved methods for their preparation and harmonization of methodological approaches for their control.

Results and discussion. Research related to optimizing the control of probiotics should help to improve efficiency, adaptation to the conditions of mass production of drugs, reducing the complexity, duration and material costs.

The number of immunobiological products, registered in Ukraine, is growing every year. The most common domestic probiotic preparations are presented such bacteria as: *Lactobacillus, Bifidobacterium, Escherichia, Aerococcuses* (Bifidumbacterin, Lactobacterin, Bifikol and A-bacterin).

Requirements for the quality control of such preparations are high quite, because probiotics do not always have therapeutic action. They can die in the acidic environment of the stomach under the influence of stomach acid, antibiotics and antimicrobials, and without getting into the intestine. It is known that the effectiveness of any probiotic is determined by the characteristics of the bacterial culture, which is consists of probiotic.

Conclusions. One of the basic requirements for probiotic bacteria are: resistance to aggressive environments gastrointestinal tract; the lack of conditional pathogenicity; sufficient antagonistic activity against pathogenic microorganisms; high biosynthetic activity (synthesis of organic acids, vitamins, polysaccharides and bacteriocins); rapid reactivation of the biomass; immunomodulating properties; the high growth rate of population; stimulating effect on the representatives of normoflora; natural resistance to antibiotics. Compliance of the probiotics to the quality indicators ensures their effectiveness during the action on the human body.

DOPING FOR ATHLETES BASED ON ERYTHROPOETIN

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Introduction. Today the concept of professional sport and doping is continuously connected. Because of the strong competition for the right to dominate in the world today, athletes are increasingly resorting to dangerous drugs, which lead to irreparable consequences. Bodybuilders and other athletes use different drugs and their complex combinations. Some are effective and generally accepted, and others raise questions and misunderstandings. Currently, doping agents are divided into five main groups: blood doping (central nervous system stimulants, analgesics); narcotics (narcotic analgesics); anabolic steroids; β-blockers; diuretics.

Erythropoietin (EPO) is a hormone that stimulates the blood cells production. In medical practice, the EPO is used to treat anemia caused by chronic renal failure. EPO can be used by athletes to increase the transport of oxygen in the body, the concentration of which increases with the amount of red blood cells, resulting in increased endurance. The negative consequences of receiving erythropoietin are: increased blood viscosity; increased risk of blood clots formation; the risk of virus infections such as hepatitis and HIV infection.

The **aim** of our work is to study the effect of erythropoietin on the human body, and whether it is appropriate for use as a doping drug; to learn clinical blood analysis techniques.

At the moment is almost impossible to reliably authenticated cases of administration of exogenous EPO in the body. To date, there are no universal methods of detection of EPO in the blood as an athlete doping. Since the natural and recombinant erythropoietin (rh-EPO) have the same amino acid structure and rh-EPO is virtually indistinguishable from its natural counterpart. The direct detection method is based on the minor differences in different isoforms of erythropoietin. Natural EPO predominantly glycosidic moieties are associated with more acidity, while rh-EPO have alkaline properties.

Materials and methods. The material for the EPO detecting is the urine. Methods of the urine sample purification and separation are fairly complex and requires a large amount of urine (to 1 liter). As indirect methods some oscillations of physiological blood parameters which are detected after the administration of EPO for the preliminary control such as the maximum value of the hematocrit, the maximum permissible values of hemoglobin are used. This is possible only when using blood as a sample for doping test. Certain biochemical tests, such as serum soluble transferrin receptor (sTfR) measurement are also used in doping control.

THE STUDY OF EFFECT OF YEASTS ON QUALITITATIVE CHARACTERISTICS OF CIDER

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Introduction. Apple cider – low alcohol drink which is obtained by fermentation of apple juice. A drink known from times of the Middle Ages and since then its popularity has not faded, conversely, eventually production technologies were improved and scaled, a new varieties of apple have improved and were deduced. here are other ways of making cider which can replace the long processes of cultivation and preparation of apples for processing against the backdrop of modern methods and technologies of preparation of cider. One of such methods is the preparation of cider from apple juice with the addition of cider yeast.

Results and discussion. At the Department of Biotechnology of the National University of Pharmacy works on the development of composition and technology of apple cider, which is produced by the fermentation of apple juice by various yeast species are carried. In the first stage of experimental studies a few samples of the fermented beverage have been prepared. Apple juice of trademarks “Sadochok” and “Nash sik” were used as raw materials, in which the organoleptic indexes, and active and titrated acidity were pre-determined. The inoculums was added to each sample, 1% for each 1 liter. Alcohol and cider yeasts were used as the inoculums. They were pre-prepared(aged in the thermostat TSO-80 at 30 °C for 30 minutes). The samples were dispensed into 4 previously sterilized containers and yeasts were added in. Then hydraulic locks were installed, for anaerobic fermentation, for 6 days at a temperature of (18-20) °C. After finishing the fermentation process in the samples obtained fermented beverage active and titrated acidity, as well as sensory properties were determined. The results of study showed that the titrated acidity of almost all samples grew by (16-18) T of other than drink juice-based brand "Sadochok" and alcohol yeasts - to 28 °T. This active acidity has not changed much for beverages based juice "Nash sik" and for drinks on the basis of the trade mark "Sadochok" – increased by 0.07-0.09 units.

Conclusions. The study of the organoleptic properties of all the intermediate products have received a satisfactory evaluation. The best flavor characteristics of the samples were allocated on the basis of apple juice "Nash sik", but the smell of the yeast reduced the overall impression. After quality control, semi-finished products were filtered, bottled in containers for carbonization stage. Thus, the results of the study will be used in the development of composition and technology of fermented apple cider drink.

ASPECTS OF PRODUCTION OF FRUIT VINEGAR. RED AND WHITE WINE VINEGAR

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Introduction. Natural vinegar – result of fermentation of alcohol-containing raw materials by means of acetic bacteria. Content of acetic acid in it makes 4-6%. Natural fruit vinegar differs from usual in uniqueness of medicinal properties and a surprising set of components. Almost without loss pass all useful substances of fruit into him (macro - and minerals, vitamins, enzymes, amino acids, propionic, dairy, vinnokamenny, lemon and other acids, aldehydes, complex alcohols and air) which presence creates aroma and a bouquet of vinegar. Wine vinegar happens two types: red and white.

Classical red wine vinegar is received by a sbrazhivaniye of red wines – as a rule, grades of "Cabernet", "Malbek" and "Merlot" are used. Wine is filled in in barrels from an oak which impacts to vinegar special relish. White wine vinegar is done of dry white wines, it easier to taste. Unlike red, process of fermentation comes not in expensive wooden barrels, and in cheaper capacities from stainless steel. Thanks to such approach white vinegar cheaper, than red.

Draw both types of vinegar long enough – till 12 years.

Taste of wine vinegar of both types more sweet, than at other fruit vinegar, aroma difficult and soft. Potassium entering in the complement of vine vinegar beneficially affects nervous system, destroys pathogenic bacteria, and also assists strengthening of hair and nails.

Another microelement included in a sufficient amount in winy vinegar is magnesium, stimulates work of heart.

Doctors recommend to use wine vinegar in the menu as it is possible for a thicket. He actively interferes with emergence of cholesteric plaques, flavonoids, anti-inflammatory substances, antioxidants– resveratrol which possesses powerful cardiotyre-tread, antineoplastic and anti-inflammatory action are his part.

Conclusions. Medical researches show that the use of wine vinegar is excellent prevention of cardiovascular diseases, including a stroke. Wine vinegar increases immunity and is a good defender both against usual cold, and against serious diseases, for example cancer. He slows down aging processes, has the rejuvenating effect on skin and hair. The rejuvenating and general improving action low-calorie (9 kcal in 100 g) wine vinegar considerably if it constantly is in the menu of your table. Vinegar can be used for cuts, bruises and skin whiteting. It also effective for sunburns healing.

STATUS OF FERMENTED BEVERAGES IN UKRAINE

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Introduction. The global beverages industry at all times occupied a special place in the food industry. Recently, with increasing of production volume there is a significant expansion of their range. There are different classifications of drinks, but overall they can be divided into two main types – fermented and unfermented. The latter include juices and also drinks with the use of substitutes for natural raw materials. The most promising type is fermented beverages. The vast majority of them are drinks obtained by the action of the complex enzymes that are concentrated inside the cell, on its surface and outside membranes of microorganisms. These drinks are produced by fermentation of aqueous solutions of natural raw materials (wort) contains nutrients for the microorganisms of the substances. These include: beer, kvass, cider, kombucha, mead, a drink from the tibetan mushroom, mushroom rice, etc. It is common knowledge that any fermented drink is more useful for the human body due to the enrichment of biologically active substances formed during the fermentation and transition in fermented wort bioactive constituents of microorganisms. They primarily include the essential amino acids and extremely important to the human body B vitamins, which are actively involved in many metabolic processes, have a positive effect on the physical condition of the person providing the blood. Unfermented carbohydrates and pectic substances play an important role in the processes of digestion. Fermented drinks contain essential for human body enzymes, in particular hydrolytic (amylase, protease, lipase, etc.). Today Ukraine has the potential to take a leading position on the global market for the production of such fermented beverages, like beer and bread kvass. To realize this potential the industry already has their production and the soil and climatic conditions, which fully meet the needs in raw materials. But the necessary condition is to conduct complex research, marketing operations and the corresponding reconstructions of the workshops of the manufacture. Recently fermented beverage under the trivial name "kombucha mushroom tea" became very popular. In the market of Ukraine it is represented by a fermented drink called "Vitalon". With regard to the production of honey fermented beverages on an industrial scale in Ukraine, it is virtually absent and preserved only in their cooking at the household level, mainly in beekeepers. It should be noted that, Public Union "Ukrainian industrial Association of the living drinks" was established in Ukraine.

Conclusion. So, responsible consumption is an important component of the culture of consumption of fermented beverages.

THE PERSPECTIVE OF DEVELOPMENT OF PROPHYLACTIC ENZYMATIC MEAT PRODUCTS

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Introduction. Nowadays the largest number of processed collagen raw material used for the production of food products, and less directed to the production of meat products. At present, we developed and thoroughly studied the various ways bio modification of raw materials that achieve the optimal possible properties of the finished product. The most promising and underexplored method is the enzymatic treatment. Enzymatic processes involve materials handling processing enzyme preparations and microorganism's ferments. Fermented foods - improved animal products that are based on waste products of microorganisms. Currently on the market range of fermented foods is limited, but their number is constantly increasing. These include a variety of sausages, pates, beverages based on milk serum.

Results and discussion. Fermented meat products are a delicacy, which to the probiotic properties of the dominant in the finished product is recommended for use in children and special diet. The need for such products is significantly. The longer the food is exposed to the fermentation process, the better and easier to digest its components. Fermentation is used for preserving food and just for a healthy diet. Furthermore, fermented foods are good for the intestinal microflora and replenish the amount of enzymes in the human body. The advantage of these products is also increasing intestinal microflora as well as water binding ability. During reproduction of microorganisms, yeasts belonging to the vitamin content and increased digestibility of the nutritional components: protein, fat and carbohydrates. Fermented foods are a source of beneficial bacteria - probiotics natural and rich in enzymes, vitamins and amino acids. The same advantage is to obtain a food increased shelf life. The products have been subjected to a fermentation process have sensory characteristics - smell and taste. Nowadays range of enzyme meat products on the Ukrainian market is very small and presented foods low calorie (with a small amount of animal fats), products for preventive nutrition of patients with anemia (a source of iron components - pork liver) and products for children with β-carotene, vitamins - ascorbic acid, thiamin, riboflavin, retinol, tocopherol, calcium and minerals. Particular attention is paid to the development of specialty sausages for preschool and school feeding adapted to the physiological needs of the child.

Conclusion. Therefore, at the Department of Biotechnology of the National Pharmaceutical University work on the development of composition and technology of fermented products for preventive nutrition-based animal feed is started.

THE MODERN STATE BIOTECHNOLGIES DRUGS ON THE MARKET OF UKRAINE

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Introduction. Biotechnology is one of the fastest growing industries in all countries, focus on progress. Industrial production of penicillin, insulin, interferons, on the basis of biological synthesis - all these are the first steps of pharmaceutical biotechnology, became history. The leading area of the industry today is the development and commercialization of new drugs for the prevention and treatment of infectious diseases (e.g., influenza, tuberculosis, HIV) and diseases of other etiology (diabetes, cancer), as well as for gene therapy of congenital pathologies. The introduction of domestic developments in this area is very rare, however in Ukraine there is a fundamental level of biotechnological innovation and production of biotechnological medicines carried out in several factories.

Today in Ukraine the production of biotechnological medicines are pharmaceutical factories: "Enzim" (Ladyzhyn); "Dniprofarm" (Dnepropetrovsk); "Pharmstandard - biolek (Kharkiv, Ukraine); "PharmBiotek" (Kyiv); "Biostimulator" (Odessa); "INDAR" (Kyiv); "Biopharma" (Kyiv). Among these enterprises are the largest "INDAR" specializing in the production of insulin, "biolek" and "Biopharma" that produce drugs - normality, proteins of human blood, vaccines and sera for the prevention and treatment of many infectious diseases, as well as different test systems. Kiev factory "Biopharma" produces the following products: "Subalin" - a biological product on the basis of genetically modified aerobic spore - forming bacteria with a high antiviral and antibacterial activity for the treatment of diseases of mixed etiology; the "human Immunoglobulins" - against the herpes simplex virus type II, Epstein - Barr, against Toxoplasma gondii, etc.; "Biosporin" - a highly effective preparation based on Bacillus subtilis and Bacillus licheniformis B. for the prevention and treatment of dysbacteriosis and acute diseases of the gastro - intestinal tract of humans.

The **aim** of this work is the analysis of the current state of biotechnological products and their further development in the Ukrainian market. The leading countries of the world community strongly encourage the development of biotechnology, as have long appreciated the advantages of biotechnological production – the relative cheapness and environmental safety. Problem in our country are complex socio – economic conditions that restrict biotechnology development in Ukraine, although in the future this should pay off in full.

THE STUDY OF BIOGENIC STIMULATORS ON THE BASIS OF BEE PRODUCTS

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Introduction. Biogenic stimulators are biologically active substances that stimulate regeneration and metabolism processes in the body and have a tonic influence. Bio-stimulators show some biological activity and non-specific stimulatory effect on the body metabolism. Bio-stimulators are used for stimulating and improving the metabolic processes in the body in case of inflammatory degenerative and atrophic diseases. Natural bio- stimulators include hive products; they have properties to stimulate the metabolic processes in a human body. One such product is royal jelly, the main principle of the biological effects of which is the improvement of the human body'' immune system to the highest level, when it independently copes with a variety of diseases.

Results and discussion. The composition of royal jelly is very complex. The chemical composition of it is a combination of various components in proportions Compliant physiological needs of the living organism. The main components of royal jelly:water - 60-70% proteins (albumin and globulins represented) - 10-18% carbohydrates - 9-15% fat - 1,5-7% minerals - 0.7-1.5%

All the basic properties necessary for building and well-being of a human organism have been found in the composition of the royal jelly such as: amino acids, proteins, vitamins, fats, carbohydrates, enzymes, fatty acids and hormone-type substances. According to the conclusions of the experienced scientists bee royal jelly in its composition has a balanced mix of micro-elements useful for the human body. Due to which this natural remedy has special pharmacological effects. The composition of the royal jelly also contains deoxyribonucleic acid (230-240 mg/g), contributing to the rejuvenation of the body, as a result of the regenerative effect directly on the aging tissue and cells.

Royal jelly is a phenomenal product of beekeeping and is a very powerful biological stimulator. It is widely used for the prevention of complex diseases of different kinds; there are also data on the improvement of women’s separation of milk who are breastfeeding a child with regular admission of royal jelly.

Conclusion. Due to the high biological activity of royal jelly, we are interested in the possibility of its use as part of biogenic stimulators, the development of composition and the technology of which are being carried out at the Biotechnology Department at the National University of Pharmacy of Ukraine.

PROBLEMS OF PRODUCTION OF THE CURD GLAZED CHEESES

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Introduction. One of most quickly developing to date segments of milk industry for the last 10 years, producing of the curd glazed cheeses. A total production of this group of soul-milk foods volume in Ukraine increased more than in 3 times. Experts say that production will grow. And it is not surprising, as an all greater number of population realizes the necessity of introduction in to the ration of feed more foods providing the normal functioning of organism.

The glazed curd cheese is the product made from curd mass and glazed. On State standard, the glazed cheese is the wet-process curd mass, got from the subpressed curd, covered by a food glaze, by mass no more than 75 gramme. The glazed cheeses differ in a high food value due to high maintenance of proteins and carbohydrates. The proteins of curd are better mastered by an organism, than proteins of fresh milk. The product does not get heat treatment. That's why it saves all properties of fresh curd. Curd have lots of proteins, fats, carbohydrates, and organic acids. Organic acids normalizes work of gastrointestinal tract. 100 gramme of curd mass have day norm of A vitamin, and lots of B vitamin. These vitamins keep our emotional health. Also curd mass has a lot of minerals such as calcium, phosphorus, magnesium, potassium, manganese, and others. Besides it has lipotropic. Lipotropic normalize fat metabolism. It inhibits accumulation of fats in the liver. Curd mass have lactobacillus. Lactobacillus improves digestion and protect from gastrointestinal tract cancer. Curd mass have only one problem its calorie content.

Now our **aim** is, to light up the modern production of the curd glazed cheeses in Ukraine, and to ground the necessity of verification of these products to the corresponding requirements. First requirement is organoleptic indicators, second is physical and chemical indicators. Organoleptic indicators to be check are: appearance, taste, smell and color. Physical and chemical indicators to be check are: acidity, mass fraction of fats and moisture. On state standard 52790-2007, acidity should be 160-220 °T including. Mass fraction of fats should be 5-26% including. Mass fraction of moisture should be 55-33% including. According to the got results, it is necessary to define perspective in creation of not only delicious but also useful foods. That means, we need to create products with good organoleptic indicators and more useful for human body using natural, no synthetic analogs. And implement it in to the production.

Results and discussion. Mostly basic components of the curd glazed cheeses are: curd, sugar, fat vegetable, modified starch, sodium alginate, guar gum, flavoring

identical to natural, vanillin, sorbate of potassium, palm-oil, cacao-powder, lecithin. Glazed curd cheeses are made from curd with low mass fraction of moisture. Making is going on in a mixing machine, according to composition. Received mixture cools to 5-9°C and puts in the bunker of molding vehicle. Mixture goes out as molded streams from molding vehicle. This streams is automatically cut to pieces, by mass for a 40 grams. These cheeses enter frosting machine, where they covered by a couverture. Stream of warm air retires superfluous glaze from cheeses. The underbody of cheeses is glazes by revolved rollers of enrobing machine. Further conveyer brings curds in the chamber of the air cooling, where at a temperature -1-1 °C a glaze hardens. Prepared cheeses pack and lay in boxes. Keep the prepared products at the temperature no more than 8 °C. It should be noted that the curd glazed cheeses presented at the modern market contain the least of useful substances, and their basis is a vegetable fat and sugar. Experts often finds in dangerous ingredients not indicated on packing. All other in composition is an enormous amount of harmful sugar, cheap fats, starch, colorants, flavours, stabilizers, emulsifiers. Synthetic components can easily hide low quality of raw materials. Also producers can give almost full synthetic product instead natural. The examination conducted by the program "The Control purchase" educed, that in cheese of trade mark of "Rostagroexport" were found out the preservatives not indicated on packing, and in cheese of trade mark of "Danone" the amount of yeasts in 7 times exceeded a norm, that is dangerous for a consumer. In addition, the glazed cheeses of " Dmitrov a suckling plant" and "Carat" contained to the coliforms, and in cheese of trade mark of " Dmitrov milk plant" was found out mould. Besides it harm of these cheeses consists in high enough indexes of cholesterol, that grounds fully to eliminate it product from the ration of feed of some groups of people. For example, people with diabetes, by an ovenweight and suffering the diseases of the cardiovascular system. Aurococcus discovered in one of the standards investigated in the program. Aurococcus causes weakening of immunity, festering infections, stomach-aches, diarrhoea, vomiting, furunculosis et cetera. Collibacillus of E. coli, discovered exactly in the half of the standards investigated in the program. Collibacillus, causes the accumulation of toxic substances, failures in-process gastrointestinal tract process, negatively influences on the functions of buds, liver, immunity. Infection by the collibacillus of E. coli even can result in a fatal outcome for children. Scientists think that all this violation happens because of ignoring hygiene regulations. Similar researches show the necessity of creation of not only delicious but also useful, safety for human health foods.

Conclusions. That’s why the department of biotechnology of NPhaU works on development of composition and technology of the curd glazed cheeses. This goal still actual and perspective in nowadays.

THE STUDY OF THE PHYTOPATHOGENIC FUNGUS RHYTISMA ACERINUM MORPHOLOGY AND ASCI FORMATION

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Introduction. *Rhytisma acerinum* is the microscopic ascomycete that locally affects the leaves of the trees and is a biotrophic parasite. The fungus is parasitic mainly on Acer platanoides leaves and can affects young pine needles. Infection is especially noticeable in urban areas, squares and parks of major cities. The Teleomorphic stage of this microorganism is called *Rhytisma acerinum,* Anamorphic stage is called *Melasmia acerina.* This fungus is belongs to kingdom - *Fungi*, class - *Leotiomycetes,* family - *Rhytismataceae,* genus - *Rhytisma*, species - *P. acerinum.*

The disease manifests itself in the leaf spot formation. Vividly symptoms are seen in the second half of the summer. Spots are black, shiny, slightly protruding, surrounded by a yellowish border, size (10-15) mm. They appear on leaves. The spots appear on the upper leaf side and can be very numerous. Plant infection occurs most intensively in high humidity and temperature changes. The fungus survives in the fallen leaves, and next spring there is an infection of young leaves.

Contact with the affected leaves is not a danger to human and animal. The main harmfulness of the disease is to reduce the ornamental trees.

One of the main measures to combat this fungus is raking fallen leaves and composting them in closed pits, or burning. There are also *P. acerinum* infection control chemical methods. They are spraying fungicide, copper sulfate, bordoss mixture, kuprikol. But their use is limited in localities.

Despite the fact that the fungus is a phytopathogenic, several disease cases and mortality from atypical myopathy of horses that were grazing near the maple trees infected with fungus *Rhytisma acerinum* have been known in the Netherlands.

Removing fallen leaves from the city's parks and the impact of the dry wind may affect the *Rhytisma acerinum* presence in urban centers.

The absence of this fungus in large cities may also be due to the its ascospores sensitivity to contaminants (especially sulfur dioxide) during germination. An abundance of black spots on the leaves is used as a visual indicator of air quality.

Aim. To investigate the teleomorfa stage of the fungus life cycle we have conducted a series of experiments, the purpose of which was the natural processes, in which the formation of *Rhytisma acerinum* asci and ascospore maturation have been modeled under laboratory conditions.

In the course of the experiments we studied:

- for the detection of the fruiting bodies of the fungus - leaves with characteristic lesions, collected in the fall;

- for the experimental induction of asci formation- leaves subjected to freezing at minus 10c to simulate the natural conditions for 1 month, followed by thawing and holding at room temperature with intermittent lighting for 14 days;

- to study the release of ascospores - leaves, overwintered in a natural way, and after freezing in laboratory conditions.

The asci formation we studied by using the biological material cutting into small pieces, bearing one or more lesions (spots) each. The prepared material was placed upper epidermis up into a Petri dish with wet filter paper.

The light microscopy techniques of temporary agents we used to evaluate the results of experiments.

Results and discussion. As a result of asci inducing experiment conducted in the laboratory in "crushed drop" preparation we seen the formation of asci.

During the study on the infected leaves surface we observed black spots stroma using a stereoscopic microscope.

Apothecia combs had curved extensions. The hymenium was in places of such discontinuity ridges.

Asci were with a typical elongated shape with a thickening at one end, were colorless, filled with ascospores. Their were filamentous paraphysis between them. In some asci the ascospores yield that have needle-like shape and arranged around the periphery of the ascus and the smear was observed.

In the study of the surface of infected leaves, overwintered in nature a similar picture was observed.

Conclusions. *Rhytisma acerinum* is an excellent model object for studying the characteristics of the ascomycetes lifecycle. The life cycle of this biotrophic parasite is finely adapted to the owner, as well as to the seasons changing.

Rhytisma acerinum is particularly attractive to investigate in a university laboratory in the study of many disciplines such as mycology, plant pathology, microbiology, ecobiotechnology, the biology of biologically active substances producers, as the fungus has the anamorphic and teleomorfic state change which can easily be demonstrated.

DEVELOPMENT OF FUNCTIONAL DRINKS ON THE BASIS OF STARTERS

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Introduction. Lactic acid bacteria are the group of gram-positive microaerophilic microorganisms useful for the functioning of the human body. Lactic acid bacteria belong to the family of Lactobacillaceae which includes:

1. subfamily Lactobacilleae (includes the genus Lactobacillus);

2. subfamily Streptococceae (includes the genus Streptococcus, Leuconostoc, Pediococcus).

Depending on the fermentation products, lactic acid bacteria are divided into: 1. homofermentative - lactic acid is released during the fermentation of carbon; 2. heterofermentative - lactic acid formed by the decomposition of carbohydrates.

Species of the genus Streptococcus in the fermentation of sugar converted to lactic acid, and only the minimum sugar turns to alcohol and acetic acid. The most widely used in the practice of the human species of this genus are: Str.lactis, Str.citrovorus, Str.cremoris, Str.thermophilus, Str.diacetilactis.

Results and discussion. Lactic fermentation is faster under the influence of Lactobacillus genus of bacteria, among which the most widely used following types: L.casei, L.brevis, L.acidophilum, L.plantarum. Also bacteria of the genus Bifidobacterium have of great importance to humans, which are among the first representatives of the normal flora colonizing the mucous of babies. Lactobacilli support the normal balance of the intestinal microflora, are inhibitors of pathogens, have immunomodulatory activity, reduce cholesterol levels in the blood and amines, and reduce the risk of tumor tissue, synthesized vitamins, amino acids, enzymes. The use of lactic acid bacteria improves human health, increases its resistance to infection. Representatives of the normal flora of the normal human have long been used in probiotic products and preparations. Today is very popular among the population use starters, which you can use at home to get tasty and healthy functional foods. It can be found several firms in Ukraine in pharmacies and grocery stores: Good Food, Vivo, Genesis, Fit, etc.; there are available yogurt, yogurt, sour cream, cheese, cottage cheese and others on the basis of their. Technology and the amount of starters increases, as a positive effect from the reception of functional products based on them is a fact.

Conclusion. In this regard, a series of functional products on the basis of starters that are useful to humans and the production of which would be easy for home cooking are developing at the department of biotechnology of NUPh.

ALTERNATIVE KINDS OF FERMENTED BEER

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Introduction. Nowadays there in a decline in demand for traditional sorts of beer made on classical technology on the basis of malt and hop. Alternative kinds with new original organoleptical properties are in demand.

Different kinds of beer products are presented in the world market. They contain medicinal herbs, spices, pine-needle, ginger, oak bark, camomile, wild rose, cardamom, hypericum, coriander, walnut, linden, black pepper, basil, cumin, vanilla, mint, licorice, tea berries, juniper etc. The technology of production of such beer is complicated by the necessity of strict control of physiological activity of seed material, yeast as many herbs and spices have alternative and bacteriostatic properties. Moreover, these kinds are oriented on the narrow segment of consumers.

Results and discussion. It is also possible to see beer which is produced by must fermentation of fruit raw material (cherries, blueberries, raspberries, currants, wild ash, cactus, oranges, lemons, limes, peaches, apricots, apples, plums) or with addition of berry and fruit juice and extracts. Consumers are very interested in bragget. This light beer with addition of oat-flakes has a sweetish taste and is recommended when having gastrointestinal issues. Beer must which contains 40-45% of wheat grain and 50% of barley malt with addition of oat is considered to be non-traditional. Beer with anise, licorice, nuts and green apples is well-known. For preparing British and Irish beer barley malt, hop, water, sugar and also barley, rice or corn starch is used. It has light colour and slight beer flavour.

Among the alternative types of beer drinks potato beer stands out. This is a historically traditional drink in Germany. Today it is produced at some brewing enterprises of Europe. It has got specific hop bitterness, tints of taste: tastes of mellow grain, yeast, alcohols. It is produced on the basis of potatoes, barley malt, einkorn and water using top and low fermentation methods. In the production process of beer potatoes are washed, cleaned and mashed potatoes are prepared, which later serves as wort. Then, purified water was added thereto, hops and boiled for 30 minutes. The wort is filtered and placed in a brewery where the yeast was added. Fermentation was carried out anaerobically 7-10 days, and then poured into containers and beer is carbonated. Potato beer is a perspective consuming product.

Conclusion. Therefore at the department of biotechnology of the National University of Pharmacy work on the development of ingredients and technology on the basis of potatoes has been started.

THE STUDY OF INFLUENCE OF BIOACTIVE SUBSTANCES ON PHYSIOLOGICAL ACTIVITY OF YEASTS

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Introduction. Yeast is relayed to the minute organisms which widespread use in the biotechnology to get receive product metabolism and biomass. The most widespread variety yeast is Saccharomyces cerevisie. Yeast the most widespread in food industry. Their important function in the bread making decondensation dough as a results in fermentation of sugar flour and maltose which formed from amylum with singling out alcohol and carbon dioxide. In viniculture - in fermentation fructose and glucose grapes juice with the formation of ethyl alcohol.

Results and discussion. At the medicine sphere they use in the restorative, antiallergenic preparation, dietary supplement. So the wideness of the application and useful characteristics yeast determine constant research their process of metabolism and find components which could increase their physiological activity. In the capacity of substrate the main components for the yeast is glucose and fructose, their breakdown realize glycolytic way. And other components could fermentation such as: hexoze and oligosaccharides. Very rare variety of yeast fermentate lactose and melibiose. And they can fermentate polysaccharides, which consist of hexose rests. Metabolism yeast can make by breathing and fermentation. The arrangement of these process at the primery stage are similar. They continue from the line of the medium stages, and then at the certain stage they device and follow to the final product. During the breathing carbon dioxide and water are the final products, and the fermentation ethyl alcohol and carbon dioxide are too. Many kinds of yeast can change from the barmy process to the respiratory process and backward according to the conditions: together this the oxygen fermentation inhibition and yeast stat to breath, without oxygen start the process of alcoholic fermentation. The growth factors are the complementary matters, which influence to the growth yeast. They are vitamins, amino acides, purine, pyrimidines which are parts of nucleic acids and proteins and consist coenzyme. Composition of coenzyme yeast consist from vitamins group B and lipoic acid, pantothenic acid, biotin, inositol, folic acid, retinol, tocopherol. At the morden biotechnologies they are used as subsidiary dietary supplements, which stimulate the process of metabolism. Chlorella and spirulina often are used for enrichment of food production. The enteroduction of elements make a good results to the yeast, improve accretion biomass, microbiological index, that influence to the barmy process.

Conclusion. So, the search biology activity things are important and could make better physiological activity yeast.

THE STUDY OF SOME SYNTHETICS DRINKS ON THE HUMAN MYCROFLORA

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Introduction. The discussions around the most prominent representatives of a number of synthetic beverages, such as: «Coca-cola», «Sprite», «Pepsi», «Fanta», constantly worried titles of medical journals, and the Internet has lots of information about adverse effects on the normal functioning of the human body of product, that's why this problem can not be ignored nor nutritionists or people who are actively involved in issues of healthy lifestyles.

Results and discussion. For example, according to Forbes magazine, is the drop in sales of «Coca-Cola Ukraine" for the fourth year in a row. At that time, as the relevance of public attention to the topic of nutrition and health improvement is growing every year. In this connection there is more questions about the use of synthetic beverages. Most often in the carbonated drinks include: water, sugar and sweeteners, acid, caffeine, benzene, and carbon dioxide. The microflora of the human is a collection of many microbiocenoses characterized by certain relationships and habitat. Gastrointestinal (GI) - a system of bodies, food processing, extract the nutrients, absorb nutrients into the blood, leading out of the body undigested. Microbiocenosis gastrointestinal tract is one of the most complex body fluids. High diversity (over 500 species) and density of microbial contamination, in which very finely balanced interaction between the protective systems of host and microbial associations. Violation of the functions of the digestive tract has a negative impact on the organism as a whole. The subject of our study were bacteria of the genus Lactobacillus, which are the normal microflora of the gastrointestinal tract. These organisms have a pronounced antagonistic activity against a broad spectrum of pathogenic and conditionally pathogenic microorganisms, displacing them from the intestine, contribute to the restoration of disturbed microflora. The properties to improve the absorption of iron, calcium, releasing large amounts of immunoglobulins. Normalize and maintain a high level of hemoglobin and metabolism. The foundation in the study of quantitative and qualitative development of bacteria will be the product which contains the necessary for the analysis of microorganisms. It probiotics and dairy products.

Conclusion. Since topic work directly related organisms, then the goal is: Comparison of activity Lactobacillus genus bacteria by using biotechnological knowledge indication of negative or positive change in the qualitative and quantitative composition of microorganisms despite the fact that the true composition of the synthetic beverages (except soda "Coca-cola"), is a commercial mystery.

ANTIVIRAL ACTIVITY OF CERIUM OXIDE NANOPARTICLES ON TOBACCO MOSAIC VIRUS MODEL

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Introduction. Nanocrystalline ceria dioxide (NCD) is very interesting material in terms of the possibilities of its application in biomedicine due to its physical and chemical properties. In addition to antioxidant, UV-shielding, antibacterial, antifungal and several other properties, it shows antiviral activity against animals and humans viruses, in particular against HSV-2 in vivo (model of guinea pig genital herpes) and in vitro (renal rabbit cell RK-13). In this connection, it is a topical question to determine its activity against plant viruses.

Aim. Purpose of work – investigation of the antiviral activity of cerium dioxide nanoparticles in conditions of plant viral infection caused by tobacco mosaic virus (TMV).

Materials and methods. The research of the antiviral activity of cerium dioxide nanoparticles was performed using the plants *Datura stramonium* and *Nicotiana tabacum,* in which TMV causes the local lesions in the form of necrosis. From plants there were selected clean leaves without deformation and loss of pigmentation for the experiment. The leaves were infected by TMV by mechanical inoculation using silicon carbide. After the infection the leaves were cut in stencil and cut in half through the veins. One segment of the leaf was placed in a petri dish with 3 ml of distilled water (positive control), and second (experiment) – in 3 mL of 10 mM sol NCD (synthesized by A. B. Shcherbakov, Zabolotny Institute of Microbiology and Virology NAS of Ukraine, Kyiv, Ukraine). The development of cytopathic action of the virus (necrotic formation) was observed on the 4th day of incubation the leaves in the cups at room temperature.

Results and discussion. TMV in both of the model plants caused local reactions in the form of necrosis. Virus symptoms were reduced in the segment of the leaves which after infection were placed in the NCD sol: inhibition of viral necrosis of 85.43% and 50% respectively for *D. stramonium* and *N. tabacum*. The results suggest that the NCD able to penetrate into the TMV-infected leaf segment through the vascular system of plants and inhibit reproduction of the virus.

Conclusions. The application of NCD in model plants *D. stramonium* and *N. tabacum*, infected with highly pathogenic TMV accompanied by inhibition the development of specific viral necrotic lesions, that indicates its antiphytoviral activity.

ABOUT THE MAINTENANCE IN THE ACTIVE STATE OF HIGH-PRODUCTIVE VARIANT OF EREMOTHECIUM ASHBYII

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Introduction. Maintaining of a collection of producers of essential oil is an important component for their preservation in an active state, and a further introduction to the biotechnology. To maintain the viability and activity of the microorganisms it is necessary, to crop on different agarized culture media and to do the periodic subcultures on fresh media.

Aim. The aim of this study is the search of opportunities to sustain on nutrient media of different composition of high-productive variant Eremothecium ashbyi.

Materials and methods. The object of the study is a highly variant 36 O-b, received by multi-step selection of the strain Eremothecium ashbyi Guill. VKPM F-36 belongs to the genus Eremothecium , the family Eremotheciaceae Kurtzman 1995. The culture was maintained on agar media beveled: soy sucrose (g / l sucrose - 10.0; soy flour - 40.0; agar - 20.0) Saburo (g / l: glucose - 40.0; peptone - 10.0; agar - 18,0-20,0) and potato-glucose (dextrose) (g / l: potatoes - 200.0; glucose (dextrose) - 20.0; agar - 30.0; pH 6.0). Seeds were grown by the deep way in a liquid glucose-peptone medium with the yeast extract (g / l: glucose - 7.5; peptone - 4.0; yeast extract - 1.2, sodium succinate – 2.0; K_2HPO_4 - 0 5; inositol - 0.14, pH 6.5) by the continuous shaking at 240 oscillations per minute for 51 hours at 28 ° C. Microscopic analysis of methylene blue microslides was conducted , the microslides were fixed with Carnoy's solution, using MiniMed-5321 microscope (XSZ-2107) at 10-, 40-, 100-fold magnification.

Results. In the experiment it was noted that by the growing of seed materials for subsequent fermentation the culture growth from the potato dextrose agar medium was much more active and more significant than from Sabouro medium and soy-sucrose agar. The inoculum was a liquid with the mycelial mass containing residual nutrients and metabolic products, including essential oils, riboflavin, and others. Moreover, the culture liquid obtained by mikomateriala taken from a potato dextrose agar was more bright orange colour, the mycelial mass was abundant, fine, flaky and had a floral aroma. It should be noted that the increase of the biomass began after a day compared to other media. The inoculum was obtained from the culture on soya-sucrose agar was saturated bright yellow, there was a large number of

the fungic mass and the strong floral aroma. The culture medium in which the seeding of the variant 36 O-b from the Saburo agar was carried out , was less than the saturated color of a lemon at the end of cultivation, but the mycelial mass was thick and the smell was also significant.

To determine the quality and the condition of the culture it is necessary to conduct the microscopic analysis. Dichotomous branching mycelium, its coloration caused by the presence of riboflavin, sporangia, ascospores have the diagnostic significance. By analyzing of inoculum 36 O-b, obtained from the potato dextrose agar, the dichotomous branching of mycelium, significantly thicker vacuolated hyphae , whole and broken polysporous single sporangia and ascospores of curved shape with tapering ends were observed. Microscopic picture of inoculum obtained from the Saburo agar, is characterized by a thin hyphae having thickening and numerous ascospores of curved shape, diverging from the disclosed asci. By microscopic analysis of the inoculum produced from the soy-sucrose agar the thin and considerably thickened hyphae, polysporous sporangia and separated numerous ascospores of curved shape with tapered ends were observed .

Conclusions. In the course of the study it was found that the cultures 36 O-b, maintained on potato dextrose agar and soy-sucrose agar, remain more activity during prolonged storage than culture on Saburo agar ; by growing of the seed the culture 36 O-b accumulates more actively the fungic mass, has more vivid coloring and more significant sweet floral aroma. Mycelium of producer obtained by subculture in the seed medium from the potato-dextrose agar developed at the fastest pace; at the least pace- from the Saburo agar, which was confirmed by microscopic analysis of the inoculum.

Thus, the study and research of the storage medium for the culture Eremothecium is an important and integral part of its rational use in biotechnological processes for obtaining of aromaproducts.

THE STUDY OF SOME MODERN DOMESTIC ANTIMICROBIAL DRUGS

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Introduction. Throughout history, mankind has been fighting tirelessly with microorganisms that cause infectious diseases. Despite the fact that in recent years medicine has achieved great results in the studies and the impact on the pathogen, and is equipped with a large number of antimicrobial drugs, infection with which existing drugs fail or are not effective progress with increasing speed. Now for Pharmacology most problematic area is the search for effective and safe antimicrobial drugs, modern antimicrobials occupy a leading position in the treatment of infectious diseases. They are used in 70-100% of cases with various infectious and inflammatory diseases in patients with surgery, gynecology.

Results and discussion. Every year the world's infections killed 17 million people. This suggests that existing member antimicrobial drugs are not effective enough. Difficulties treatment of infectious pathologies and inefficiency caused by drugs:

1. Variety of forms of biological agents;
2. The constant emergence of MDR;
3. The appearance of new types of dangerous pathogens;
4. The increase of allergic reactions in the application of the majority of antimicrobial agents;
5. Having a strong toxic effect on human organs and systems.

Antimicrobial resistance (AMR), including antibiotic resistance, is the resistance of a microbe to an antimicrobial medication that used to be effective in treating or preventing an infection caused by that microbe.

The cause of antimicrobial resistant strains is that they are not controlled. It is not always justified application both in veterinary and in human medicine.

All these factors determine the need for constant monitoring of existing medicines and the creation of new ones with improved pharmacokinetic properties and to reduce the toxicity.

Conclusion. Based on these data, research in order to study the stability of various microorganisms to antibacterial drugs of Ukrainian origin are conducted at the Department of Biotechnology.

DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF FERMENTED BEVERAGES SUCH AS A «BREW»

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Introduction. Brew or kvass is a traditional Slavic sour drink that is prepared based on the fermentation of flour and malt (wheat, barley) or from dry rye bread, sometimes with the addition of fragrant herbs, honey. Well-known expert on national cuisines V.V.Pohlebkin successfully described the brew as a "living product of living systems". There are several varieties of kvass: bread, hash, fruit, milk, honey.

There are a variety of fruit and berry varieties of kvass: pear, cranberry, cherry, lemon and others. Brews of this kind are common or bread kvass, juice or flavored jam of these fruits and berries, or they are prepared directly from the juice of berries, without the addition of bread or flour. Preventive action of brew is manifested in the regulation of the gastrointestinal tract and the cardiovascular system, improve metabolism. The use of kvass prevents to development of pathogens, raises the tone of the body.

Currently, set of synthetic substitutes of brew is also available for the industry (so-called "kvass drinks"). They usually consist of soda (a solution of carbon dioxide), sweeteners, flavoring - simulated taste of kvass, and sold in plastic bottles.

Results and discussion. Experimental works at testing the technology of different varieties of brew and studying of their properties are carried out at the department of biotechnology NUPh.

The microbiological composition, physico-chemical and medical-prophylactic properties of brew are studied experimentally.

The study was conducted in two stages: the first was the preparation of the drink, the second was the study of its properties: determination of pH (acidity), organoleptic, chemical and microbiological composition. During studying of the organoleptic properties it was found: brew is a drink of dark brown color with a slight opalescence and sediment natural raw materials, the drink has a pleasant aroma of rye bread and sweet-sour taste.

Conclusion. Investigation of microbiological composition is showed the presence of brew yeast cultures, belonging to the species Saccharomyces minor (M race), Saccharomyces mines cesevisiae kvass, and lactic acid bacteria belonging to the species Lactobasillus fermenti. Acidity of beverage is ranged from 1.5 to 7 units due to the accumulation in the drink various organic acids (oxalic, tartaric, formic, malic, citric, succinic, lactic and acetic), in the process of microorganisms. Works to the study of the different varieties of brew will be continued due to their actuality.

THE INFLUENCE OF THE GENES AT THE RHYTHM OR LIFE

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Introduction. The theme of "the influence of genes on the rhythm of life" interesting study of topical scientific issues such as circadian rhythms, sleep, aging, sleep quality, depending on the person's age and the influence of sleep on the body's health.

Aim. The dependence of the amount of sleep and wakefulness, depending on the person's age. To study the properties of the suprachiasmatic nucleus of the hypothalamus. To determine what diseases may occur due to a chronic lack of sleep and elaborate precautions.

Materials and methods. Theoretical materials. Statistically processed reports of experimental studies.

Results and discussion. It was found that with age, the person feels hot flashes vivacity much less than in his youth. It is caused by degeneration of neurons in the suprachiasmatic nucleus of the hypothalamus and the change in the structure of the locus coeruleus (locus coeruleus, LC) – the region of the brain stem. The suprachiasmatic nucleus is the main regulator of circadian rhythms, influences the blue nucleus and cerebral cortex, from which is already dependent on human performance. For this reason, older people are more difficult to tolerate the forced omission of sleep or changing sleep patterns. But despite this, the feeling of sleepiness in the elderly does not differ much from the young. The circadian rhythm can be a kind of "counter" days due to the fact that in a dream observed gene expression that never manifest expression in the waking state of the organism. Statistically it determined that people, who sleep less than 6 hours of sleep or more than 10 hours a day for 2-14 years, fall into the zone of risk of diabetes of the second type. Over 1 year in people chronically enough sleep may develop metabolic syndrome, impaired glucose tolerance. In men, frequent awakenings, and shorter sleep may be a sign of diabetes.

Conclusions. Identified side effects of sleep disorders. Determine the effects of chronic sleep deprivation. Investigations into age groups shows that older people less awake, but do not become more drowsy except in patients with the syndrome of senile drowsiness. The mechanism of the nervous regulation of sleep and how sleep affects the condition of the body at different ages. It is proved that the dream is too long or chronic sleep deprivation can cause the development of diabetes of the second type.

THE PHARMACOGNOSTIC AND MICROBIOLOGICAL ANALYSIS OF RUBUS IDAEUS LEAVES

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Introduction. Everyone knows the beneficial properties of raspberry. It is an indispensable source of vitamins. At this time, the healing properties of its fruits are sufficiently studied, but now we need to pay attention to its leaves as not less significant useful substances.

Today *Rubus idaeus* leaves are a promising source of a large amount of useful substances for the medicinal preparations manufacture, fermented tea and infusions., *Rubus idaeus* is a popular plant and grows in almost every front garden in Ukraine.

The **aim** of our work is to identify useful and therapeutic properties of Rubus idaeus leaves by the **pharmacognostic** and microbiological analysis.

Results and discussion. *Rubus idaeus* leaves are alternate, lower leaves are pinnate, with 5-7 leaflets on petioles, upper leaves are trifoliate with broad firmly attached to the petiole stipules, the upper side is darker than the bottom, where it is pannose. *Rubus idaeus* leaves have a wealth of chemical composition include salicylic acid, flavonoids , coumarins, ascorbic acid, tannins, polysaccharides.

Rubus idaeus is a perennial branched shrub. It is used in popular medicine and traditional medicine. It is gentle and safe drug, its leaves are commonly used for hemorrhoids, colds, as an antipyretic and diaphoretic drug. Flavonoids as a part of the leaf exhibit hemostatic properties. *Rubus idaeus* leaves have strengthens and immunostimulatory effects., Raspberry tea is traditionally used as a female tonic to relieve menstrual pain. The vitamin tea is especially popular.

Raspberry leaves are harvested during its flowering (May - June), because the maximum number of stored nutrients are in the leaves in this period.

The only green leaves with no signs of disease and injury are suitable to collect. When collecting raw materials it is not recommended to break and trample down shrubs, especially its annual shoots.

Conclusions. In the research process we identified pharmacological and microbiological properties of plant material, as well as aqueous and alcoholic extracts made from *Rubus idaeus* such as:

- quality parameters - the identity, purity, goodness;
- macro- and microscopic properties;
- a numerical and quantitative of the active ingredients markers;
- microbiological purity;
- antimicrobial activity.

STUDYING THE PROPERTIES OF THE MICROBIAL CONSORTIUM "KOMBUCHA" AND CREATION NEW PRODUCTS ON THEIR BASIS

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Introduction. Modern human is exposed to stress and environmental hazards, so the problem of a balanced diet based on functional foods and soft drinks is very relevant. Widely publicized imported products can be substituted by creating original recipes non-alcoholic drinks based on *Kombucha*.

The **aim** of this work is to develop cultivation technologies *Kombucha* with the addition of herbal extracts and fruit juices.

Results and discussion. *Kombucha* (*Medusomyces gisevi*) is a consortium of symbiotic yeast and acetobacters. *Medusomyces gisevi* consists of the microorganisms: yeasts (*Saccharomyces cerevisiae, Brettanomyces bruxellensis, Candida stellata*, etc.) and acetobacters (*Acetobacter xylinum, Gluconobacter oxydans*, etc.). Strains of microorganisms which constitute "mushroom body" can vary depending on the place of origin, and culture conditions. Morphologically *Kombucha* is a mucous amorphous film, floating on the surface of the liquid nutrient medium (sweet tea, juice).

From the biochemical side, yeast ferment sugar with the formation of ethanol and carbon dioxide, and bacteria oxidize ethanol to acetic acid, and then to carbon dioxide and water. The culture fluid (usually 4-9% sugar solution in the infusion of black tea) under the action of enzymes *Kombucha* within 7-10 days turns into a sour-sweet carbonated drink - "tea kvass." Infusion *Kombucha* contains gluconic, citric, lactic, acetic, malic acids, enzymes, ethanol, and vitamin B, vitamin C and PP, caffeine and other physiologically active substances. The main source of metabolic power for the cultivation of tea fungus is black or green tea with sugar. Aromatic, tannic components contained in the tea infusion, hardly used symbiotic microorganisms Kombucha. Since the tea infusion is a source of biologically active compounds, it plays an important role in the biosynthesis and influences meduzomitseta antimicrobial properties infusion. Soft drinks based on meduzomitset have antioxidant and tonic properties. Black or green tea and sucrose are the main source of metabolic power for cultivation meduzomitset. Symbiotic microorganisms Kombucha didn't consume aromatic, tannic components contained in the tea infusion. Since the tea infusion is a source of biologically active compounds, it plays an important role in the biosynthesis of *Kombucha* and contributes to the antimicrobial properties of infusion.

Cultivation temperature (20-25 °C), light and other environmental factors affect the growth of *Kombucha*. Interestingly, the film *Zoogloea* (symbiotic culture consisting of *Acetobacter xylinum* and yeast) formed on the sixth day of storage at 22-25 ° C in the presence of a preservative such as sodium benzoate and sorbic acid. *Kombucha* adapts to the power supply flexibly. Usually *Kombucha* is grown in non-sterile home environment, so that's why there is a possibility of charging a liquid culture of pathogenic microflora. Meantime, the risk of serious infection is small, since *Kombucha* developed a protective mechanism (pH ≈ 3, the presence of antibiotic compounds, etc.). To increase the range of drinks as aromatic raw materials for the production of a number of the original drinks with the tonic effect used extracts of wild rose, St. John's wort, lemon balm, lemon peel, blackcurrant, and fruit juice concentrates (apple, orange, cherry, blackcurrant). When we chose the flavor components for the development of functional soft drinks we were accounting for "the principle of compatibility of nutrients".

During the organoleptic studies we determined the optimal ratio of components in fermented beverages. We also developed 7 original recipes drinks on *Kombucha* basis with the addition of the above listed aromatic raw materials:

1. *Kombucha* + the infusion of wild rose + apple concentrate;
2. *Kombucha* + the infusion of St. John's wort + apple concentrate;
3. *Kombucha* + the infusion of lemon balm + orange concentrate;
4. *Kombucha* + blackcurrant extract + blackcurrant concentrate;
5. *Kombucha* + the infusion of St. John's wort + cherry concentrate;
6. *Kombucha* + lemon peel extract + orange concentrate;
7. *Kombucha* + the infusion of lemon balm + apple concentrate.

To take into account the views of potential consumers of functional drinks based on *Kombucha* we conducted tasting event with a group of 20 people.

On the basis of the physic-chemical and organoleptic research as a tech for the production of soft drinks we chose the most favorite samples for the tasters. Thus, the inclusion these drinks in human diet helps protect the body against pathogens, sate vitamins B, C, D, bioflavonoids, enzymes etc. It was preferable to introduce extracts of medicinal plants and fruit juice concentrates to the soft drinks to improve the flavor and aroma characteristics.

Conclusions. Due to modern research medical industry has created medicaments based on the *Kombucha.* One of them is "*Kombuka*". This drug is made in Germany. It is a concentrate of *Kombucha,* created by vacuum distillation on the basis of fermented *Kombucha* juice (obtained by pressing the young Zoogloea) and acid. During production the preparation *Kombucha* keeps all the active substances besides ethyl alcohol and acetic acid. Alcohol is added to the juice to protect them from damage. This drug is widely used for the treatment of senile diseases.

THE STUDY OF MICROORGANISMS MORPHOLOGICAL FEATURES ON PERMANENT PREPARATIONS

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Introduction. Research of the microorganisms tinctorial properties and morphological characteristics is the first stage of their identification. For this purpose simple, complex, and differential smear preparations staining techniques followed by light microscopy are used.

Accurate identification of microorganisms is important when working with bacteria and fungi, which are producers in biotechnological production, are used in environmental bioremediation and in environmental monitoring, agriculture, energetics and also have medical value.

Aim. The aim of our work is the creation of a bacteria and fungi several species permanent smear preparations collection, which are the objects of study in the laboratory of National University of Pharmacy Department of Biotechnology.

Materials and methods. We studied the species of microorganisms *Escherichia coli, Klebsiella pneumoniae, Bacillus subtilis, Staphylococcus aureus, , Corynebacterium pseudodiphtheriticum, Mycobacterium bovis BCG, Candida albicans.*

We used the following methods – staining by methylene blue solution; Gram staining; Ziehl - Nielsen staining; bacteria inclusions staining by Raskina; capsules staining by Burri; bacterial spores staining by Peshkov; nuclear elements staining by Romanovsky.

Smears were made according to traditional methods.

To prepare permanent preparations use ready smears made from pure microorganisms cultures. Drop of polystyrene dissolved in xylene was placed over the swab and then was covered with a clean cover glass.

After polystyrene solidification the microscopy of permanent smear preparations was carried out.

Prepared permanent preparations were stored in the packages of dark paper.

Results and discussion. The genus *Escherichia* are rod-shaped, Gram-negative bacteria. *Escherichia coli* is a member of the humans and animals gastrointestinal tract microflora. Several strains which are effective probiotic that reduce inflammation in the digestive tract diseases have been derived. They are the components of medical products such as Hylak forte, Bincolum, Colibacterin and others. Some strains can cause food poisoning in humans.

The genus *Klebsiella* are straight Gram-negative bacilli. The genus of opportunistic bacteria belonging to the Enterobacteriaceae family. They form capsules that protect cells from damage and drying. Some species cause pneumonia, urogenital infections, conjunctivitis, meningitis, sepsis, intestinal infections.

The genus *Bacillus* are gram-positive, spore-forming bacillus. They can tolerate high or low temperatures and are resistant to high or low pH values. They are opportunistic bacteria that can cause food poisoning. They are used for enzymes, antibiotics, biological products of high purity, including odor enhancers and food additives production.

The genus *Staphylococcus* are coccoid Gram-positive bacteria. May cause skin disease - furuncles, acne, impetigo; and lethal diseases - pneumonia, sepsis, toxic shock.

Corynebacterium is a genus of gram-positive rod-shaped bacteria. They do not form spores and capsules. In smears their cells are located in characteristic groups, chains, a stockade. In recent years the different Corynebacterium species value in human and animal pathology significantly increased. They are isolated in pneumonia, endocarditis, septic arthritis, diseases of the genitourinary tract. Some species can infect animals that can serve as a source of human infection. Some Corynebacterium species used in biotechnology.

Mycobacterium is a genus from Mycobacteriaceae family of actinomycetes. They are Gram-positive rod-shaped bacteria, bacterial spores and capsules do not form, are acid resistant. Most species are saprophytes and opportunistic patogenes. Such species as *Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium leprae* are widely known as the causative agents of dangerous human and animal diseases.

The genus *Candida* are yeast eukaryotic microorganisms, the etiological factors of candidiasis. The disease is caused not only by the presence of Candida but by their reproduction in large quantities or more ingress pathogenic fungus strains.

Conclusions. The microorganisms permanent smear preparations collection, which are the objects of biotechnological use, are important in medicine, veterinary medicine, agriculture and other industries, which students study on disciplines such as microbiology, general biotechnology, environmental biotechnology, fundamentals biochemical engineering and other has been collected in the Department of Biotechnology of National University of Pharmacy. Our students can use his collection in the course of scientific works. The collection will be constantly replenished with new preparations of actual microbial strains, the study of which will contribute to the deepening of knowledge and skills of future biotechnologists.

COMPARATIVE CHARACTERISTIC OF ORGANOLEPTIC PROPERTIES OF RED WINES, DEPENDING ON THE REGION OF PRODUCTION

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Introduction . Red dry wines are becoming increasingly popular in the world thanks to its toning and refreshing properties, they are more valuable on the composition of the biologically active substances in comparison with the white and have a wider range of colors.

Coloring is one of the most important characteristics of red wine, because it allows evaluating its composition, age and quality. It depends on the technology, climate, soils, degree of phenolic maturity and grape varieties. Color control is required when production of both high quality wines, and with the release of mass production.

Aim . The aim of the research was to determine the physico-chemical and organoleptic parameters of red wines produced in different climatic zones and comparative analysis.

Materials and methods. Objects of research chosen were red dry wines made from the same grape varieties in the production countries, Chile, France and Ukraine in the amount of 3-x samples. For research, it was used descriptive tasting method, method of determining absorbance spectrophotometer, settlement-graphic method of color vector.

All analyses were conducted according to accepted in winemaking techniques in three repetitions.

Results and discussions. The subjects investigated wines shades of color, using descriptive method of tasting (G. G. Valujko, E. P. Scholz-Kulikov). Color picker samples included bulbous and brick tones of dark-ruby color. Measured optical characteristics of wines at these wavelengths (nm): 420, 445, 495, 520, 550, 625. Received data allowed to determine the intensity of the colors(I), which is the red color of anthocyanin and brownish-red tones, caused by condensation products of phenolic substances also defined shade of coloring (T), which tells about the age of the wine. Wine color vectors were constructed according to the optical measurements in a triple system of coordinates.

Conclusions. Studies on color defined ranges of optical characteristics of a number of wines from various regions and conducted a comparative assessment of these indicators.

TYPES OF RAW MATERIALS AND THEIR PROCESSING FOR FORMULATION OF ALBUMIN

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Introduction. Animal blood is a cheap source of natural raw material for processing of medical and veterinary drugs. It can also be used as a proteinic mineral feeding in fur farming. The high content of native proteins and bioactive substances, fair amount of iron in blood of beef cattle (BF) and pigs defines its significance as a raw material for production of wholefood that has a beneficial effect on treatment of diseases caused by iron-deficiency anemia that is suffered by the considerable part of population, especially children and women.

During industrial processing of blood of meat-producing animals, dried blood, dark and bright albumin are formulated. The short range of traditional solutions for processing and usage of blood and its fractions results in cases when the most of blood is processed solely into meat and bone meal.

Aim. The aim of our studies was the analysis of known methods of formulation of biologic drugs based on animal blood, modern regulations of blood sampling, its transportation and storage, detecting of relevant types of raw materials for formulation of albumin as well as the ways of conservation before processing.

Materials and methods. The blood of BD sampled during butchering at the private farm was chosen as the material of our studies. Experimental studies were carried out though the methods of mechanical mixing, centrifugation, filtering, drying etc. using laboratory equipment. The methods of physicochemical analysis (qualitation of proteins, titration, osmometry etc.) were used for control.

Results and discussions. Blood quantity and count differ in different animals, different sex, breed, economic use. Generic differences refer to density, content of proteins, hematoglobulin, fat etc. These differences are essentially important for blood biotechnology. The comparative study of blood count of a number of animals, the cost and availability determined the selection of blood of BD as the object of the study. To prevent blood clotting, the following anticoagulants and their combinations were used: sodium oxalate, potassium or ammonium, sodium citrate, sodium fluoride, heparin. We suggested the usage of two-component anticoagulant for stabilization of blood of beef cattle during formulation of albumin.

Conclusions. The performed theoretical and experimental studies will be used for development of technologies that will provide more complete usage of alimentary blood and its fractions for production of bright ant dark albumin, fibrin and hematogen as basic and most promising biologic drugs.

STUDY OF SPIRULINA PLATENSIS CULTIVATION CONDITIONS

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Introduction. Spirulina (Arthrospira) is a genus of cyanobacteria or blue-green algae from order Oscillatoriales. Members of the genus Arthrospira are cultivated around the world, and spirulina is traditionally harvested in Chad, of the many lakes and ponds around Lake Chad. Two species Arthrospira platensis and Arthrospira maxima are edible for human and can be used for animal feed with the commercial name "Spirulina". Spirulina is used as a food additive and independent product available in the form of tablets and powder, and also as a feed additive for breeding in fish-farming and poultry. The different Arthrospira platensis strains biomass is rich on easily digestible protein (51-71%) comprising all essential amino acids, carbohydrates, lipids, fatty acids (particularly large amount of linoleic and γ-linolenic acid), a wide range of vitamins B, the presence of β-carotene, phycocyanin, chlorophyll A, etc.

Results and discussion. There are a lot of Spirulina cultivating methods with special cultivation conditions. The medium used for the Spirulina production is a solution of mineral salts in water. This medium must provide spirulina all chemical elements, it needs. The nutrient medium pH factor should be between 8 and 11. The medium temperature has a direct impact on the Spirulina growth rate. Noticeable Spirulina growth begins at a temperature above 20 °C and at it reaches maximum at 35-37 °C. The sharp changes in temperature reduce Spirulina productivity. It is important, at least from time to time (2-4 times a day) to stir spirulina. Excessive agitation may damage spirulina causing the appearance of foam. The emergence of direct options cultivators creates certain difficulties in the biomass process associated with the purity algological culture establishment, the filterability of the culture fluid deterioration. Greenhouses industrial spirulina cultivation use a photosynthetic units as close as possible to the heat and sun. Grown Spirulina is washed, filtered and dried at 65 °C. The advantage of the closed type spirulina cultivation is the possibility of preserving pure cultures, high productivity algal strains, production automation. Conducted numerous studies indicate that the capacitive photobioreactors use for the industrial-type installations have the economic profitability.

Conclusion. In summary it can be said that Arthrospira platensis cultivation conditions and biomass production further study will allow solving some contemporary problems of man and his environment as a whole.

IMPACT OF FOOD ADDITIVES ON IMPROVING QALITY OF GOAT PASTES

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Introduction. In recent years, the countries of the world and Ukraine increased production volumes of goat milk. However, the number of technologies developed by its processing in fermented milk products on an industrial basis is insignificant.

The aim of the study: to develop ways to improve the organoleptic properties (taste, smell, texture and color) sour paste of functionality of goat milk with the addition of grain by adding additives (β - carotene, titanium dioxide and Elamin).

The main material research. To achieve the above-mentioned objectives in the department of technology of processing and standardization of animal products at Kharkiv State Veterinary Academy. It was made 4 parties of goats paste.

Production technology provides additional molding paste cottage cheese with grain additive to (57 ± 2)% moisture.

As a control (C) we took paste without making additions to it. In the production of pilot lots D2, D3 and D4 were made additives such as: β - carotene and a number of Elamin, respectively 0.04 - 0.05 each and 0.01 - 0.02 weight%. titanium dioxide.

Results and discussion. The table shows data of organoleptic changes introduced under the influence of imposed to dairy goats graze food additives.

Options for changing organoleptic characteristics paste dairy

Indicators of goats paste	Research results		
	Taste and smell	Consistence	Colour
Control	Do not expressed	Soft	White with grey shade
D1. With Elamin	Refreshing	Grainy	With green shade

D2. with β - carotene	Expressed milk	As dense	White yellowish
D3. with titanium dioxide	Mild cheese	Grainy	White

From the data table shows that under the influence of Elamin goat paste was improved taste and smell, appearance it refreshing flavor and smell and greenish hue. Using rational dose β- carotene contributed manifestation of it as sour milk taste and smell, and color change from gray to attractive - white with a yellowish tint. With this addition of titanium dioxide contributed to the appearance of it white color instead of grey shades compared to controls.

Conclusions:

1. All food additives contributed to the elimination of grey shades in goat paste, which is considered a defect.

2. Taste and smell, research product versions has improved through the use of food additives as Elamin and β - carotene. However, under the influence of titanium dioxide substantially improved organoleptic characteristics paste did not happen.

3. Enrichment paste food additives such as Elamin and β - carotene, enable it to carry product functionality. This suggests the possibility of including paste enriched food supplements to the diet of the population of Ukraine.

THE STUDY OF MICROFLORA OF KOUMISS AND ITS ANTIMICROBIAL PROPERTIES

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Introduction. Today the increase in the tendency of people to a healthy lifestyle is observed; the consumption of high-quality food is one of the constituents of this tendency. The development of composition and technology of functional products is carried out at the department of biotechnology of NUPh, the non-traditional for our region dairy drink – koumiss is interest. Koumiss is obtained by fermentation of milk with lactic acid bacteria and yeast that synthesize vitamins C and B to form an alcohol, carbon dioxide actively. It is known that the mare has pronounced healing properties, antimicrobial activity that is related to their content of antibiotic substances, which increase the body's resistance to infections, normalize digestion, improve the secretory activity of the gastro - intestinal tract heals and has a prophylactic effect in diseases of the respiratory tract. Drink restores the human body after a serious illness. Koumiss has a positive effect on the composition and properties of blood. It increases red blood cells and white blood cells, which fight with alien microorganisms. The drink improves metabolism, improves the body's absorption of fats, proteins, carbohydrates, and is a source of the essential amino acids needed for tissue growth. The composition and technology of several kinds of koumiss beverages based on cow's milk, alcohol flora and lactic flora are developed at the department of biotechnology.

Results and discussion. This paper presents the results of studying the antimicrobial activity of the drink based on bread-yeast as an alcohol microflora and sour cream as a lactic flora. Determination of antimicrobial activity beverage is carried a conventional microbiology diffusion method in agar against such a model microorganisms: *Candida albicans*, *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and determination of antimicrobial activity was conducted on the first day of preparation (young koumiss), third and fifth days (intermediate koumiss) and seventh days (strong koumiss). We used industrial designs of kefir and biokefir as a control. The results showed that the greatest antimicrobial activity is manifested for the intermediate koumiss, so, growth inhibitory zone *E. coli* is 14 mm, *B. subtilis* - 13 mm, *S. aureus* - 14 mm, *C. albicans* - 12 mm. For strong koumiss inhibitory zone is absent; it appears only bacteriostatic effect.

Conclusion. Thus, preliminary studies showed the presence of anti-microbial effect for the new functional fermented beverage koumiss, that making it a promising for further studies.

DIAGNOSIS OF ONYCHOMYCOSIS

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Introduction. Onychomycosis is the most common cause of abnormal nails, but some diseases and nail trauma may mimic the clinical picture of onychomycosis and nail changes are mistaken for onychomycosis.

Aim. To identify the sensitivity of several diagnostic tests for onychomycosis.

Materials and methods. 25 patients with clinical manifestations of pathology nails are supervised. Patients were examined by standard methods (direct microscopy and fungal culture) and method of the polymerase chain reaction (PCR). Isolation DNA of nails was performed using phenol method, then the resulting DNA amplification was performed using punfungal primers ITS 4 and ITS 5. After the detection of the amplification reaction products is carried electrophoresis in 1.5% agarose gel in Tris-acetate buffer, 0.5 mM etydium bromide for 15 min and then analyzed by transilluminator with light with a wavelength of 310 nm. If a positive result amplicon detected a certain value and determine the species of fungus belonging

Result and discussion. The diagnosis of onychomycosis was confirmed microscopically in 14 (56%) patients. Culture fungi was obtained in 9 (37.5%) patients from 14, (5 - *Trichophyton rubrum*, 3 - *Trichophyton* mentagrophytes var interdigitale, 1 - Candida spp. The positive result was obtained in 18 patients (72%) by PCR. T. rubrum DNA was detected in 10 patients, positive reaction to panhrybkovi primers were 3, combined positive reaction to punfungal DNA primer + T. rubrum was in 5 patients. Analysis of etiological structure of onychomycosis, conducted by PCR-diagnostics and culture studies showed a significant percentage similarity of both methods for identifying pathogens and prevalence of dermatophytes. Of all the methods to identify pathological nail mycelium the cultural method was the least informative, as showed the smallest percentage of patients with onychomycosis, and the longest execution time (10-14 days). PCR method requires 24 hours to determine the type of fungus and the method of microscopy requires one hour but the kind of infectious agent is not defined.

Conclusions. The analysis of our results shows that the information content of the method of PCR in the diagnosis of onychomycosis is greater than the standard research methods: direct microscopy and fungal culture. Method PCR using pan fungal primers that specifically detect conserved regions of DNA of pathogens is the most promising species-specific and cost-effective.

THE MODERN ASPECTS OF THE LOW-ALCOHOL FERMENTED BEVERGES PRODUCTION

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Introduction. One of the major problems in currently society - satisfaction population needs for high quality of fermented beverages. Today, the consumer, buying goods, paying particular attention to the component composition of drinks, that the product contains only natural ingredients. Particular attention is given to products with therapeutic or curative properties. Development consumer market in Ukraine increases the interest of producers in the expansion of the range of beverages. One area for this is the production of low alcohol beverages with different organoleptic and physic-chemical properties. In this respect, it is of interest sidr - natural low-alcohol beverage obtained in the fermentation of apple juice to other fruit (pear, plum, grape, cranberry) with further possible saturation of carbon dioxide.

Results and discussion. Due to the high mass concentration of organic acids, phenolics, minerals (macro and micro elements) and vitamins and low particle volume of ethyl alcohol ciders are characterized by high therapeutic and prophylactic properties -diuretic, protivopodagrennymi, anti rheumatic, anti-alcoholic and derive radionuclides and heavy metals from the body. On the Ukrainian market are the following types of cider: Somersby, Cidre Royal, Cidre Royal, Royal Fruit, APPS, Zonk, CIBER. They are made of natural apple juice from these varieties apple as Antonovka ordinary, Askold, bilberry, Perry Moscow, Doneshta, and Eder, Priscilla, Rennet, etc., - by natural fermentation. This sugary drinks, with a refreshing apple flavor and a slight fruity-floral scent does not contain dyes and preservatives, the greatest demand in the hot season. Excellent quench thirst, thanks tonic properties of apples. A promising market is the emergence of cider kinds of fermented drink based on apple juice with the addition of the biologically active components of plant origin (extracts of herbs, cherry, plum and currant puree, extracts of aronia, etc.). Thus, among european consumers is Kelvish product of natural fermentation. Made of natural apple juice with no added alcohol. Only natural flavorings are used for the production of apple cider with fruit flavors. Apple cider with fruit taste (with taste of pear, black currant, cherry, raspberry, strawberry with mint and strawberry). Today declared the appearance on the market of Ukraine cider production companies APPS so flavored elderberry and lime and apricot.

Conclusion. Thus, the increase in demand for alcoholic beverages of fruit juices, determines the relevance of the development of composition and technology of the new fermented beverage based on vegetable raw materials.

DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF NEW FUNCTIONAL FOODS - KOUMISS, THANE, AYRAN

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Introduction. Scientifically proved that the most part of so-called civilization diseases, like cardiovascular, diabetes, allergies, anemia, metabolic disorders can be adjusted with special products with physiological effect - antioxidant, immunomodulating and regulatory action. Accordingly, food fortification technology by essential ingredients became so important.

Nowadays, one of the most popular group of functional food are dairy products. Everyone, who leads a healthy lifestyle knows about the benefits of dairy products. The growth of consumer interest in dairy products has been caused by bringing their positive effects on human body. For our region traditional dairy products are kefir, yogurt, fermented baked milk, sour cream. Because of the relevance of a healthy diet on the market the non-traditional for our regions dairy products on the basis of traditional cow's milk and on the basis of other types of raw mil have appeared. To new products for our market include ayran, than, koumiss and so on.

Koumiss is produced by fermenting milk with lactic acid bacteria and yeast, which synthesize vitamins C and B, alcohol, carbon dioxide, to make koumiss refreshing sparkling beverage.

Ayran is made from cow's milk with the water and salt. Sometimes goat or sheep milk are used instead of cow milk. Ayran is pruduced with *Lactobacillus bulgaricus* and *Streptococcus thermophilus* leaven. Typically ayran contains 94% of water, 1.2-1.5% of fats, 1.7% of proteins and 0.75% of the lactic acid.

Than is the dairy beverage, which is prepared with cow's or goat's milk and yeast for lactic fermentation, with an addition of salted water. The than benefit is caused by the presence of vitamins and minerals. It contains live microorganisms and have a positive effect on the stomach and intestines. It destroys unhealthy microorganisms and help with dysbiosis treatment. Moreover, this beverage improves the digestive tract and effective for constipation.

Koumiss has a strong antimicrobial activity due to the presence of antibiotic substances, produced by microorganisms during fermentation. It has a great nutritional value and can stimulate biological processes in the organism. Alcohol, carbon dioxide and lactic acid presense is activiting gastric glands and improves digestion. Antibiotic substances in koumiss increasing the organism's resistance to infection, lactic acid bacteria making a favorable intestinal microflora and depress

putrefaction which leads to the poisoning of organism. The koumiss treatment improves appetite, gastric acid secretion and absorption of food, increases the protein and fat digestibility, gained weight.

Today koumiss production technology realized with different raw of materials. Production of koumiss with mare's milk restricted by horse-breeding areas. In some regions koumiss is not produsing due to the lack of raw materials, but necessity exists.

Results and discussion. The intention of this work was developing the technology and composition of functional dairy beverage koumiss type, based on traditional for our region the raw materials and its therapeutic effects researching, specifically antimicrobial activity.

The objects of studing were laboratory samples of functional dairy beverage koumiss type, which were made according to our technology with relevant to our region ingredients: pasteurized skimmed cow's milk - the main raw milk, milk powder - proteins enriching component, dry bakery yeast - as the source of alcohol microflora, biokefir or kefir fungus - as the source of lactic acid microorganisms, honey - as carbohydrate substrate for yeast and the component, which enriched the product with healing properties.

To estimate the efficiency of fermentation process, were determined the number of yeast cells and titrated acidity. The total number of yeast cells counted in the Goryaeva chamber using an optical microscope. Titrated acidity were determined in accordance with GOST 3624-92.

The qualitative composition of the samples (the presence of lactic acid bacteria and yeast) were performed by differential diagnostic method Gram staining. The quantitative products composition (number of lactic acid bacteria and yeast cells) were performed by serial dilutions and inoculation on a solid substratum (Koch cup method).

Antimicrobial properties were studied by modified method of co-culturing with the test-strains of bacteria *Escherichia coli ATCC 25922* and *Staphylococcus aureus ATCC 25923,* which were previously grown for 24 h with the temperature (37±1) °C.

Conclusions. This research allowed to choose the components and their optimal ratio in the product composition (20% of the leaven, the ratio of lactic acid and yeast flora in the leaven is 2:1). Was choosen the most rational method of fermentation - fermentation separately. Research have shown high quantum of lactic acid and yeast flora in the product with its rational ratio and high antimicrobial effect against *E. coli* and *S. Aureus*. It shows potential therapeutic effect of the product and allows to recommend it as the microflora recovery remedy for human with infectious and inflammatory diseases of the gastrointestinal tract.

MICROBIOLOGICAL ANALYSIS OF SURFACE WATER

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Introduction. Surface waters are the waters that flow or collect on the surface of the earth. The surface waters include seas, lakes, rivers, marshes and other watercourses and ponds.

The main factors of surface water pollution include: discharge into waterways of untreated sewage, pesticides wash heavy rainfall, gases emissions, leakage of oil and oil products.

In modern conditions the danger of such epidemic diseases as cholera, typhoid, dysentery, etc increases. The indicators of water epidemic safety include sanitary-microbiological and sanitary-parasitological and sanitary-chemical indicators of water pollution.

Aim. To determine the microbiological purity of the surface reservoirs water on the territory of Kharkiv region.

Materials and methods. Water samples from the river Kharkiv was made twice with an interval of 14 days.

Water analysis was conducted in accordance with the regulations. The degree of bacteriological contamination of water was determined by the number of bacteria contained in 1 cm^3 of water. The total microbial count was determined as total number of colonies growing for 24 h at 37 °C by sowing 1 cm^3 of water on 1.5% agar plate. According to sanitary rules and norms the total microbial count for open water is <=500 colony-forming units/100 cm^3, the thermotolerant coliforms count is <=100 colony-forming units/100 cm^3 and the number of coliphages is <=10 plaque-forming unit/100 cm^3.

To assess the contamination of water by pathogenic bacteria the content of Escherichia coli was determined. Bacterial contamination was measured by the coli-titer and coli-index. To the bacteria group of E. coli belong the genera Escherichia, Enterobacter, Klebsiella, Citrobacter and other members of the Enterobacteriaceae family.

Conclusions. Protection of water resources from depletion and pollution, their rational use are the most important problems that require urgent solutions. Problems of surface water epidemiological purity are very relevant for large cities. The cleaning procedure of the surface waters of the reservoir is promising for the biotechnology industry, as cleaning methods allow to increase the purity of water in reservoirs.

THE ALGAE MUSEUM SPECIMENS PREPARATION

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Introduction. The herbarium is a collection of the dried (flat) samples of the plants prepared in consent with certain rules.

The purposes and problems of herbariums are diverse. A herbarium is the main basis for works on systematization of plants. The herbarium documents structure of flora of this or that territory, region and also distribution (areas) of separate taxons. The herbarium is used for research of plants morphology, their ecological, geographical and individual variability.

Aim. The purpose of the work, which is carried out at department of biotechnology of NUPH, is preparation of museum specimens of seaweed, which are a subject of studying of discipline "Biology of biologically active agents producers".

Materials and methods. Representatives of brown algae (Phaeophyta) Division, genus Fucus and Diktyota and green algae (Chlorophyta) Division, the genus Valonia were objects of research.

Several brown and green algae biology features, their importance in nature and practical human activity were studied during the work.

Biological material have been dried up with a herbarium grid use. Each sample has been placed on an individual sheet after which it was wrapped in a paper cover. On the sample label systematic position (Division, Genus, Species), a habitat, the place of collecting, date of collecting, names of people who have collected algae and have defined it, were specified.

By means of these herbariums it is possible to compare morphology of different representatives of seaweed as well as the peculiarities of each of them.

The part of seaweed has been placed in glasswares in which the preserving solution consisting of water – 30%, alcohol – 30% and formaldehyde – 30% has been poured.

Results and discussion. Fucus vesiculosus, known by the common name bladder wrack or bladderwrack, is a brown alga which grows as a bush with lamellar dichotomizing branched parts, reaching a height of 100-150 cm. The Fucus is attached to underwater boulders and rocks, and the upper part has an appearance of freely floating lamellar segments with slices of the middle vein, containing a pair of pneumatic bubble both sides. With air bubble a alga always takes a vertical position.

A habitat of this alga is the coastal stony zone in the lower and average water layers of the Arctic and Atlantic Ocean, the Barents, Northern, White and Baltic seas. These algae are edible for humans. A Fucus provide a human body with vitamins,

amino acids, polynonsaturated fatty acids. Besides, its fucoidan component possessing antiviral, antineoplastic, immunoregulatory properties. Fucus is widely used in medicine.

It allows to rid the body of radionuclides and heavy metals. It also helps to strengthen the immune system, it helps to normalize metabolism, prevents the blood clots formation.

Dictyota dichotoma has thallus height of 10-20 cm, rough leathery, flat, branched dichotomously. Segments are 2-8 mm wide; almost uniformly wide or slightly narrowed to the apex and are parallel to each other. Dictyota attaches to the substrate with numerous rhizoids forming felt near the bottom. It grows on rocks or on other algae in the subtidal and lower intertidal zone. Dictyota habitat is the Caspian Sea, the Mediterranean Sea and the Indian, Atlantic, Pacific Oceans.

Green algae are characterized by a green color due to the predominance of chlorophyll in their cells. Green algae include the same pigments as that of higher plants (chlorophyll a and b, carotenes and xanthophylls) and almost at the same ratio. There are unicellular, colonial, and multicellular green algae. Multicellular Green algae are often filamentous, less plate-shaped. Some green algae have a non-cellular structure. Green algae is used in agriculture as fertilizers. They are eaten, some are used as indicators of water pollution. Several green algae species are lichen phycobionts.

Valonia is the green seaweed genus from Family Valoniaceae Order Cladophorales. The noncellular thallus is 5 – 15 cm large, bushy, with small rhizoids at the base. Due to the large cell size Valonia is a convenient object for experimental study of intracellular processes. It lives in the tropical and subtropical seas. It has recently become a popular inhabitant of the marine aquarium.

Results and conclusions. Herbarium is used for conduction a comparative analysis of the algae on morphological, ecological and systematic characteristics, reinforcement of theoretical knowledge of plant morphology and taxonomy. The herbarium preparations and preserved seaweed preparations can also be studied repeatedly to give new information as required.

THE DEVELOPMENT OF THE PRODUCTION TECHNOLOGIES OF BEER

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Introduction. Beer is a valuable product in the world and the third most popular after water and tea, and the most favorite alcoholic drink. Beer - is lower alcoholic drink which is obtained by alcoholic fermentation malting wort using brewer's yeast, with the addition of hop.

Results and discussion. At the Department of Biotechnology, composition and technology of preparation light beer is developed. At the first stage of the experimental researches for selection of optimal temperature conditions fermentation malt wort the experimental samples of light beer were prepared according to the following technique. The barley was washed and soaked for obtaining malt. It was growing during 3 days and process was stopped at the moment of achieve sprouts height 3 cm. After that sprouts barley was dried at a temperature of (35-40) °C for 3 days then malt was purified from sprouts and sieved. A ready malt was ground and mash was prepared. For this purpose 3 kg of malt and 5 liters of water were mixed and heated to 96 °C. The mash was boiled for 15 minutes, added 1/3 required quantity hop. Then it was heated a further 30 minutes and added second portion of hop, and 40 minutes later - remaining quantity. After that wort was cooled to (24-26) °C and filtered. Then it was transfused into mini-brewery, and yeasts were added. Because the stage of wort fermentation is decisive for the product were used is three temperature conditions: (10-12) °C, (14-16) °C and (20-25) °C within 8 days. Then the intermediate product was poured into the bottles with the addition of glucose (4 g/l) and was allowed to stand for 8 days at a temperature (8-10) °C for the carbonation. At the expiration of carbonation time the obtained samples of light beer were determined by organoleptic and physicochemical quality indicators for. Results of the studies showed that beer was with temperature mode of fermentation (10-12) °C was characterized by the expressionless, weak, unusual for a beer to sensorial characteristics and high acidity. The beer, which was obtained at (14-16) °C, had odor of malt drink, light brown color, characteristic beer taste, and on indicators of acidity and transparency meet the requirements of normative documents. Beer, which was obtained at (20-25) °C had more muddy color with bitter taste and sharp smell of alcohol.

Conclusion. Thus, optimal temperature conditions for the light beer from malt based on barley with the addition of yeast brand Nottingham is a (14-16) °C. Obtained data can be used in future for the development of composition and technology of new types of light beer.

THE RESEARCH OF THE ACTIVITY OF SOME ANTIFUNGUL DRUGS

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Introduction. In Ukraine, as elsewhere in the world in recent years increase in morbidity mycosis have observed. This contributed significantly to the social, medical and pharmacological factors. This deterioration in health education work and expand the network of services for the population rendered pools, saunas, a beauty parlor, which provided non-compliance with the relevant rules can become centers of infection, and some problems with the treatment of patients with fungal diseases from socially disadvantaged segments of the population and the use of invasive diagnostic techniques, increasing the pathologies that are often accompanied by a fungal" we infections (diabetes, cancer, HIV infection, etc.). In addition, there is a general deterioration of immunity among the population. These causes contribute to increased incidence of systemic fungal infections (cryptococcosis, histoplasmosis, parakoktsydiomikoz etc.) that the high cost of treating the underlying disease become important pharmaco-economic importance. Antifungal agents are extremely attractive pharmacotherapeutic group for manufacturers and distributors of products because some of the drugs or even individual doses allowed to sell without a prescription, that patient can buy them on their own initiative under the influence of advertising for the purpose of self. In Ukraine, nearly 100 registered trade names of antifungal drugs, and in 1999 there were 60. However, if four years ago, about 80% of its imports is, but now its share has dropped to 75%, which should be regarded as a positive structural shift in the Ukrainian pharmaceutical market. In 1999 antifungals it represented 12 domestic manufacturers and 66 foreign companies in 2002 were respectively 13 and 45.

Conclusions. In the current socio-economic environment it is important to take into account the economic availability of medicines, which should adequately correlated with the clinical and microbiological efficacy. In this regard, as desired further search of new antifungal agents given the drawbacks and side effects of existing drugs and the latest research to develop more sophisticated schemes of their application for reduction of unwanted effects on the patient as quickly as possible and achieve a therapeutic effect. It should be noted that advancements in this area relate to the emergence of new azoles. Difficult to predict their broad economic availability in the near future, so we must continue to examine the existing system antimycotics, particularly those that can be applied at superficial fungal infections, and in systemic onihomikozah effective on a broad spectrum of pathogens and have satisfactory ratio price / quality.

THE STUDY OF THE MORPHOLOGY OF LICHENS ON HERBARIUM SPECIMENS

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Introduction. There are more than 26,000 species of lichen worldwide. Lichens in forest Biogeocenoses play a protective role for trees, increase soil fertility. Also some lichens are the main food for the reindeer. Certain species are edible and are used as human food. As producers of a variety of biologically active substances lichens are used in the pharmaceutical industry, perfumery and for medicinal purposes. In Ukraine 380 species of lichens were found. They can be meet in all regions of Ukraine, usually grow on rocks or tree trunks, sometimes on the soil. The main area of lichens use in Ukraine is lichenoindication - an assessment of the atmospheric environment pollution degree, because they are not tolerate the presence of sulfur-containing gases in the atmosphere, nitrogen oxide and other pollutants.

Aim. The aim of our study was the lichen species identification and their morphology studying by a herbarium specimens collection using.

Materials and methods. Studies performed on lichens collected in different geographical regions of Ukraine and Western Europe. During lichen identification we studied the thallus morphology, fruiting bodies, substrate attached organs. For some lichens biochemical tests were performed to determine which substances are present in their thallus that is important to consider as systematic position.

Results and discussion. Objects of research were different by the thallus structure, color and size.They belonged to three different main morphological groups and the transitional forms also. The lichens morphology study could assign them to the division Ascomycota class Lecanoromycetes. We have identified lichens of the following types: crustaceous lichen - *Haematomma ventosum, Rhizocarpon geographicum;* foliose lichen *Cetraria islandica, Hypogymnia physodes, Lobaria verrucosa, Xanthoria parietina;* fruticose lichens: *Cladonia bacillaris, Cl. deformis, Cl. fimbriata, Cl. rangiferina, Usnea dasypoga;* foliated bushy-: *Pseudevernia furfuracea.* After species identification were decorated lichen herbarium specimens.

Conclusion. Collection of lichens in nature and their subsequent identification based on external, internal structure and biochemical properties, allow us to conclude pollution lichen habitat. The results can be used to environmental prediction and methods for environmental clean development. The collection of lichens herbarium specimens established at the Department of Biotechnology NUPh will be used in the educational process, in the courses of biology producers of biologically active substances, microbiology, ecobiotechnology and other.

THE SOFT MEDICINAL FORMS WITH BIOLOGICAL ACTIVE SUBSTANCES

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Introduction. The soft medicinal forms are widely used in various fields of medicine, namely, dermatology, surgery, ophthalmology, gynecology and in cosmetology. In accordance with the State Pharmacopoeia Ukraine to soft medicinal forms include ointments, creams, pastes, gels, liniments, suppositories, patches. Of particular interest are ointments and creams that are applied externally and can provide both local resorptive effect on the body as a whole. Used for the prevention and diagnosis of various diseases.

Results and discussion. Ointments are widely used for topical application, for the prevention and treatment of wounds. They consist of an ointment base and the active ingredient. Creams are dispersed system, which are emulsion "water in oil" or "oil in water". In the structure may contain medicinal substances, fats, vitamins, oils and other. Vegetable oils that are part of ointments and creams nourish and moisturize the different layers of the skin. To date, the production of soft medicinal forms on the basis of biologically active substances involved in a variety of cosmetic and pharmaceutical companies. As a raw material is used purified water, glycerin as a wetting agent, preservatives, and oils for food and enrichment with vitamins and other skin nutrients. Nowadays promising are ointments and creams with prebiotic and probiotic ingredients. Cream with probiotics universal that are suitable for all skin types and all ages. The cream has a soothing and regenerating effect. To date, there are only a cream with lysates of probiotic microorganisms. Lysate - a product that results from the splitting into fractions of bacterial cells (cell wall and its intracellular content). Lysates contain large amounts of vitamins, free amino acids, polysaccharides, peptides, also save pH level. These useful components create a suitable environment for the breeding of normal microflora on the surface of the dermis. They increase the level of regeneration and repair, deeply moisturize, improve skin tone and stimulates collagen synthesis and are used to eliminate edema. Lysates of probiotics today are an innovation among cosmetics. Since they are natural and ecological basis of their properties and positive effect on the skin and significantly improves its condition. It is known that living forms of probiotics have not yet used for the manufacture of soft medicinal forms, which is associated with the complexities of the process of their production.

Conclusion. Therefore, the production of soft medicinal forms containing live probiotic microorganisms, is relevant today.

THE DEVELOPMENT OF THE FERMENTED MILK PRODUCT WITH BIFIDOBACTERIA

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Introduction. An increase in the percentage of dysbiotic disorders of the gastrointestinal tract in children's is associated with environmental issues, stress, a regimen of a balanced diet. This problem can be solved with the use of functional food, namely, fermented milk products containing representatives of the normal microflora of humans: Lactobacillus spp., Bifidobacterium spp. Therefore, the development of composition and technology of fermented cheese, containing Bifidobacterium bifidum is important.

Results and discussion. At the Department of biotechnology is working on the selection of the optimum ratio of fermenting cultures of microorganisms for cottage cheese enriched with bifidobacteria. At the first stage of experimental investigations was prepared six samples containing milk (trade mark "Zareche", fat content - 2,5%) and probiotic starter culture microorganisms (live bacteria leaven "Cheese VIVO cultured milk", experienced manufacturer of State enterprise of Institute of food resources National Academy of Agrarian Sciences of Ukraine, and Bifidobacterium bifidum (freeze-dried preparation "Bifidumbacterin" the production of Private joint-stock company "Biopharma"). A ferment, containing 10^7 the colony-forming unit (CFU) of probiotic microorganisms in 1 ml was added in an amount of 1% relative to raw milk, the ripening was performed for 12 hours at a temperature of (37±2) °C, which determined the time of formation of clot, the degree of separation of the serum and titratable acidity. The results showed that the fastest – after 4.5 hours clot formed in the sample containing leaven without the addition of bifidumbacteria. When the content of the leaven from 13 to 53% of bifidumbacteria, time of ripening, was more than 7 hours. In samples of leavens which contained more than 55% of bifidumbacteria dense clot was not formed, and serum wasn`t separated. At the end of fermentation was determined by the number of lactic acid bacteria and the number of bifidumbacteria. Cultivation was performed in a thermostat TSO-80 at a temperature of (37±2) °C within 48 hours. The results showed that all experimental samples contain from 10^{12} to 10^{14} CFU/ ml lactic acid bacteria. Determination of bifidumbacteria has allowed to establish that the optimum ratio of fermenting cultures: "Cheese VIVO cultured milk" - (70-75) %, br - 25-30 %. This ratio allows to obtain enriched curd fermented milk containing 10^8-10^{12} CFU/ml of bifidobacteria.

Conclusion. The results will be used in production technology of enriched cottage cheese.

BIOPREPARATIONS INFLUENCE ON PLANT GROWTH AND DEVELOPMENT

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Introduction. Biological preparations (biologicals) are the preparations of biological origin, which are received due to the microbiological synthesis. They are used for introduction into plant seeds along or with organic fertilizer.

By means of biotechnology new pheromones, attractants, repellents and biologically active substances, growth regulators, antibiotics, to breed predatory and parasitic insects, phytophages that suppress harmful insects, diseases, weeds were began to receive.

It is consider that biological products are more environmentally safe, harmless to humans, animals and insects than pesticides. So them are consider safer then pesticides.

The mechanism of biological preparations action is associated with the fact that the microorganisms into the soil conquers his living space in bacteria that is already there. Microorganisms recycle the soil, doing therein nutrients "edible" plants, do not allow the roots to harmful bacteria. Useful substances produced by microorganisms faster reach the cells of the plant.

Biological preparations are used to stimulate development of the root system and plants in general, to improve the germination of seeds, strengthening of plant immunity and enhance resistance to diseases and abiotic factors, to protect from pests, for the treatment of organic waste for digestion remedies, increasing yield and soil fertility. They provide plants with nutrients required during germination. Designed for grains, beans, oilseeds and cereal crops, beets, corn, vegetables (cucumbers, tomatoes, cabbage, and others), flowers, tubers, also used for berry crops, herbs, soil.

In Ukraine there is a large spectrum of biologicals products. They are biofungicides-Field®-R, Mikosan, biocomplex®-BTU-p, the insecticides-Lepidocide®-BTU-R, Bitoxibacillin®-BTU-R, biodestruktor-Organic-balance®-R and others.

Nitrogen-fixing bacteria are in the majority of biologics. Nitrogen-fixing bacteria are belong to gram-negative bacteria from the free-living nitrogen fixers group. Representatives of this group of bacteria inhabit neutral and alkaline soils, water and are symbiotic with certain plants. They play an important role in the nitrogen cycle in nature. Nitrogen-fixing bacteria can be aerobic and anaerobic, living freely in the soil (Azotobacter, Clostridium) and living in symbiosis with plants.

The energy source for the reduction of nitrogen in aerobic bacteria is the processes of respiration, anaerobic is the processes of fermentation. In free-living nitrogen-fixing activity is influenced by the content of soil organic matter, macro and micronutrients, its acidity, temperature and humidity.

Nitrogen-fixing bacteria of the genus Azotobacter are in the majority of Biological preparations.

Members of the genus Azotobacter are bacteria living in the soil, which in the process of nitrogen fixation is able to transfer gaseous nitrogen into a soluble form for absorption plants.

Aim. The aim of our research is to study the effect of biological preparation on the germination, energy of germination of seeds and growth of tomato seedlings.

Materials and methods. We studied the universal biological preparation AZOTOPHYT® (manufacturer: PE "BTU-Center", Ukraine, Vinnitsa region, Ladyzhyn).

Treatment of seeds and seedlings was performed with a AZOTOPHYT® solution, which was prepared according to the manufacturer's recommendations.

The experiments and statistical analysis of results was conducted according to State Standard 12038-84 “Seeds of agricultural crops, methods of determination of germination”.

Results and discussion. The biopreparation AZOTOPHYT® contains cell bacteria of the species Azotobacter chroococcum as a valid base, as well as micro - and macronutrients, enzymes, amino acids, vitamins, phytohormones, antifungal substance.

Species Azotobacter chroococcum is a free living obligate aerobic bacterium. To obtain a biologics culture the producer is grown by the method of deep cultivation, in addition enter the sulphates of iron and manganese salt of molybdenum acid, pH 5.7-6.5.

As the object of research we choose the tomato Volgograd cultivar. The are a high content of carotenoids, vitamins (B1, B2, B3, B5), organic acids (folic, ascorbic, citric, malic, oxalic and others), high-molecular fat (palmitic, stearic and others), and carboxylic acids In the tomato fruit. Choline, which is present in tomatoes, helps to lower cholesterol levels in the blood, prevents fatty degeneration of the liver, strengthens the immune system, increases hemoglobin content. Tomatoes are a common vegetable crop in the industrial and private horticulture.

Conclusions. The results, obtained in the conducted experiments, can be used in the selection of biological preparations to increase the yield of vegetables and the creation of new and effective biological products for use in agriculture.

STUDY OF COSMETICS WITH BACTERIOPHAGES

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Introduction. Bacteriophages, also known as viruses that kill bacteria, are perfect antibacterial agents. They only act on "their own" microorganism, don't have any adverse events and it's not necessary to keep treatment regimen strictly when you use them. For that reason bacteriophages came in view of scientists again nowadays. Different kinds of bacteriophages are used in medicine. These are: staphylococcal, streptococcal, dysenteric multivalent, klebsiella, piobacteriophage, colibacteriophage, proteus and coliproteus bacteriophages and so on. Bacteriophages are also used in gene engineering.

The safest and "ecologically cleanest" method of controlling with microbial infections is the usage of natural regulation levers of population level also known as biological limiters. Natural biological limiter for bacteria is bacteriophages. The use of bacteriophages with narrowly-specific lytic activity at the stage of anti-inflammatory and antibiotic therapy allows not only to destroy pathogenic microorganism population (including antibiotic-resistant stain), but also improves "beneficial" normal flora bacteria development conditions.

Contemporary issues of phagotherapy are in a major focus of interest nowadays. The generalization of the accumulated data on the results of the use of phage-containing agents and close co-operation of virologists, microbiologists, practicing physicians, biotechnologists and veterinaries allows to create such agents that have no analogues in the world of microorganisms. It's also possible to use them for prevention of microbial etiology diseases by purification from opportunistic bacteria. One of such argents is Gel Sengara for make-up removal. It has bacteriophages and prebiotics in its content.

The main **aim** of the work is to show all the prospects of cosmetic products based on bacteriophages as well as objectivation of the need for biotechnology researches of cosmetics on the activity of stated bacteriophages.

Results and discussion. Currently at the Department of Biotechnology of National University of Pharmacy it being planned a research of bacteriophages used at production of cosmetics "Sengara" for its peculiarity. As an object we have chosen gel Sengara for make-up removal with bacteriophages and prebiotics in it (manufacturer is LLC "NVC Agrovetzashchita S.-P.", Russia, for request of LLC "Sengara" for PLC "Faberlic").

Conclusions. Its peculiarity is characterized by the presence or absence of bacteriophages lytic activity. The gel is being researched for the presence of mentioned above bacteriophage (Wolinella Spp., Actinovyces Spp., Actinobacillus actinomycetemcomitans, Porfiromonas gingivalis, Campylobacter Spp., Bacteroides Spp., Staphylococcus aureus, Streptococcus pyogenes, Streptococcus mutans, Pstudomonas aeruginosa, Proteus vulgaris, Klebsiella).

THE STUDY OF THE PROPERTIES OF CERTAIN TYPES OF CHEESE WITH MOLD

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Introduction. Cheese relates to high nutritional and biological value food. It is composed of proteins, lipids, carbohydrates, minerals, organic acids, vitamins, etc. Produced cheese assortments are truly various. Various types of cheese are made of cow's, sheep's, goat's milk, or its mixtures, and they differ in organoleptic characteristics, size, shape and weight. The most popular cheese is the one that is ripening with moldy mushrooms. The product appeared on Ukrainian shelves pretty much recently. To this day, the domestic manufacturers of dairy products such as TM "Dobryana", "Genatsvale", "Lazur" mastered modern technology and engaged in production of cheese with mold.

Results and discussion. Cheese with white mold. This is the smallest group, but this group particularly contains the famous Brie and Camembert. These assortments are covered with the specific white plaque, which builds up in special cellars, whose walls are covered with penicillium mold species.

Cheese with red mold. These assortments, livarot cheese and Muenster among them, are covered with the red mold that appears on the product in the process of ripening, when it is processed by special bacteria.

Cheese with greenish and blue mold. Unlike the first two groups of cheese with mold, this third group contains mold within the product, and does not cover its surface. This cheese stage is achieved through the use of special cheese cooking techniques. Mold is added to the curd with special tubes, where it brings the cheese to the desired condition successfully. The most famous cheese in this group is Roquefort cheese.

Cheese with mold is very healthy. They saturate human's body with all necessary nutrients such as calcium, protein, amino acids, and phosphoric salts; improve metabolism; have soothing and anti-stress effect, have antibacterial ingredients. Their use normalizes blood pressure, improves eyesight and skin condition, increases efficiency; it reduces the risk of cardiovascular diseases.

Keep in mind that, because mushroom mildew has the high concentration of natural antibiotic, it can disrupt the intestinal microflora, which leads to dysbacteriosis and allergic reactions. Also, it is not recommended to eat cheese delicacy to pregnant women, little children and obese people.

Conclusion. To this day, the Department of Biotechnology is conducting studies about the moldy cheese technology and its microbiological and organoleptic properties.

MANIPULATING THE PRECURSOR SUPPLY TO IMPROVE TEICOPLANIN BIOSYNTHESIS LEVELS IN *A. TEICHOMYCETICUS*

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Introduction. Glycopeptide antibiotics are one of the most important classes of antibacterial compounds. Glycopeptides are widely used in clinics as "last line of defense" drugs against multi-resistant Gram-positive pathogens. Although novel semisynthetic glycopeptide antibiotics like dalbavancyn, telavancyn and oritavancyn have successfully passed clinical trials, the main burden of medical use is imposed on "old" glycopeptides: teicoplanin and vancomycin (produced by *A. teichomyceticus* and *Amycolatopsis orientalis* respectively). In comparison to vancomycin, teicoplanin has proven better pharmacokinetics and effectiveness; however, the production level of the later in *A. teichomyceticus* is very low and unstable. Therefore, there is a considerable need in rational improvement of teicoplanin production in *A. teichomyceticus*.

All glycopeptides contain a lot of aromatic amino acids derived from tyrosine or tyrosine itself in aglicone. Such a big demand in tyrosine as a precursor of antibiotic biosynthesis is reflected in the content of glycopeptide biosynthetic clusters (GBCs): all of them contain genes that encode additional copies of the key enzymes of tyrosine biosynthesis. In particular these are the genes coding for 3-deoxy-D-arabino-heptulosonate 7-phosphate synthase (DAHPS) that catalyzes initial reaction of shikimate pathway converting erythrose 4-phosphate into 3-deoxy-D-arabino-heptulosonate 7-phosphate) and prephenate dehydrogenase (PDH), which converts arogenate into tyrosine.

Aim. Recent experiments on balhimycin producer - *A. balhimycina* have shown that cluster-encoded enzymes of tyrosine biosynthesis can be used as a valuable tool for glycopeptide biosynthesis improvement. In current work we decided to apply the same metabolic engineering approach to a producer of industrially valuable glycopeptide – teicoplanin. To this aim, construction a set of teicoplanin overproducing strains by means of precursor supply engineering, particularly by over-expressing of DAHPSs and PDH genes in *A. teichomyceticus*, was performed.

Materials and methods. All molecular cloning procedures were performed according to standard protocols. Heterologous genes, $dahp_{sec}$ and pdh_{sec}, from *A. balhimycina*, as well as *tei*24* from teicoplanin biosynthesis cluster, were subcloned

in pSETPAm integrative vector under the control of strong apramycin resistance gene promoter. The *tei*14* gene was cloned into a moderate copy number vector pKC1139 under the control of its own promoter. All obtained constructs were delivered into *A. teichomyceticus* by means of intergeneric conjugation. Teicoplanin production in recombinant strains with over-expressions of above-mentioned genes (*tei14*$^{*+}$, *tei24*$^{*+}$, *dahp*$_{sec}^{+}$, *pdh*$_{sec}^{+}$) was checked after 6 days of growth in TM1 production media by means of HPLC.

Results and discussion. The teicoplanin biosynthesis cluster contains two genes *tei14** and *tei24** that encode DAHPS and PDH, respectively. Although Tei14* and Tei24* are homologous to $DAHP_{sec}$ and PDH_{sec} encoded in balhimycin biosynthetic cluster, deeper *in silico* analysis has revealed some major differences. Tei14* belongs to Iβ subtype of DAHPS, and therefore has the structure different than $DAHP_{sec}$ (Iα DAHPS). Tei24* is an orthologue of PDH_{sec} but possesses an additional domain. This is a regulatory ACT-domain, probably involved in a negative feedback inhibition of PDH with the product of its reaction: tyrosine.

Since, different GBCs have in their disposal two types of DAHPSs, Iα and Iβ, and PDHs with ACT-domain and without, we have decided to overexpress all corresponding genes in *A. teichomyceticus* and study their effects on teicoplanin production. The strain with additional copies of the *tei*14* gene produced 5 times more teicoplanin reaching the concentrations of 400 mg/l; the amounts of teicoplanin for *A. teichomyceticus dahp*$_{sec}^{+}$ were in range of 250 mg/l. The over-expression of *pdh*$_{sec}$ had rather no impact on teicoplanin biosynthesis, resembling the situation observed in *A. balhimycina*. Surprisingly, *A. teichomyceticus tei24*$^{*+}$ strain exhibited obvious increase in teicoplanin production levels, yielding 3 times more teicoplanin than a wild type strain (up to 350 mg/l).

Conclusions. To summarize obtained data, we can conclude that GBCs have evolutionary obtained different types of DAHPSs in response to high demand of tyrosine. Despite $DAHP_{sec}$ and Tei14* belong to completely different subtypes of DAHPSs, they both positively influence glycopeptide production. The role of PDHs in the precursor supply of antibiotic biosynthesis appears to be less important: some PDHs (like PDH_{sec} from balhimycin cluster) have lost their regulatory ACT-domain and became rather nonfunctional. However, the version of PDH with ACT-domain has positive effect on the biosynthesis of teicoplanin.

TO THE CANDIDA GLABRATA IDENTIFICATION AND SUSCEPTIBILITY TO ANTIFUNGAL DRUGS DETERMINATION

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Introduction. Fungi of the genus Candida are found in the normal microflora of the mouth, vagina, gastrointestinal and urogenital tract in healthy individuals. They are opportunistic organisms. Candidiasis develops under certain conditions that contribute to the rapid multiplication of these fungi.

The Candida detecting gold standard is a microbiological method of cultivation on nutrient media (inoculation into liquid or solid Sabouraud medium). When identifying should pay attention to the C. glabrata morphological and cultural characteristics. It do not form pseudomycelium. Some strains usually form a smooth, glossy surface colonies with a soft texture. When C. glabrata is cultured on Sabouraud glucose agar with specific indicators, colonies acquire specific pink color. Also C. glabrata zymogram includes a positive trehalose reaction and negative maltose, saccharose, galactose and lactose reactions.

Results and discussion. The sensitivity of the isolated microorganisms to antimycotic drugs determination is used mainly for lack of treatment efficacy or during the transition from parenteral antifungal drugs to oral another anti-fungals (fluconazole), if the long-term Candida infections (for example Candida meningitis, endocarditis or osteomyelitis)treatment is necessary. In the treatment of Candida infections amphotericin B, fluconazole, itraconazole, ketokanozol are often used. After analyzing their minimum inhibitory concentration (MIC) it can be concluded about these medicines effectiveness. Itraconazole was the most effective (MIC 0.5-4.0 mcg/ml); Ketokanozol (MIC 1.0-4.0 mcg/ml); Amphotericin B (MIC 2.0 mcg/ml). Fluconazole (MIC 32-64 mcg/ml) was the least effective.

Nowadays, many infectious diseases are difficult to antibiotic therapy. Therefore, it is important to determine the sensitivity of microorganisms to antibiotics. Methods for determining the sensitivity of fungi and microorganisms to antibiotics and antifungal, divided into 2 groups: the diffusion and dilution methods. Now the polymerase chain reaction for the specific microbes and fungi responsible for drug resistance formation genes detection is widely used.

Conclusions. After studying the C. glabrata identification methods and its sensitivity to antimycotic preparations it can be concluded that the fungus can be identified without any costs (using glucose in the medium). For Candida glabrata infections treatment Itraconazole, Ketokanozol, Amphotericin B and Fluconazole are usually prescribed. C. glabrata showed the greatest sensitivity for Itrakanozol, and the smallest to Flucanozole.

IDENTIFICATION OF CANDIDA ALBICANS ON MORPHOLOGICAL FEATURES

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Introduction. Fungi of the genus *Candida* are commensals on human mucosal surfaces, but can become one of the most important invasive pathogens causing a variety of superficial fungal lesions forms and severe invasive fungal infections, especially in immunocompromised patients and during antibiotic treatment. Therefore, the accurate identification of *Candida* species may provide important information for the effective treatment of patients.

In recent decades the incidence of diseases caused by *C. albicans* is steadily increasing, accounting for more than 15% of the inflammatory nosology total etiological structure. In the 40-60% of disease cases remains undiagnosed or diagnosed late.

For the identification of *C. albicans* cultural, microscopic, molecular-genetic and serological methods are commonly used.

Aim. The purpose of this work is to study the various methods of yeasts isolates morphological characteristics research for their primary species identification.

Materials and methods. In experiments the museum strain of *C. albicans* and two clinical isolates that were identified during vaginal and intestinal candidiasis were used.

When studying the cultural and morphological characteristics Sabouraud medium, potato, rice and corn agar and bovine serum were used.

For the *Candida* cultures microscopic examination the native (crushed drop) and painted (by methylene blue solution) smear preparations were examined.

Results and discussion. To study the yeasts cultural properties the inoculation into liquid and solid Sabouraud medium are used. In simple nutrient media under (25-27)°C *C. albicans* form yeast cells and pseudomycelium.

The colonies are convex, shiny, creamy, opaque. In tissue *Candida* grow as yeast cells and form pseudohyphae.

Candida species differ by filamentation type (Mycotoruloides and Mycotorula) when growth on glucose-potato and rice agar: glomeruli location - small rounded clusters of yeast cells around pseudomycelia.

To growth types diagnostics the inoculation on potato agar supplemented with 1% glucose, rice and corn agar was carried out.

The germ tubes formation is a *C. albicans* invasive properties manifestation. The germ tube growth was detected by cultivating in liquid protein media (bovine serum) at 37°C for 2-4 hours.

Blastospores are the asexual reproductive cells of fungi and yeast, which produced by budding. The yeasts blastospores capable to filamentation (i.e. elongate and form a pseudomycelia). Pseudomycelia differ from the true mycelium by lack of common coat.

Detection of pseudomycelia by pathological material microscopy is important for laboratory confirmation of the pathogen yeast-like nature.

Chlamydospores are the spores of vegetative propagation of fungi, with thick (often double) cell wall. They are generated by the hyphen decay into single cells. Chlamydospores can be terminal or intercalary (in the middle of mycelial filament). This type of yeast-like fungi reproduction may also be performed by mycelium or individual cells budding.

Chlamydospores include reserve nutrients necessary for cell activity, are involve in physiological processes and play a protective function.

For the chlamydospores detection the inoculation area on the rice agar was covered with a sterile coverslip and after incubation at 25 °C for 2-5 days the microscopy was carried out.

Conclusions. The experimental results confirm the importance of the *C. albicans* primary identification based on morphological characteristics by using of inexpensive routine microbiological tests available to most laboratories for the detection of fungus increased invasiveness and pathogenicity for more effective candidiasis diagnosis.

SECTION № 6

PHYSIOLOGICAL AND BIOCHEMICAL BASIS OF ACTION OF BIOLOGICALLY ACTIVE COMPOUNDS

COMPLIANCE WITH THE KEY METABOLITES OF SOME MODERN SYNTHETIC CANNABINOIDS IN HUMANS AND LABORATORY ANIMALS

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Introduction. The drug addiction problem in Russia is particularly acute for the last few years. Some of the most popular and at the same time dangerous drugs - smoking blends (SPICE) - are widely distributed on the illicit market. There are several ways to determine whether the use of prohibited substances, but the most common is the analysis of drug metabolites in urine.

Aim. A necessary step in the identification of drug metabolites in his collection is a biological fluid of a person who took a banned substance. Thus, to identify drug and its metabolites must have poisoned and availability data bases containing information about already metabolites. Establishing the presence or absence of a matching key metabolites of PB-22 and PB-22F, determined by GC-MS, under given conditions, in humans and laboratory rats.

Materials and methods. Gas chromatograph Agilent 7890A mass spectrometer Agilent 5975C, non-polar column HP-5ms. The analysis used the urine of male rats weighing 180-250 grams, the exposed synthetic cannabimimetics PB-22 and PB-22F. When used sample preparation method of alkaline hydrolysis followed by extraction with a mixture of heptane: ethyl acetate (7: 1). As applied methylation derivatization kuprirovannym methyl iodide.

Results and discussion. An analysis results of the chromatograms could establish the presence of the main metabolites (markers) substances PB-22 PB-22F and urine laboratory animals. The mass spectra of metabolites found in the urine of animals completely coincide with mass spectra of the human metabolite, taken from the literature.

Conclusion. Availability of basic "human" synthetic cannabimimetics metabolites in the urine of laboratory animals allows us to speak about the prospects of research data for forensic purposes.

THE INFLUNENCE OF POLYPHENOL CONCENTRATES FROM GRAPES WITH STEVIA ON THE LIPID CONTENT UNDER EXPERIMENTAL DIABETES MELLITUS

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Introduction. More than 230 million people worldwide suffer from diabetes, accounting for 6% of the adult population of the world. In the present work we have studied the effect of a substance containing a complex of polyphenols of grapes vinifera and carbohydrate derivatives of stevia, on the effects of experimental diabetes in rats. The **aim** of this study was to investigate the influence of dry extract from the stevia leaves on metabolic disorders under experimental insulin resistance development in rats.

Materials and methods. DM1 ave been modeled by a single intraperitoneal injection of streptozotocin solution (STZ) in 1 M citrate buffer pH 4.5 at a dose of 55 mg / kg of a body weight. Polyphenol concentrate, containing the stevia extract (PCS) has been injected intragastrically. The content of free fatty acids (FFA) has been determined by reacting them with salts of copper diethyldithiocarbamate. The concentration of glycerides has been measured using a standard enzymatic assay. The content of cholesterol (LDL) has been determined by the standard enzymatic cholesterolxidase sets. Total lipid concentration has been determined using a standard assay – the reaction with a vanillin reagent. Statistical data processing has been carried out using the variation statistics.

Results and discussion. In our experiments it has been shown that among the animals with type 1 diabetes there is an increase in the content of AR, TAG, FFA in 1.69; 1.86; 2.1 and 1.5 times, respectively. PL content in the liver of the rats has been significantly reduced with a factor of 1.7. The injection to the animals the studying polyphenol concentrates has resulted in a significant decrease in these parameters. However, it should be noted that the injection of the investigated substances has not led to the normalization of the studied parameters. This fact seems to be playing a leading role in the fact that under DM1 the injected substances do not have a strong effect on normalizing lipid metabolism. This is evidenced by a fairly high level of triglycerides, free fatty acids and a reduced content of FFL. Similar changes have been also observed in type 2 diabetes.

Conclusions. Using PCS has prevented hyperlipidemia and reduced the hepatic parameters of lipotoxicity in a liver of the experimental animals. Thus, the studies have shown the feasibility of a combination of grape polyphenols with stevioside in the complex treatment of diabetes.

REPARATIVE ACTION OF NANOMATERIALS FROM RARE EARTH METAL FOR THE TREATMENT COMPLICATIONS OF DIABETES

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Introduction. Due to development the epidemic of diabetes worldwide grows its importance as a morbidity factor due to the development of diabetic foot syndrome. Ulcers on the foot in case of infections are the cause of disability, morbidity and even mortality. The social significance of the development of new drugs with reparative activity is to raise the effectiveness of the treatment of patients with diabetes.

In recent years, perspective as antidiabetic agents considered containing compounds of rare earth metal that can mimic the action of insulin, reduce insulin resistance, and exercise insulin-retaining activity. Therefore, using of the compounds in the form of nanoparticles makes perspective efforts to create medicines with high reparative activity. It is reasonable to study of fundamental issues - namely, correlation of biometrical parameters of nanoparticles (form-factor) and the parameters of their environment with biological activity of new compounds. In addition, full use of the advantages of nanotechnology in medicine requires an adequate assessment of dangers associated with nanomaterials, that is, the study of parameters of accumulation and distribution of nanoparticles in the body.

Aim. To development a reparative properties new innovative non-toxic compounds in form of nanomaterials for the treatment of complications of diabetes.

Materials and methods. Our experiments were carried out on outbred mice weighing 18 – 28 g that were on a standard diet of food and water according to sanitary norms. All animal studies were conducted according to international principles of the "European Convention for the Protection of vertebrate animals used for experimental and other scientific purposes" (Strasbourg, 1986) and "General ethical principles of animal research" (Ukraine, 2001). Modelling of diabetes in mice was reproduced by intraperitoneal introduction of streptozotocin at a dose of 45 mg/kg for 4 days. After 6 weeks it was carried out wounding operation. Mice were anesthetized; the dorsal skin was shaved, treated with depilatory cream and cleansed with iodine solution. Mice were kept warm during anesthesia and surgery using a heat lamp. Four full-thickness round wounds were created on the dorsal surface of the

mice. Wounds were next covered with gel of nanoparticles, basis of gel or Wundahyl for 14 days of intact and diabetic mice. The control wounds were not covered. Nanoparticles were made in Institute for Scintillation Materials of the NAS of Ukraine. Wounds were photographed on days 1, 3, 5, 8, 11, 14 days using a digital camera. A ruler was included in each image for spatial calibration. Three independent readers evaluated wounds for percent closure. The wound area was determined by Universal Desktop Ruler, measuring this area in square mm. At 0 and 14 days was measured blood glucose level. Mice were euthanized 14 days after wounding. Comparison of the results with the initial parameters of the sampling and the data of control group was made using Mann-Whitney test with the Statistica 6.0. P values ≤ 0.05 were considered statistically significant.

Results and discussion. When we evaluated the closure of full-thickness skin wounds on the dorsum of mice without diabetes, we found that the nanoparticles-treated and Wundahyl-treated wounds showed a more rapid healing of wounds relative to control. Wounds covered with nanoparticles closed earlier than Wundahyl-covered wounds, wound was smaller and less risk of infection. Wundahyl treatment displayed an increase of wound area at the first five days as compared to first day, wound healing occurs from 11 day.

Wounds heal more slowly in diabetic mice than in mice without diabetes. Wounds covered with the basis of gel were not displayed statistically significant differences with wound at 14 day of diabetic mice without treatment. Nanoparticles-treated wounds revealed more rapid wound healing and smaller wounds area as compared to control. Wundahyl treatment showed a faster healing of wounds in mice with diabetes than the closure wounds without treatment. The wounds area at 14 day observed no difference between wounds of non-diabetic mice.

Conclusions. These results indicate that Nanoparticles from rare earth metal may provide a means to improve healing of poorly healing diabetic wounds and treatment the complications of diabetes.

THE RESEARCH OF AN ANTIOXIDANT ACTION OF NEW COSMETIC MEDICINES

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Introduction. Wide distribution NSAIDs forced pay attention to the side effects of these relatively safe drugs. The most commonly found side-effects are associated with the digestive tract and the kidneys. One promising area of anti-inflammatory drugs safety problems solving is the use of remedies based on a biologically active substances basis of various plants.

The **aim** of this study was to investigate the antiexudative activity of an therapeutic cosmetic medication under the models of inflammation of rat's hind limb using different phlogogenes.

Materials and methods. As a phlogogene we have used 0.1 ml of 1% solution carrageenan, 0.1% solution of histamine and 2% of zymosan suspension, which have been administered subplantary due to hte rate of 0.1 ml per an animal weighing 180-200 g. After the phlogogene administration he rats have been applied with a remedy and cosmetic preparations of comparison to the rear limbs. The animals in the control group have been applied with some distilled water. As the comparison medications we have used the cream "Panthenol" and ointment "Vundehil". The size of a swelling has been measured in 0.5; 1; 2, 3, 4, 5 and 24 hours after the use of phlogogene with the help of oncometre.

Antiexudative activity has been calculated due to the formula and expressed as a percentage. All factual material has been processed statistically using t-criterion by Student.

Results. The analysis of the obtained data indicates that the use of the investigational cosmetic remedy, we have experienced a significant reduction in the swelling of rats' hind limbs. On the model of carrageenan edema the antiexudative activity has been equal to 45.5%, zymozan one - 42.8% histamine one - 37.5%.

Conclusions. The obtained data show that under the models of acute carrageenan, zymozan and histamine inflammations the therapeutic cosmetic remedy shows an antiexudative activity that slightly exceeds the medication of comparison. This could be due to the presence in the composition of the investigational remedy a wide range of substances that are capable of inhibiting inflammatory mediators: serotonin, histamine, bradycine, prostaglandins, leukotrienes.

COMPARISON OF THE OF GINSENG, ELEUTHEROCOCCUS AND SCHISANDRA SINGLE DOSES EFFECT ON RATS EMOTHIONAL AND BEHAVIORAL REACTIVITY

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Introduction. At present the prevalence of depressive disorders is becoming increasingly importance. According to WHO statistics this pathologies occupy one of the first places for reasons not to return to work, as well as disability. It is not only become the cause of social welfare is not the individual, but also an economic problem of the state. Thus more and more attention attract both the depression prevention methods and the most early and rapid treatment or correction of symptoms of the disease. And one of the most promising directions of this problem is the adaptogens usage for mono correction or for their use in the complex treatment of the disease. In any case, for the most effective and important adaptogens application is understanding of the relationship between their stimulating and toning effects for the possibility of adaptogen selection or justified its change in the course of therapy.

Aim. Compare the stimulating effect of Ginseng, Eleutherococcus and Schisandra on emotional and behavioral reactivity in rats.

Materials and methods. The experimental study was performed on the pre-selected white rats (170-210g, 6 months, male). Rats were divided into 4 groups. 1) control; 2) given Ginseng; 3) given Eleutherococcus; 4) given Schisandra; (The dose calculated in terms of a therapeutic dose for humans by a factor of recalculation doses Y.V. Rybolovlev). The calculated doses were administered intragastrically in 1 ml of water. The control group received the appropriate amount of water. The final results obtained in the "open field" tests. The test took place one hour after drug administration.

Results and discussion. According to the test results, the impact of these adaptogens on the emotional reactivity is statistically the same. It revealed a small feature of Ginseng, which was a little less inclined to locomotor activity, while maintaining the cognitive activity just above the level of Eleutherococcus and Schisandra. But the pattern is not confirmed statistically, the difference was within the margin of error.

Conclusions. Thus, in the context of our experiment differ stimulating action of Eleutherococcus, ginseng and lemongrass recommended therapeutic doses are not found. However, this does not contradict the possible differences in the mechanism of its implementation. To clarify this aspect is necessary in the course of carrying out further studies of EEG.

CHANGES IN EXTRACELLULAR LIPID METABOLISM PARAMETERS UNDER EXPERIMENTAL METABOLIC SYNDROME

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Introduction. Metabolic syndrome and type 2 diabetes make up the main, the most global problems of health, and their level is increasing at an alarming rate. Hepatic lipase (HL) - lipolytic enzyme, which is involved in the regulation of plasma triglycerides level. High triglyceride levels can increase the risk of coronary heart disease. HL facilitates the TG output from the pool of the very low density lipoproteins (VLDL), and this function is controlled by the composition and structure of the particles of high-density lipoprotein (HDL). The composition of HDL regulates the "liberation" of the HL from the liver, and the structure of HDL controls the HL transportation and activation of it in the bloodstream. Changes in the HDL composition can disrupt the function of the HL by disruption the output and the activation of the enzyme. The structure of HDL could therefore affect the plasma levels of TG and risk of coronary heart disease.

Aim. The aim of present work was to investigate some correlations between activity of HL and blood lipoproteins content and composition.

Materials and methods. In our work we measured HL activity and some parameters of lipid metabolism under experimental metabolic syndrome caused by fructose-enriched high calorie diet in hamsters.

Results and discussion. It has been shown that levels of apolipoprotein B-containing lipoproteins, LDL, and chylomicrons were increased and it was connected with the atherosclerosis development. Podendotelial delay and modification of ApoB - containing lipoproteins are milestones in the initiation of atherosclerosis. In podendotelia implantation of modified lipoproteins by macrophages leads to the formation of fat cells that store excessive amounts of cholesterol ethers and subsequently to apoptosis. Deactivating the hepatic lipase hamsters that are fed according to a diet high in cholesterol, caused dyslipidemia including hypercholesterolemia, hypertriglyceridemia and increased levels nonesterefecized fatty acids. These changes were accompanied by intolerance to glucose, and hepatic inflammation of the pancreas. Moreover, that promotes deposition of monocytes and macrophages on the subendotelial layer of the artery cells. Deposition of lipids in monocytes and macrophages leads to the further development of atherosclerosis.

Conclusions. Our results indicate that dyslipidaemia caused by deficiency HL in combination with a high calorie causes atherogenic changes. Thorough understanding of these mechanisms will help to develop new therapeutic strategies.

THE STUDY OF ANTIOXIDANT PROPERTIES OF THE PLUM LEAVES EXTRACT

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Introduction. One of a topical problems of the modern pharmaceutical science is to create a new more efficient than those are being used remedies to treat diseases of the hepatobiliary system. A prospective group of substances to be studied is natural polyphenols. This is due to the fact that polyphenolic compounds exhibit a wide range of pharmacological activity and play an important role in regulating an oxidative balance in humans and animals. Taking to the account the tradition of the folk medicine to use plums, the search for medications based on the active ingredients of the fruit culture is the urgent task of the pharmaceutical science.

Aim. The test for the pharmacological activity has become the experimental study of the mentioned extract for its antioxidant properties.

Materials and methods. The study of antioxidant properties of the extract from the plums leaves in the system *in vitro* has been performed on a model of spontaneous lipid peroxidation (LPO) in a liver homogenate.

Results and discussion. Experimental data suggest the presence of the substances of the extract from the plums leaves some expressed antioxidant properties. As a result of the addition to the an incubation medium the mentioned extract in an amount of 0.5 mg per 1 g of a liver tissue, it has resulted in a reduction of TBA - active products in the studying samples to 46.5% compared to the control.

The impact of the studying substance on the flow of spontaneous oxidation by increasing its concentration in the reaction medium is characterized by a more expressive inhibition of lipid peroxidation. At a concentration of 1 mg / g of the extract from the leaves of plum has reduced the content of TBA-reagents on average by 75.6%, while the α-tocopherol at a concentration of 1 mg / g - to 56.6%. The most significant activity against lipid peroxidation inhibition the studying extract has revealed at a concentration of 2 mg / d, in which it has reduced the level of lipid peroxidation at 88.1%.

Conclusions. Thus, it has been found out that the substance of the plums leaves extract in the studied concentrations reveals a marked capacity for the inhibition of lipid peroxidation in conditions *in vitro*, and in concentrations of 1 and 2 mg / g is not inferior to the antioxidant properties of α-tocopherol.

ANTIPHYTOVIRAL ACTIVITY OF TILORONE ON DATURA STRAMONIUM INFECTED WITH TOBACCO MOSAIC VIRUS

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Introduction. The well-known antiviral agent – tilorone hydrochloride – is one of the first oral low molecular weight inducers of interferon. The tilorone's mode of antiviral action is the subject of debate since the 70-ies of the last century to the present time, but there is still no consensus on the subject. In this interferon induction is still regarded as almost the sole mechanism of action, despite the many contradictions with experimental results. It is known that plant cells do not have the interferon synthesis system, as well as receptors to interferon. That is why the research of antiviral activity of tilorone during infectious process in plant allows us to confirm or deny the existence of interferon-free antiviral activity.

Aim. The main aim of this work is the research of efficiency of tilorone usage on Datura stramonium, during the tobacco mosaic virus infection.

Materials and methods. Standardized leaves of Datura stramonium were covered with tobacco mosaic virus solution. Leaves were placed with their petioles into the tilorone hydrochloride (substances of Amixin, «Interchem», Odessa, Ukraine) solution and incubated in room conditions. Four days later the quantity of viral necrotic lesions were counted on each leaf. Antiviral efficiency of tilorone about control group leaves was evaluated. Experimental data were presented as the median and interquartile range Me [LQ-UQ], where Me – median (50% percentile), LQ – 25% percentile, UQ – 75% percentile. Evaluations were made using Microsoft Excel 2010.

Results and discussion. It is shown, that tilorone decreases the quantity of necrotic lesions on Datura stramonium leaf surface. This activity depends on dose: the higher concentration is more effective. The evaluated antiviral efficiency reaches 38% [18% – 60%] and 65% [49% – 76%] for 10 and 50 μg/ml tilorone solutions respectively.

Conclusions. The results show an antiphytoviral activity of tilorone on Datura stramonium during the tobacco mosaic virus infection which probably caused by direct influence of tilorone as intercalator on viral RNA and does not depend on activation of the missing in plants interferon system.

RESEARCH OF THE THICK EXTRACT FROM THE LEAVES OF CORYLUS AVELLANA AS FLEBOTROPIC REMEDY

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Introduction. High prevalence of varicose veins and its complications is an emerging problem in the 21st century, and it leads to an increase in disability and the cost of treatment. Varicose veins are superficial vessels in the lower extremity that are abnormally twisted, lengthened and dilated, and often associated with incompetent valves within the vein. Pharmacotherapy includes the use of phlebotropic drugs belong to several different chemical families. Some have been produced by chemical synthesis, but the majority of them are plant-derived compounds, that represents various flavonoids and their combinations. Nowadays it's important to search for the new plant-derived compounds that can adjust as much as possible spectrum of venous disorders, and that would be accessible to a wide range of consumers. The promising substance for pharmacological study as phlebotropic remedy is Corylus avellana, which according to the literature, is used in folk medicine for varicose ulcers, capillary hemorrhage and contains in its structure: flavonoids (myricetin, quercetin, kaempferol, afzelin). It is widely known that the hallmark of all bioflavonoids are capillary protective effects and decrease of vascular permeability, which makes anti-inflammatory and anti-edema effects, reduction in venous congestion of the capillaries, improvement of the venous circulation. However, in the pharmaceutical market of Ukraine there are no medications on the basis of Corylus avellana, indicating the pharmacological studies feasibility of the medicinal raw materials.

Aim. So, the object of our research has been extract from the leaves of Corylus avellana at a dose of 60 mg/kg obtained at the Department of Chemistry of Natural Compounds at the National Pharmaceutical University led by professor Khvorost O. P. Whereas venous diseases the development of inflammation is accompanied by venous wall structure disorder and increases its permeability that leads to edema and venous congestion, the next goal of our research has been to study the thick extract from the leaves of Corylus avellana on the course of inflammation in venous stasis of a rat's tail to confirm the prospects of studying Corylus avellana as phlebotropic remedy.

Materials and methods. Venous stasis at the tail has been caused by the occlusion of an overlay alloy on the base of the tail for 3 hours to load a metal weight. At the same time the permeability of blood vessels remains the same, but

by 2/3 venous outflow has been hampered from the tail. As a result, developing venostaz accompanied by transsidative edema. On the development of edema we have figured out due to the increase of the volume of the tail, which has been measured in the dynamics within 3 hours after the imposition of ligatures and after 1, 2 and 24 hours after removal of ligature. To assess the effectiveness of the integrated samples in this condition the expected rate of an antiexudative activity, measured by the degree of reduction of edema in the experimental animals, has been compared with the control and expressed as a percentage. Statistical data processing has been carried out using the software package Statistica 6.0. Statistical analysis has been performed using Newman-Keylsa criterion for significance level $P < 0.05$.

Results and discussion. It has been determined that occlusion, which has been imposed for 3 hours at the base of the tail, reduces the resistance of capillaries and causes the development of edema. It has been proved that the antiexudative activity of the extract for three hours of the experiment has been 47.8%, 28.5% and 16.2% respectively. Eskuvit (the comparator tablets) within the first hour after the imposition of ligatures has also reduced the volume of the tail, but slightly inferior to the effect of the Corylus avellana extract treatment group from the leaves. In a second experiment the activity of Eskuvita has been almost at the level of the treatment group of the investigated extract. In the third hour the occlusion of the tail and an hour after the removal of ligature influenced prototypes tail volume has slightly decreased, but not significantly due to the group of control animal pathology. Two hours after removing the tail the ligation volume in the animals, which have been treated with the investigational extracts and tablets Eskuvit, has decreased and an antiexudative activity has amounted to 66.7% and 61.0% respectively. A day later in the control animals and the animals treated with Eskuvit have remained negligible swellings, and in the group of the Corylus avellana extract treatment from the swelling has completely gone.

Conclusions. Thus, the thick extract from the leaves of Corylus avellana at a dose of 60 mg/kg has a pronounced veinprotective activity on the model of venous stasis in the rat's tail. In some moments the extract is more active than the comparator Eskuvit. That is all confirms the prospects of further study of the extract as phlebotropic remedy.

ESTROGENES ALLEVIATE MITOCHONDRIAL DYSFUNCTION IN THE HEART OF OVARIECTOMISED RATS WITH METABOLIC SYNDROME

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Introduction. It is believed that premenopausal females have a reduced incidence of cardiovascular disease. Much of this protection is attributed to beneficial effects of estrogen on the lipid profile and endothelial cell function, but recent data have suggested that estrogen also can protect cardiomyocytes and mitochondria are a major target of cardioprotective signaling.

Aim. To assess the effects of 17β-estradiol (E_2) on mitochondrial respiratory chain activity and oxidative status in the heart of ovariectomised rats with fructose-induced insulin resistance.

Materials and methods. Female Wistar rats were divided into four groups: control intact rats (C, n=8), ovariectomised rats fed on a regular diet (OVX, n=8), OVX rats which had free access to 250 g/L solutions of fructose for 8 weeks (OVX+HFD, n=8), and OVX rats treated with E_2 (20 μg/kg/day per os) during 2 months of HFD feeding (OVX+HFD+E_2). Mitochondria were isolated by differential centrifugation from the hearts of rats. Oxygen consumption rate was measured polarographically at 37ºC using a Clark-type oxygen electrode with either glutamate/malate or succinate as energy substrates of Complex I or II, respectively. Levels of lipid hydroperoxides, reduced glutathione (GSH), superoxide dismutase (Mn-SOD) and cytochrome c oxidase activity were determined in mitochondrial preparations.

Results and discussion. Respiration studies on isolated heart mitochondria revealed that estrogen deficiency decreased the respiratory control index (RCI; state 3/state 4) for Complexes I and II by 26 % and 34%, respectively, and cytochrome c oxidase activity compared to intact control. HFD feeding induced a decrease of RCI for Complex I in OVX animals by44%, but did not significantly affect succinate oxidation (Complex II) in the state 3 and the state 4 of respiration. Administration of E_2 increased RCI for Complex I, normalised the ratio of state 3 to state 4 respiration at Complex II and cytochrome c oxidase activity. In addition, E_2 provided also 50% reduction in lipid hydroperoxides contents, enhanced Mn-SOD activity and normalised GSH level in heart mitochondria of ovariectomised rats with fructose-induced insulin resistance.

Conclusion. These data demonstrate 17β-estradiol replacement inhibited the development of mitochondrial dysfunction and oxidative stress in the heart of ovariectomised rats with fructose-induced insulin resistance.

APPLICATION OF INDIRECT IMMUNOFLUORESCENCE REACTION FOR DIAGNOSIS OF BABESIOSIS

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Introduction. Babesiosis as a relatively new and little-studied present-day haemoparasitic infection requires use of innovative methods of diagnosis, where the leading place is taken by indirect immunofluorescence reaction (IIR).

Materials and methods. In the process of development of the technique of IIR for revealing the level of antiBabesia antibodies in blood serum we used three types of complete combined cell antigens (CCCA) of *Babesia* species: *B. microti, B. divergens* and *B. canis*. IIR was tested by examination of 130 blood serum samples (BSS) of different origin: from patients with Lyme disease (n = 30), seropositive rheumatoid arthritis (n = 10), toxoplasmosis (n = 15), clinically healthy donors (n = 60); animals (n = 20). IIR results were visually assessed under a luminescence microscope with a 4-cross positional system (400x; 1,000x).

Results and discussion. It was found out that testing of 130 BSS (in 1:8 dilution) produced 10 (2.7 %) positive results of the reaction. *B. canis* was not revealed in any case of reaction with CCCA. A relatively higher number of positive results of IIR with CCCA were observed with *B. divergens* (5.4 %); *B. microti* was found in 2.3 %. The level of antibodies against *Babesia* species in BSS from patients with Lyme disease reached 16.7 %. In cases of samples from cattle the above indices were equal to 20.0 %. Diagnostically significant titres of antiBabesia IgG (≥ 1:128) were revealed in 13.3 % of BSS from patients with Lyme disease and in 1.7 % of BSS from blood donors, whereas specific IgM were only in 13.3 % of BSS from the above patients. In 16.7 % of BSS from patients with Lyme disease, who on the whole revealed diagnostically significant titres of Babesia infection antibodies, the latter were represented in 60 % of these BSS with both classes of Ig (IgG and IgM = 0.63), while in 40 % a diagnostically significant titre was reached only by one of them (IgG or IgM), thereby necessitating simultaneous determination of specific IgG and IgM or total Ig during immunological diagnosis of babesiosis.

Conclusions. Advantages of using the method of IIR for diagnosis of babesiosis are combined with certain disadvantages (the subjective principle of assessment of results, a relatively low sensitivity at the initial stage of the disease, probable false positive results owing to immunological cross reactions, absence of validated test systems and protocols of investigations for diagnosing diseases, caused by *B. divergens*, etc.). Consequently, reasonable is the tactics of its limited use: for diagnosis of the acute phase of babesiosis only in cases with negative results of investigations, conducted by other methods (microscopy, polymerase chain reaction), and in the presence of a strong suspicion that the patient may have haemoparasitosis.

THE INFLUENCE OF THE EXTRACT FROM THE STEVIA LEAVES ON THE DIABETES DEVELOPMENT

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Introduction. The International Diabetes Federation (IDF) in 2014 published updated figures showing that more than 382 million people are sick for diabetes worldwide. For the treatment of mild forms of diabetes commonly used medicinal plants. One such plant is Stevia rebaudiana. In addition, given that the main component of the extract, stevioside is sweet, but non-nutritive substance, it becomes a good sugar substitute for diabetics. The traditional therapy of diabetes is based on the use of hypoglycemic medications and insulin. At the same time, the arrival of xenobiotics in the human organism is a potent activator of microsomal processes and, therefore, free radical oxidation.

During some preliminary investigations we have found the hypoglycemic effect of stevia. However, it has been shown that the stevia has no hypoglycemic action for people without diabetes. This adaptogenic effect determines the safety of the plant. While studying the hypoglycemic effect of an aqueous extract from the leaves of stevia per os injected to the animals with alloxan diabetes, a dose-dependent effect has been detected. Supplementation in the rats diet, containing large amounts of carbohydrates, 0.1% stevioside solution has resulted in a reduction of glycogen levels in a liver but has no effect on blood glucose. When the experimental animals have been given the food with a high fat diet supplemented with 0.1% stevioside solution, we have found no changes in those indicators that have been observed in the animals that have not been treated with stevioside. A diet of a high amount of carbohydrates with 10% of the powder from the leaves of Stevia has induced a significant decrease of glucose level in blood and glycogen in a liver within 4 weeks of use.

Plant polyphenols, which contained in stevia, normalize glucose, insulin, fatty acids and triacylglycerols in the rats with the experimental diabetes of the first type. Moreover, diterpene glycosides promote the normalization of glucose concentration in blood and restoration of impaired metabolic process that facilitates the course of diabetes; they have the ability to feed the pancreas, restoring its normal function.

Conclusions. It should be noted that the hypoglycemic effects of the medications of stevia are not always observed, and it is often short-lived and requires a further study. But nowadays we have found out that the product is useful for diabetics. Thus, the use of the remedy derived from stevia, can be justified, and appropriate in the complex therapy of diabetes.

EFFECT OF HYPERICUM PERFORATUM AND CHISANDRA CHINENSIS ON PSYCHOPHYSICAL STATE UNDER EXPERINENTAL NEURASTHENIA

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Introduction. The World Health Organization declared the 21st century as the depression epidemical. Depression is ranked first in the world among the causes of absenteeism and the second - among the diseases leading to disability (annually about 150 million people). In 60% of cases it is the cause of depression is suicide. 50% of Ukraine's population suffer from borderline states (all sorts of neuroses). Neurasthenia (F48.0) is the most common form of such states. Neurasthenia is a mental disorder from the group of neuroses, which manifests itself in increased irritability, fatigue, loss of the long-term mental and physical stress adaptation ability. There are three stages of neurasthenia: hypersthenic neurasthenia, irritable weakness and hyposthenic neurasthenia. Each of which has features in therapy.

Aim. Studying the influence of plant originating drugs (based on Hypericum perforatum and Schisandra chinensis), in the psychophysical state when hyposthenic neurasthenia. As well as the consideration of the feasibility of their combined use.

Materials and methods. The experimental study was performed on the pre-selected 24 white rats (145-185g, 5 months, male). Hyposthenic neurasthenia modulated by keeping in a confined space for 21 days. Rats were divided into 6 groups. 1) control; 2) given Hypericum perforatum; 3) given Schisandra chinensis; 4) given Hypericum perforatum and Schisandra chinensis; 5) given Schisandra chinensis daily dose in the morning and daily dose of Hypericum perforatum in the evening; 6) given a single dose of Schisandra chinensis in the morning and a single dose of Hypericum perforatum in the evening. (The dose calculated in terms of a therapeutic dose for humans). The calculated doses were administered intragastrically in 1 ml of water twice daily. The control group received the appropriate amount of water. The final results obtained in the "open field" tests, swimming according to Porsolt and swimming with the additional load.

Results and discussion. Based on these data statistically significantly better ratio of locomotor activity to cognitive activity in group Schisandra and group Schisandra combination Hypericum compared with a group of Hypericum. Also the groups with Schisandra showed the better results of physical endurance in swimming experiment with additional weights 10%.

Conclusions. The combined use of Schisandra chinensis and Hypericum perforatum looks quite promising and needs more detailed investigations.

THE STUDY OF ANTI-INFLAMMATORY PROPERTIES OF THE PLUM LEAVES EXTRACT

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Introduction. Scientific researches in the field of creation of new anti-inflammatory medications are held constantly, but the range of these medications is still relatively limited. The emphasis in recent times on the choice of the objectives for a research is given to the biologically active compounds obtained from some plant materials. We are interested in plums, especially its leaves, which is rich in phytochemicals compositions. At the Department of Chemistry of Natural Compounds of the National University of Pharmacy has received the extract from the plums leaves and identified the presence of a diverse group of flavonoids, which have unlimited spectrum of a biological activity. Therefore, we have chosen the study of anti-inflammatory properties. **Aim**. Evaluation of anti-inflammatory activity of the plum leaves extract has begun with the study of the effects of the studying extract on the development of carrageenan foot edema among rats.

Materials and methods. The animals of the control group has been subplantary injected with 0.1 ml of 1% solution of carrageenan to the aponeurosis of a hind limb. The animals of the second and third groups have been intragastrically injected with the investigational extract at a dose of 25 mg / kg and Silibor at a dose of 25 mg / kg, respectively. The animals of the fourth group have been injected with Ortofen at a dose of 8 mg / kg. The degree of edema has been assessed three hours later after the carrageenan injection. We are aware of the fact that in the pathogenesis of carrageenan inflammation in 1.5-5.5 hours after the phlogogene injection the prostaglandins play a leading role, this leads to the conclusion about the impact of the studying substance on the cyclooxygenase system. As comparison medictions we have used Ortofen at a dose of 8 mg / kg, and gepatoprotector Silibor at a dose of 25 mg / kg.

Results and discussion. The studies have shown that the studying extract has shown a modest anti-inflammatory activity and reduced swelling value at 25.1%, trailing in terms of expressiveness to the antiexudative action of Ortofen. Silibor has not shown any significant effects on the intensity of the inflammatory process.

PROPHYLAXIS OF ENDOTHELIAL DYSFUNCTION EVELOPMENT UNDER INSULIN RESISTANCE IN RATS

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Introduction. Insulin resistance (IR) is a key factor in the development of diabetes mellitus type 2 (DM2). Vessel endothelium metabolism disorders, primarily endothelial dysfunction (ED), play an important role in DM2 pathogenesis. Nitrogen oxide (NO) is synthesized from arginine and this reaction is catalyzed by NO-synthase (NOS). There is evidence that some components from bilberry (*Vaccinium myrtillu*) leaves, such as quercetin, increased the expression of endothelial NOS (eNOS), NO formation and its release from endotheliocytes. The **aim** of this investigation was to explore the effect of the polyphenol complexes from bilberry leaves with the addition of inositol and arginine on the ED development under the experimental IR. The extract was obtained by the supervision of Dr. O.H. Koshevoy.

Materials and methods. IR in rats was modeled by feeding the animals high-fructose diet (HFD). For the aim of experiment 18-month-old male *Wistar* rats were divided into 4 experimental groups: 1) intact animals; 2) animals, which were fed HFD during 6 weeks; 3) animals, which were fed HFD during 4 weeks and further the diet and bilberry extract enriched by inositol (no 1, 2.5 mg/100 g body mass); 4) animals, which were fed HFD during 4 weeks and further the diet and bilberry extract enriched by inositol and arginine (no 2, 2.5 mg/100 g body mass). The content of glucose, insulin, triacylglycerols (TAG), cholesterol, arginine, citrulline and nitrites and nitrates were measured in blood serum.

Results and discussion. Feeding the fructose diet leads to almost threefold increase in blood glucose level, development of hyperglycemia, increased cholesterol and TAG concentrations. All these changes indicate the development of IR. The significant reduction of nitrite and nitrate and citrulline content was found in the blood serum of animals under the IR, the content of arginine was increased significantly. Such disorders may be caused by oxidative damage of the enzyme or by the lowering content of coenzyme - tetrahydrobiopterin.

Conclusions. The administration of complex enriched both by inositol and arginine, normalized studied indices more pronounced compared to another complex. Moreover, the indices that characterized NO-system – nitrites and nitrates, and citrulline content were increased and the arginine level was reduced almost completely to that in intact animals. This is obviously due to the presence of arginine. So, the addition of arginine and inositol to the bilberry leaves extract improved it useful properties.

SOME NEW DATA ON F_0F_1-ATP-SYNTHASE STRUCTURE AND FUNCTION

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Introduction. The question how energy of oxidation of fueling molecules is transformed and conserved in the universal form of ATP in the cell is an issue of critical importance for scientists in the field of bioenergetics for some 5-6 last decades. Many theories were proposed to answer this question, but the most rational explanation was given by the Nobel laureate Peter Mitchell in his chemiosmotic model. The author postulated that working electron transport chain creates the electrochemical potential on the inner mitochondrial membrane - $\Delta\mu_H^+$, and this potential is the proton-motive force which drives the biosynthesis of ATP. Such force makes protons to cross the membrane from the intermembrane space back into the mitochondrial matrix via proton pores in F_0 of the ATP synthase complex. The same force provides the energy for ATP synthesis by F_1 connected to F_0.

Aim. On the eve of Millennium II it was shown that ATP synthase revealed a turbine activity. The F_0 domain that is plunged into the inner mitochondrial membrane includes 3 types of subunits – a (1), b (2) and c (varies from 8 to 15 depending on organism species) – and contains a proton pore. The c subunits are identical, small hydrophobic proteins arranged in a ring which is rotated as hydrogen ions cross F_0. The F_1 domain is composed of 9 subunits of 5 types – α (3), β (3), γ, ϭ, ε. Each of the β subunits carries a catalytic area where ATP biosynthesis occurs. These catalytic areas may be present in 3 different conformations with different nucleotide-binding sites. Three conformational states gave rise to the names of β subunit status – β-ATP, β-ADP and β-empty. All the 9 subunits form a stalk and a pileus of a microscopic "mushroom" headed into the matrix.

Results and discussion. Another Nobel laureate Paul Boyer who for a long period of time strongly defended a "conformational" theory of oxidative phosphorylation, now with high probability considers a rotational mechanism of ATP synthesis. According to the mechanism a given β subunit starts to participate in ATP synthesis in the β-ADP conformation. It binds ADP and Pi from the medium and turns into the ATP state. Being in the ATP conformation, the subunit fulfils the ATP formation and firmly keeps the molecule of ATP on its surface. Then the conformation of the unit is changed to β-empty. Such conformation possesses a low affinity to ATP, and the new molecule of ATP easily leaves the subunit.

Conclusion. What energy supplies all these conformational transformations? This is the energy of protons moving across the inner mitochondrial membrane through the F_0 domain of ATP synthase. The proton-driving force makes the cylinder of c subunits rotate together with the connected γ subunit (the stalk), which at each120° turn switches onto a new pair of αβ subunits (3 αβ pairs) changing the conformation of β unit into the β-empty form. At the same time one neighboring β subunit takes the β-ADP conformation, and the third β subunit – the β-ATP one. The rate of the cylinder rotation in intact mitochondria can reach 100 rotations per second.

BIOLOGICAL ROLE OF d-TRANSITION ELEMENTS OF VIII GROUP

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Introdiction. The iron group in the periodic table referred to the elements iron, cobalt and nickel, that is the first row of group VIII (or VIIIB under the old numbering system.) In modern numbering, the iron group appears as three columns numbered group 8, 9 and 10. These metals, and the platinum group immediately below them, were set aside from the other elements as they show obvious similarities among themselves in their chemistry, but are not obviously related to any of the other groups. All d-microelements has their own optimal concentration in human organism. Any deviation in the direction of the deficit or excess leads to violation of substance exchange.

Aim. Review the biological properties of d-elements of VIII group.

Biological role of Iron

Iron is involved in numerous biological processes. Iron-proteins are found in all living organisms: archaeans, bacteria and eukaryotes, including humans. For example, the color of blood is due to the hemoglobin, an iron-containing protein. As illustrated by hemoglobin, iron is often bound to cofactors, e.g. in hemes. The iron-sulfur clusters are pervasive and include nitrogenase, the enzymes responsible for biological nitrogen fixation. Influential theories of evolution have invoked a role for iron sulfides in the iron-sulfur world theory.

Structure of Hemoglobin b, in the protein additional ligand(s) would be attached to Fe. Iron is a necessary trace element found in nearly all living organisms. Iron-containing enzymes and proteins, often containing hemeprosthetic groups, participate in many biological oxidations and in transport. Examples of proteins found in higher organisms include hemoglobin, cytochrome (see high-valent iron), and catalase.

Biological role of Cobalt

Cobalt is essential to humans. It is a key constituent of cobalamin, also known as vitamin B12, which is the primary biological reservoir of cobalt. In humans, B12 exists with two types of alkyl ligand: methyl and adenosyl. MeB12 promotes methyl (-CH3) group transfers. The adenosyl version of B12 catalyzes rearrangements in which a hydrogen atom is directly transferred between two adjacent atoms with concomitant exchange of the second substituent, X, which may be a carbon atom with substituents, an oxygen atom of an alcohol, or an amine.

Biological role of Nickel

Nickel is a trace element that influences the amount of iron our bodies absorb from foods and may be important in helping to make red blood cells. Also Nickel can have an impact on human health through infectious diseases arising from nickel-dependent bacteria. Nickel released from Siberian Traps volcanic eruptions (site of the modern city of Norilsk) is suspected of having had a significant impact on the role played by Methanosarcina, a genus of euryarchaeote archaea that produced methane during the biggest extinction event on record.

Platinum group

The presence of platinum group elements in the human body are not fully understood and its daily need is unknown. Their presence in human organism have toxic nature.

Organometallic complexes of platinum-group metals, such as alkylplatinum complexes, are employed as catalysts in olefin polymerization, the production of polypropylene and polyethylene, and the oxidation of ethylene to acetaldehyde. Platinum salts are finding increasing use in cancer chemotherapy as drugs marketed under the generic names carboplatin and cisplatin. Ruthenium oxide-coated electrodes are employed in the production of chlorine and sodium chlorate.

Main symptoms of deficiency of d – elements.

Deficiency of platinum metal doesn`t affect on metabolism, because of its little concentration in human body. Most pronounced deficiency symptoms refer to the iron. Total body iron averages approximately 3.8 g in men and 2.3 g in women. There are several mechanisms that control human iron metabolism and safeguard against iron deficiency. When loss of iron is not sufficiently compensated by adequate intake of iron from the diet, a state of iron deficiency develops over time. When this state is uncorrected, it leads to iron deficiency anemia: fatigue, dizziness, pallor, hair loss, twitches, irritability, weakness, brittle or grooved nails, Plummer-Vinson syndrome (painful atrophy of the mucous membrane covering the tongue, the pharynx and the esophagus), impaired immune function, pagophagia.

Conclusions: Iron group metals have a much greater influence on the metabolic processes in the human body than the platinum group metals. Biomedical research on the concentration of iron metals allow us to establish a diagnosis and choose a treatment strategy.

URIC ACID CONTENT IN BLOOD SERUM AND TISSUES OF RATS UNDER SUBCHRONIC STRESS

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Introduction. The prolonged stress leads to the hormonal disbalance and, as a result, to the tissue metabolism disorders, energy deficiency, and reactive oxygen species (ROS) formation. There is an evidence that hyperuricemia can be one the confirmation of the insulin resistance (IR). So, the hyperuricemia in hypertensive patients is the feature of IR and associated with increased cardiovascular morbidity. The **aim** was to study UA content in blood and tissues in rats under the subchronic stress.

Materials and methods. Rats were divided into two groups: intact animals and animals that were exposed prolonged neuromuscular tension by daily immobilization on the belly for 3 hours during 21 days, which were decapitated on the 8^{th}, 15^{th} and 22^{nd} day. In blood serum, liver and kidneys homogenates were determined UA content.

Results and discussion. UA blood serum concentration was already increased on the first week of experiment in 1.5 times finishing almost in twice elevation. The most significant rise was observed in the liver tissue UA content particularly on the 8^{th} day (in 2.5 times). The changes in UA content in kidneys were not so vivid, but more prolonged keeping the elevation in 1.2 times to the 22^{nd} day. Consequently, kidney UA content increase may be a result of UA excretion inhibition in kidney tubules. UA accumulation might have different consequences: on the one hand, this compound has antioxidant properties, on the other – its formation involving xanthine oxidase leads to the generation of free radicals. Also, consider that increasing the UA content causes endothelial damage that is common for patients with diabetes and hypertension and plays a role in the development of atherosclerosis. However, the increase in UA formation should be accompanied by the oxidative stress progression because of increased activity of the purine degradation key enzyme – xanthine oxidase, which is considered as one of the main sources of ROS accumulation. In spite of some UA antioxidant properties, xanthine oxidase activation is believed to shift the balance in the pro-oxidant-antioxidant system.

Conclusions. UA accumulation in rat tissues that significantly pronounced under repeated stress can be considered as one of the indices of IR, which accompanied repeated stress and in turn is additional risk factor for aterogenesis and cardiovascular system diseases.

INVESTIGATION OF GLYCOSAMINOGLICANS METABOLISM DURING REPARATIVE REGENERATION IN THE LABORATORY RAT'S SKIN UNDER NEW SOFT MEDICINAL FORMS USING

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Introduction. Wound treatment is one of the oldest problems of medicine and pharmacy. Nowadays the importance of the topic is not lost and become even more actual due to growth of military conflicts, domestic and occupational injuries. Skin integrity damages that occur at these situations are one of the most severe and sometimes incurable pathology. Medications for local use are diverse. The search of new molecules and the creation of metabolic type drugs based on them can reduce the toxicity and improve the conditions that can positively influence on the process of wound healing and, as a consequence, provide quality treatment.

The **aim** of the research was to investigate glycosaminoglicans metabolism during reparative regeneration in the laboratory rat's skin under using a metabolic type drug based on wide-spread biological molecules of human, animal and plant origin such as natural amino sugar 2-D - (+) - glucosamine and its derivates.

Materials and methods. The object of the study was the 1% cream based on the derivate of amino sugar 2-D - (+) - glucosamine and oxalic acid (oxoglucamin - OGA). The substance and medical form based on the substance was previously developed by O. I. Pavlii, I. A. Zupanets, M. O. Lyapunov, L. V. Brun.

Experiments were performed on 40 white breadless rats according to International requirements of humane animal treatment and Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes. Wound healing activity of the 1% cream OGA and glycosaminoglicans metabolism (GAG) in rat's skin were investigated in the linear cut wound model on 6-th day of pathology. The "Mefenat" ointment was chosen as a comparison drug. Histochemical study of rat's skin for glucosaminoglican (GAG) identification was performed.

Results and discussion. Reparative activity was 80.3% and 11.7% ($p<0.05$) using 1% cream OGA and "Mefenat" correspondingly. Using histochemical methods it was confirmed that in the 1% cream OGA treatment group the intensive positive reaction to GAG ("+++") was found whereas in the control group (without any treating) and in the "Mefenat" ointment application the moderate positive reaction to GAG ("+") was noted.

Conclusions. The study has shown that 1% OGA cream was a highly effective metabolic type drug with expressed wound-healing properties and due to its metabolic activity and structure features led to more delicate cosmetic scar formation.

HERBAL REMEDIES OF EXTERNAL APPLICATION TO PSORIASIS TREATMENT

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Introduction. Nowadays psoriasis, which should be regarded as a system process is one of the most common dermatoses. According to the leading dermatologists' opinion, this disease affects about 2% of the world population. Psoriasis has a multifactorial nature. In its pathogenesis an important role plays some certain immunological, enzymatic and other biochemical disorders in the organism. Unfortunately, the modern medicine does not have the means to achieve a definitive cure of this disease. Therefore, in the foreground there is a symptomatic therapy. The amount of remedies for an external treatment includes some remedies that containe salicylic acid, tar preparations, vitamin A, and corticosteroid creams and ointments as well as products based on natural raw materials.

The aim of this researchwork was to study the amount of herbal remedies for an external use for the treatment of psoriasis.

Results and discussion. The company "German Homeopathic Union (DHU)" has developed the original homeopathic herbal remedy Psoriaten, the main active ingredient of which is a 10% matrix tincture of the plant *Mahonia aquifolium*. It is found out that due to the alkaloid berberine and its derivatives yatroritsine, palmatiny and colimbamine, there is an anti-inflammatory and anti-proliferative effect of "Psoriaten". According to the local researchers, a positive clinical effect of using an ointment "Psoriaten" has been obtained in 67 – 89% of the patients with psoriasis.

Also, we can apply some herbal remedies "Kamagel" for the treatment of psoriasis. The main components of this product are: aluminum atsetotartrata 10% solution, chamomile flower extract glycol. The aluminum atsetotartrat acts locally as a mild astringent remedy and antiseptic. At the area of application it causes coagulation of proteins, which forms a protective layer on the skin and reduce the capillary permeability and exudation, inflammation and infection. Essential oil of chamomile and flavones, which are contained in an chamomile extract, also reduce inflammation and act as a mild antiseptic.

Conclusions. Numerous drugs are designed to stimulate the body's natural defense system and promote the natural recovery process. Positive qualities of homeopathic remedies are that they are nontoxic, do not cause allergic reactions and adverse side effects. The analysis of anti-psoriatic herbal remedies has shown a limited choice in the pharmaceutical market for the patients with this disease and the necessity of searching some new herbal remedies with an anti-psoriatic action.

MECHANISMS OF THE ENDOCANNABIONOID SYSTEM AFFECTS THE PAIN ADAPTATION PROCESSES TO VIGOROUS PHYSICAL ACTIVITY IN HUMANS

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Introduction. Adaptation system is a complex of humoral and metabolic transformations occurring in organism in response to environmental conditions changes. The organism's adaptation to pain during the vigorous physical activity is carried out by using stress-limiting system, which is represented in central nervous system mainly by opioid system mediators. Recently, endocannabinoids (anandamide, 2-arachidonoyl glycerol) are also referred to as stress-limiting mediators with antinociceptive activity. Endocannabinoids are the endogenous neurotransmitters with lipid properties that have the characteristic of retrograde signaling (from the presynaptic membrane to synaptic), which blocks the transmission of nerve impulses. The **aim** of this work was the theoretical study of mechanisms by which the endocannabinoid system affects the pain adaptation processes during the vigorous physical activity in humans.

Dicsussion. It is known that physical activity is accompanied by a proportional increase in the blood epinephrine level (stress-inducing hormone), which leads to increased blood pressure (BP), ascending blood glucose levels and activation of glycolysis in muscles. In terms of relative hypoxia caused by epinephrine and intensive muscle work, tissue receives the energy as a result of anaerobic glycolysis, which causes the lactic acid accumulation and the development of muscle pain. According to recent studies, pain can also be caused by microtraumas formed during the excessive stretching of myofibrils. In response to the increased levels of adrenaline the stress-limiting system is activated that is accompanied with the release of endorphins and endocannabinoids. Several studies have noted a functional synergy in the work of these two types of neurotransmitters, which can be explained by different mechanisms of action. Endorphins, similar to morphine-like substances, stimulate opioid receptors and cause analgesia. 2 Arachidonoyl glycerol through retrograde signaling mechanism inhibits the afferent nerve impulse transmission, which also reduces the sensation of pain. It is also important to note a psychoactive activity of endocannabinoids and endorphins, so against the background of physical activity athletes feel euphoria, which is called "runner's euphoria".

Conclusions. Thus it shows that endocannabinoids are important in the body's adaptation to stress-induced muscle pain during vigorous physical activity. The role of other neurotransmitters in the stress-limiting system requires further research.

INVESTIGATION OF HYPERLEPTINEMIA CORRECTION MECHANISMS AFFECTED BY HYDROXYCITRIC ACID UNDER HIGH CALORIE DIET IN RATS

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Introduction. It is well known that the metabolic syndrome (MS) pathogenesis is closely associated with obesity, insulin resistance (IR) and hyperphagia caused by an imbalance of the eating behavior humoral regulators, in particular leptin. Leptin is the peptide hormone possessing anorexigenic activity. It is synthesized in adipocytes in proportion to the adipose tissue value, which leads to the hyperleptinemia development under the obesity conditions.

Aim. The aim of our study was to investigate the impact of hydroxycitric acid on leptin level changes which are developed under hypercaloric diet in rats.

Materials and methods. IR was modeled in Wistar rats weighing 160-200 g, by keeping on high-fructose diet and long-lasting dexamethasone injections. The test substance – hydroxycitric acid was injected intragastrically in a dose of 0.1g per 100 g of body weight. The animals were tested for glucose, immunoreactive insulin (IRI) and leptin levels in blood serum. For statistical data processing used program STATISTICA.

Result and discussion. Keeping rats on a high-fructose diet with dexamethasone injections led to the glucose and immunoreactive insulin (IRI) levels significant increase in in the rats' serum (1.20 and 1.11 times, respectively), which indicates the IR progression. The leptin concentration in experimental animal's blood was also significantly increased by 1.04 times, but the expected depression of appetite did not occur, probably due to the leptin resistance development. According to the literature, insulin and leptin have a crossover mechanism of intracellular biosignaling, the disruption of which can be caused by the same factor. Under IR conditions, there is an intense release of free fatty acids, which are lipotoxic and this is a significant factor in the development of resistance to leptin.

Conclusions. Intragastric administration of hydroxycitric acid resulted in lower levels of glucose and IRI, which did not significantly differ from those of intact control. The blood concentration of leptin was within physiological norms. Thus, it can be assumed that analyte increases the cells sensitivity to the insulin and leptin action, probably through it's ability to reduce the intensity of free radical oxidation within cells and enhance signal transduction of these hormones' receptors, which, however, requires further research.

MECHANISMS OF BROMOCRIPTINE D2-DOPAMINE RECEPTORS SELECTIVE AGONIST INFLUENCE ON OBESITY CORRECTION

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Introduction. Obesity is a pathological condition characterized by a significant increase the amount of adipose tissue which leads to the metabolic diseases development, in particular diabetes mellitus type 2 (DM 2). Today the search for new correction methods of metabolic disorders against carbohydrate and lipid metabolism disorders under obesity conditions is quite promising. Bromocriptine is a selective agonist of D2-dopamine receptors, which recently shown a high efficiency in the treatment of type 2 diabetes.

Aim. The aim of our work wst to study the theoretical impact of D2-dopamine receptors selective agonist bromocriptine on the obesity correction mechanisms.

Result and discussion. It is known that weight excess leads to an imbalance in the work of many hormones, including increased prolactin level. Prolactin - anabolic peptide hormone secreted by the adenohypophysis, it mainly ensures the women reproductive system functioning. However in obesity conditions there is a hyperprolactinemia developmen, which is one of the main humoral factors of energy accumulation (fat accumulation). The regulation of prolactin production is controlled by the hypothalamic dopaminergic neurons (D2-dopamine receptors), selective stimulation of which leads to the hyperprolactinemia elimination and promotes the process of weight correction. It's important to mention that the dopamine receptors have several isoforms and they are divided based on their localization in the central nervous system, and on the effects they cause. For example, amphetamines lead to a massive release of dopamine and norepinephrine, which on the contrary leads to increased prolactin levels in the blood. That is why only selective agonists of D2 receptors can reduce the prolactin production. According to several experiments, administration of bromocriptine in low doses at the beginning of the day was accompanied by carbohydrate and lipid metabolism normalization, which took place under obesity conditions, lowered glucose in serum, increased lipolysis process, lipogenesis inhibition etc.

Conclusions. Thus, it can be assumed that the bromocriptine effectiveness in the obesity and type 2 diabetes treatment occurs through the mechanism of hyperprolactinemia correction. Perhaps the studied drug has other ways to influence the course of obesity and type 2 diabetes development that requires further research.

THE STUDY OF TOXIC PROPERTIES OF THEEXTRACT FROM THE PLUM LEAVES

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Introduction. Plum is widespread in Ukraine, has a large number of kinds. At the Department of Chemistry of Natural Compounds of the National University of Pharmacy we have obtained the total extract from the leaves of plum and studied its chemical composition.

Aim. We have been the pioneers in setting up an experiment to determine the toxic properties of the extract from the leaves of plum.

Materials and methods. The study of an acute toxicity of the extract from the leaves of plum has been conducted with the help of a rapid method by Pastushenko T.V. on mice and rats. The studying extract has been administered per os. The animals have been observed for a week. At a subsequent stage of studying the acute toxicity of the plant extract we have chosen a parenteral (intraperitoneal) administration way. Also we have determined the LD_{50} for mice and rats.

Results and discussion. The obtained experimental data indicate a high toxicity of the studying extract in a single intragastric administration, that's why while conducting the research on the rats, they have been injected with the maximum dose of 20000 mg / kg, and the death of the animals has not been observed.

The analysis of experimental data has shown that the LD D_{50} of the studying extract, in the case of an oral administration, is more for the rats and mice 15000 mg / kg. Thus, an extract from the plums leaves, according to the classification by K.K. Sidorov, can be classified as a practically harmless substances. Due to the further study of the toxic properties of the extract according to the experimental data, the LD_{50} for the mice by an intraperitoneal injection is in the range of 3160-3980 mg / kg. It has been also found that the LD_{50} of the studying extract for the rats is at the range of dosage of 3980-5000 mg / kg. LD_{50} for the rats by an intraperitoneal injection is 4310 (3510-5120) mg / kg.

Conclusions. Thus, the extract from the plum leaves is a safe remedy and refers to the VI toxicity class due to the classification by Sidorov K. K.

The results of this study extend the information about biological activity of the plum leaves substances and can be used for the further, in-depth study of the pharmacological activity of the obtained extract.

BIOPHYSICAL BASIS OF THE TECHNIQUE OF SELECTIVE PHOTOTHERMOLYSIS

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Introduction. The method of selective photothermolysis-complex non-ablative procedures carried out on devices intense pulsed light directed at correcting manifestations chrono-and photoaging, as well as in the treatment of a variety of pigmented and vascular lesions in patients of any vozrazrasta.

Aim. To make the analysis methods of laser rejuvenation features, advantages and disadvantages in the practical application of each technique as well as prospects for the development of these technologies.

Materials and methods. The principle of selective photothermolysis has been formulated in the form of guidelines:

1. The absorption of electromagnetic waves to be selective, ie certain tissue structures (targets) to be subject to change;

2. The radiation source must generate electromagnetic radiation of a certain wavelength;

3. The energy of radiation and exposure time should cause an increase in the specified target temperature to the required value;

4. The impact of radiation on the surrounding tissue should be minimized. Absorption of the light passing through the fabric, independent of its original intensity I0 of the radiation, the substance layer thickness l, through which the light of the wavelength λ of light absorbed and the absorption coefficient α according to the law of Bouguer-Lambert-Beer.

If the light is not absorbed, it is no effect on the tissue does not occur. When absorbed all the energy of the photon is transferred to a molecule or part thereof (chromophore). At the same molecule in an excited state. The most important endogenous chromophores biological tissues are melanin, hemoglobin, oxyhemoglobin, water and collagen. The choice of chromophore defined set of clinical task. chromophore absorption coefficient depends on the wavelength: $\alpha = f(\lambda)$. Therefore selective absorption of radiation must be of a certain wavelength corresponding to the peak of the absorption spectrum of the chromophore. The constant α determines the radiation penetration depth d - is the thickness of the layer, the passage of which light intensity decreases by a factor e. The molecule to absorb the energy of the radiation, can not long to arrive in the excited state. Going back to

the ground state, it gives energy to the radiative (fluorescence effect) or nonradiative transition. When nonradiative transition energy of the absorbed photon is released as heat, which leads to an increase in temperature. With the passage of the beam in biological tissue is shown the effect of scattering - light deviation from its original direction. The importance of the phenomenon of dispersion is that it quickly reduces energy flux available for absorption chromophore therefore reduces the clinical impact of radiation on tissue. According to the Rayleigh scattering intensity is inversely proportional to the fourth power of the wavelength: I ~. Therefore, an increase in wavelength contributes to the delivery of energy to the deeper lying structures. The process of the scattering of the radiation in the skin due mainly to the dermis collagen. Features: This technique allows during one procedure to effectively eliminate several problems (including professional and personal tattoos).

It can be recommended for all skin types, regardless of age and gender. Disadvantages

1. Infection (10.8%);

2. Persistent erythema associated with hyperactivation healing mechanisms and increased vascular proliferation;

3. Chronic hyper- and hypopigmentation (violation of melanocytes exchange);

4. There is a risk of scarring (scar formation)

Results and discussion. The method of selective photothermolysis has its advantages as well as disadvantages. The term refers to the phenomenon of photothermolysis tissue destruction under the influence of heat generated by the absorption of electromagnetic radiation in the optical range.

Conclusions. This method is very effective and urgent in medicine and in hardware cosmetology, as well a perspective.

CORRECTION OF LIPID METABOLISM DISTURBANCE BY THE BLUEBERRY EXTRACTS ADMINISTRATION UNDER EXPERIMENTAL INSULIN RESISTANCE

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Introduction. Insulin resistance is one of the factors of metabolic syndrome, type II diabetes and cardio-vascular complications development. Recently an increasing scientific interest has developed about polyphenols, which are very abundant in blueberry (Vaccinium myrtillus), as they have hypoglycemic and insulin mimetic properties.

The **aim** of present work was comparative investigation of the extracts from the blueberry berries ("Biolika", Kharkiv) and leaves (pharmacognosy department of NFaU under d.farm.n. Koshevoi O.M. supervision) effect on lipid metabolism disorders under experimental insulin resistance.

Materials and methods. Experimental insulin resistance was modulated by fructose-rich diet (18.3% protein, 60.3% fructose and 5.2% fat). Experimental rats were divided into 4 groups: 1) the control group received regular rat chow, 2) the study group received fructose-rich diet, 3) and 4) the study groups received fructose-rich diet with one of the extracts in dose 2.5 mg/100 g b.w. Plasma levels of triacylglycerols (TAG), free fatty acid (FFA), α- and β-cholesterol (ChS) were determined after 6 weeks of experiment. Statistical analysis of the data is carried out using the program STATISTICA (StatSoft Inc., USA, version 6.0).

Results and discussion. Fructose-rich diet caused increase of TAG, FFA and β-ChS level and decrease of α-ChS content. These data demonstrate the development of atherogenic dyslipidemia. Upon both extracts administration decrease of TAG, FFA and β-ChS levels and increase of α-ChS level were observed. This was due to the ability of polyphenols to increase tissue insulin sensitivity and reduce hyperglycemia as shown in parallel experiments. Antioxidant properties of extracts components probably also contribute to the hypolipidemic effect. Extract from the blueberry leaves had a more pronounced protective effect than extract from berries, obviously, due to the different composition of polyphenols. It is known that the leaves of investigated plant are richer in myrtyllyn (a mixture of glycosides delfynydyn and malvydyn with insulin mimetic activity), tannins and unsaturated fatty acids and have lower sugar content.

Conclusions. Investigated extract from the blueberry leaves provided a stronger hypolipidemic effect so it is perspective raw material for the development of new drugs for the treatment and prevention of insulin resistance.

INVESTIGATION OF STRESS-PROTECTIVE EFFECT OF DRIED FRUITS POLYPHENOLIC COMPOUNDS UNDER ACUTE STRESS IN RATS

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Introduction. According to scientific literature, in the pathogenesis of many diseases and pathological states a key etiopathogenetic role belongs to the stress. Antioxidant and anti-stress therapy is an important element of successful medical therapy for pathologies associated with stress. Taking into account that raisins polyphenols shows stress-protective and antioxidant activity in our previously researches, rationally was to investigate and compare other types of dried fruits – apricots and prunes the pharmacological activity. The administration of synthetic antioxidants is limited by the fact that all xenobiotics, undergoing metabolism, activate processes microsomal oxidation in the liver and, therefore, can intensify the free radicals formation. Promising compounds are natural antioxidants, primarily of plant origin. The **aim** of present work was to explore mechanisms of raisins, dried apricots and prunes polyphenolic compounds stressprotective effect on the model of acute stress induced by single subcutaneous epinephrine injection in rats.

Materials and methods. Female Wistar rats were used. Acute stress was simulate by a single subcutaneous injection of epinephrine at the rate of 2 mg per 100 g of body weight of the animal. The investigated products (raisins, dried prunes, dried apricots) was administered as a supplement to the diet at a dose, which corresponded to 350 g of dried fruit per human 70 kg weighting for 14 days. Stress-protective influence of dried fruits under the model pathology was investigated with using a standard open field test.

Results and discussion. Adding of used dried fruits to the rats diet largely facilitated the acute stress symptoms in animals. Recent data confirmed indicators of locomotor and orienting-investigatory activity, the emotional state of animals that were within the physiological norm. The results indicate that the investigated substances show the expressive stress-protective effect. This effect mainly realized by the oppression intensity of free radical processes associated with stress development. Stress-protective effect of dried fruits is mediated by the content of anthocyanins, gallic acid, vitamin C, quercetin, epicatechin, catechin protending, etc. The most obvious effect of a relatively stress protection found in raisins influence.

Conclusions. The data obtained suggest a complex stress-protective influence of dried fruits biologically active substances, which are mediate by a distinct antioxidant activity.

CONTENT

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