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СОҒЛИҚНИ САҚЛАШ ВАЗИРЛИГИ

ТОШКЕНТ ФАРМАЦЕВТИКА ИНСТИТУТИ

ИБН СИНО ЖАМОАТ ФОНДИ

**АБУ АЛИ ИБН СИНО ВА ЗАМОНАВИЙ ФАРМАЦЕВТИКАДА
ИННОВАЦИЯЛАР**

VIII ХАЛҚАРО ИЛМИЙ-АМАЛИЙ АНЖУМАН

МАҚОЛАЛАР ТЎПЛАМИ



**АБУ АЛИ ИБН СИНО И ИННОВАЦИИ
В СОВРЕМЕННОЙ ФАРМАЦЕВТИКЕ**

СБОРНИК МАТЕРИАЛОВ

VIII МЕЖДУНАРОДНОЙ НАУЧНО-ПРАКТИЧЕСКОЙ КОНФЕРЕНЦИИ

Yantoq o'simlik xom ashyosidan olingan ekstraktlarga sifat reaksiyalari o'rganildi.

1. Natriy ishqor 10% eritmasi qo'shilganda sariq rang kuzatildi,
2. Temit (III) xlorid eritmasi qo'shilganda ko'k – yashil rang hosil bolishi kuzatildi.
3. Mis (II) sulfat eritmasi bilan ishqoriy sharoitda qo'shilganda ko'k - siyoh rang hosil bolishi kuzatildi.
4. Eritmaga natriy nitrit, xlorid kislota qo'shib aralashtirib -β- naftolni ishqoriy eritmasi qo'shilganida qizil rang hosil bo'lishi aniqlandi.

Xulosa: Yantoq o'simligi hom-ashyosidan suv yordamida ekstraksiya qilingach quruq ekstrakt yig'indisi 23,41% tashkil qildi. Ekstrakt tarkibidagi moddalarga nisbatan kimyoviy sifat reaksiyalar qilinganda ijobiy natijalar olindi.

DETERMINATION OF MAPROTYLINE IN BLOOD AND URINE BY UV SPECTROPHOTOMETRIC METHOD

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Topicality. Maprotyline – (*N*-methyl-9,10-ethaneanthracene-9(10*H*)-propanamine hydrochloride) is a tetracyclic antidepressant of the non-selective neuronal monoamine reuptake inhibitor group. The drug has shown its effectiveness in the treatment of depressive disorders with an anxiety component. A case of serotonin syndrome has been reported following concomitant treatment with maprotyline and mirtazapine. Fatal maprotyline poisoning has been reported after ingestion of 4.5–6 g of the drug; analytical diagnostics have shown that maprotyline concentrations in blood and urine in various fatal cases ranged from 2.0–44.5 mg/L and 12.6 mg/L, respectively. Analytical aspects of the toxicology of maprotyline are not sufficiently developed.

The aim of the research. To develop the conditions for maprotyline determination in blood and urine by UV spectrophotometric method after liquid-liquid extraction as sample preparation step.

Materials and methods. Model samples of human biological fluids spiked with maprotyline were studied in the research. The antidepressant was isolated from blood and urine by the method of liquid-liquid extraction with methylene chloride from an alkaline aqueous medium at pH 9 in the presence of ammonium sulphate as a salting-out agent. Biogenic co-extractive impurities from biological fluids were removed by extraction with hexane from an acidic medium at pH 1. The red blood cell mass was pre-precipitated by adding 10% trichloroacetic acid solution. The quantitative content of the drug in the extracts was determined using the UV spectrophotometric method after additional TLC purification. Chromatograms were developed in two mobile phases sequentially: first in chloroform followed by using toluene-acetone-ethanol-25% ammonium hydroxide solution (45:45:7.5:2.5) mobile phase. Dragendorff-Mounier reagent was used for visualization.

Results. Maprotyline was detected on the chromatograms as orange spots with R_f 0,31±0,03. Identification of the drug in the extracts from the biological fluids was carried out by UV spectra, which coincided with the standard solution of the antidepressant under study in 0.1 M hydrochloric acid solution and had light absorption maxima at wavelengths of 265±2 and 272±2 nm. Quantitative determination of the drug in the extracts was performed at $\lambda_{\max}$ =272 nm using the equation of the calibration curve $y=(0.00320\pm5\times10^{-5})\times x+(0.03\pm0.01)$, ($r=0.999$; $S_o^2=2.0\times10^{-4}$; $S_a=0.00521$), which was linear in the range of the analyte concentrations of 20.0–360.0 µg/mL. Limit of Detection (LOD) and Limit of Quantification (LOQ) were calculated from the standard deviation of y -intercept (S_o) and a slope b ; they were, respectively, 5.4 µg/mL and 16.3 µg/mL. The optimal conditions for maprotyline isolation from blood and urine were based on the preliminary study of the extraction yield of the drug depending on the pH of the aqueous solutions, kinds of organic solvents and salting-out agents. A wide range of organic solvents, sodium sulphate and ammonium sulphate as salting-out agents were tested at the aqueous phase pH ranging from 1 to 12. The recovery of maprotyline from blood was 49.3±3.5% and from urine it was equal to 82.6±2.2%.

Conclusions. The method for maprotyline determination in blood and urine by UV spectrophotometric method after isolation using liquid-liquid extraction have been developed. Recovery values of the developed sample pretreatment steps were determined in the range of the drug concentrations of 10–50 µg/mL and 4–20 µg/mL for blood and urine respectively. The suitability of the UV spectrophotometric method for maprotyline determination in the biological fluids has been proven, which was confirmed by a number of the validation parameters relating to the expected content of the antidepressant under study in the biological fluids in fatal poisonings. The results obtained can be used for forensic toxicological examinations in acute and fatal poisonings with antidepressant drugs.

РАЗРАБОТКА ГРАНУЛИРОВАННОГО РАСТВОРИМОГО ФИТОЧАЯ, РЕКОМЕНДУЕМОГО ДЛЯ ЛЕЧЕНИЯ АНЕМИИ	115
Ташмухамедова М.А., Файзуллаева Н.С.	
РАЗРАБОТКА ОПТИМАЛЬНОГО СОСТАВА СТОМАТОЛОГИЧЕСКИХ ФИТОПЛЁНОК НА ОСНОВЕ МАСЛА ШИПОВНИКА И НАСТОЙКИ КАЛЕНДУЛЫ	116
Туреева Г.М., Носирова Н.А.	
ОПРЕДЕЛЕНИЕ ОТПЕЧАТКА ФАКЕЛА РАСПЫЛА ОСНОВЫ СПРЕЯ ДЛЯ МЕСТНОГО ПРИМЕНЕНИЯ.....	117
Треногина Д.В., Романтеева Ю.В.	
СРАВНИТЕЛЬНОЕ ИЗУЧЕНИЕ ФИЗИКО-МЕХАНИЧЕСКИХ ПОКАЗАТЕЛЕЙ ИСХОДНОГО ГЛАУКОНИТА И СУБСТАНЦИИ «ГЛАУКОНИТ-НЕО» ДЛЯ РАЗРАБОТКИ ТЕХНОЛОГИИ «FATIFILTRUM»	118
Умаралиева Н.Р., Максудова Ф.Х.	
РАЗРАБОТКА ТЕХНОЛОГИИ ПОЛУЧЕНИЯ НАСТОЙКИ ИЗ ПЛОДОВ БОЯРЫШНИКА КРОВАВО-КРАСНОГО (CRATAEGUS SANGUINEA) И ОЦЕНКА ЕЕ КАЧЕСТВА.....	119
Эрзат Н., Джиенбеков А.К.	
ПОЛУЧЕНИЕ АРОМАТНОЙ ВОДЫ МЕТОДОМ ПЕРЕГОНКИ ВОДЯНЫМ ПАРОМ ИЗ ТРАВЫ ТИМЬЯНА ПОЛЗУЧЕГО (<i>THYMUS SERPYLLUM</i>) ПРОИЗРАСТАЮЩЕГО НА ТЕРРИТОРИИ КЫРГЫЗСКОЙ РЕСПУБЛИКИ.....	119
Эркебаева А.Н., Жалалова Н.К., Муратбекова З.М.	
“ПОДАГРИН” ТАБЛЕТКА СУБСТАНЦИЯЛАРНИ ТЕХНОЛОГИК ХОССАЛАРИНИ ЎРГАНИШ.....	120
Эрназаров А.М., Юнусова Х.М.	
ГЕПАТОПРОТЕКТОР ХУСУСИЯТГА ЭГА БЎЛГАН БИОЛОГИК ФАОЛ ҚЎШИМЧАНИНГ ЯРОҚЛИЛИК МУДДАТИНИ ЎРГАНИШ	121
Эшмуратов З.Н., Ubaydullayeva X.A.	
БИОФАРМАЦЕВТИЧЕСКИЕ ИССЛЕДОВАНИЯ ТАБЛЕТОК СПАЗМОЛИТИЧЕСКОГО ДЕЙСТВИЯ	122
Юнусова Х.М., Исмаилова М.К.	

3-SEKSIYA.

DORI VOSITALARINI STANDARTLASH, FARMATSEVTIK VA TOKSIKOLOGIK KIMYOVIY TAHLIL

STANDARDIZATION OF DRUGS, PHARMACEUTICAL AND TOXICOLOGICAL CHEMICAL ANALYSIS

СТАНДАРТИЗАЦИЯ ЛЕКАРСТВЕННЫХ СРЕДСТВ, ХИМИКО-ФАРМАЦЕВТИЧЕСКИЙ И ТОКСИКОЛОГИЧЕСКИЙ АНАЛИЗ

TORASEMID DORI VOSITASINI SUVLI MUHITDAN EKSTRAKSIYA SHAROITLARINI O'RGANISH	123
Abdullabekova N.A., Usmanaliyeva Z.U.	
SYNTHESIS AND CHARACTERIZATION OF LAYERED DOUBLE HYDROXIDE TWO DIMENSIONAL NANOSTRUCTURES	124
Abdusalomov J.T., Suyundikov M.K., Azizov Sh.I., Sharipov M.A., Turayev A.S., Yong-Ill Lee.	
MEFEDRONNI SUVLI MUHITDAN EKSTRAKSIYA QILISH USLUBLARINI ISHLAB CHIQISH.....	124
Abduxaliqova N.O., Yuldashev Z.A., Primuxamedova X.I.	
YANTOQ O'SIMLIGIDAN QURUQ EKSTRAKT OLISH VA UNI TAHLILI	125
Azlarova N.X., Saidvaliev A.K.	
DETERMINATION OF MAPROTYLINE IN BLOOD AND URINE BY UV SPECTROPHOTOMETRIC METHOD	126
Baiurka S.V., Karpushyna S.A.	
FORMULATION AND EVALUATION OF DIFFERENT NANOGELS OF TAPINAROF FOR TREATMENT OF PSORIASIS.....	127
Balogh B., Pető Á., Haimhoffer Á., Sinka D., Dóra K., Argenziano M., Cavalli R., Bácskay I.	
QUANTITATIVE DETERMINATION OF ANISE OIL IN AMMONIA-ANISE DROPS BY HPLC METHOD	127
Blazheyevskiy M.Ye., Kryskiv O.S., Moroz V.P.	

ФАРМАКОЭКОНОМИЧЕСКИЕ АСПЕКТЫ ЛЕКАРСТВЕННОГО ОБЕСПЕЧЕНИЯ БОЛЬНЫХ ТУБЕРКУЛЕЗОМ	368
Рахымбаев Н.А., Абилдаева Г.У.	
РЕЗУЛЬТАТЫ АНКЕТИРОВАНИЯ ВРАЧЕЙ В г. ДУШАНБЕ ПО РАСПРОСТРАНЕННОСТИ ЗАБОЛЕВАНИЙ ИБС И АГ	368
Саидова М.Н.	
АНТИФУНГАЛ ТАЪСИРГА ЭГА БЎЛГАН КЛОТРИМАЗОЛ АСОСИДАГИ ДОРИ ТУРЛАРИ АССОРТИМЕНТИНИНГ КОНТЕНТ ТАҲЛИЛИ	369
Сайфиева А.С., Шарипова С.Т.	
КОНТЕНТ-АНАЛИЗ ЛЕКАРСТВЕННЫХ СРЕДСТВ, ПРИМЕНЯЕМЫХ ПРИ ЛЕЧЕНИИ РЕВМАТОИДНОГО АРТРИТА	370
Сейтниязова Б.М., Суюнов Н.Д.	
АНАЛИЗ ДОСТУПНОСТИ И ЦЕН НА ЖИЗНЕННО ВАЖНЫЕ ЛЕКАРСТВЕННЫЕ СРЕДСТВА В КАЗАХСТАНЕ	371
Сейтова Ж.Д., Аширов М.З.	
ФАРМАКОЭКОНОМИЧЕСКИЕ АСПЕКТЫ ТЕРАПИИ КОЖНЫХ ЗАБОЛЕВАНИЙ В КАЗАХСТАНЕ	371
Серикбаева Э.А.	
АВС/NDDD – МЕТОДОЛОГИИ ПРИ ОПРЕДЕЛЕНИИ ПОТРЕБЛЕНИЯ ПЕРОРАЛЬНЫХ ГИПОГЛИКЕМИЧЕСКИХ СРЕДСТВ	373
Хидоятова З.Ш., Азимова М.Т.	
СРАВНИТЕЛЬНЫЙ АНАЛИЗ МЕТОДОВ ЛИЦЕНЗИРОВАНИЯ АПТЕЧНОЙ ДЕЯТЕЛЬНОСТИ В РОССИЙСКОЙ ФЕДЕРАЦИИ И УЗБЕКИСТАНА	374
Хидоятова З.Ш., Азимова М.Т., Давлетьярова А.Р.	
ОБЩИЕ ВОПРОСЫ КЛИНИЧЕСКОЙ ФАРМАЦИИ В СИСТЕМЕ ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ КАЗАХСТАН, РОЛЬ ДЕЯТЕЛЬНОСТИ КЛИНИЧЕСКОГО ФАРМАЦЕВТА	374
Шопабаева А.Р., Латыпова И.М.	

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