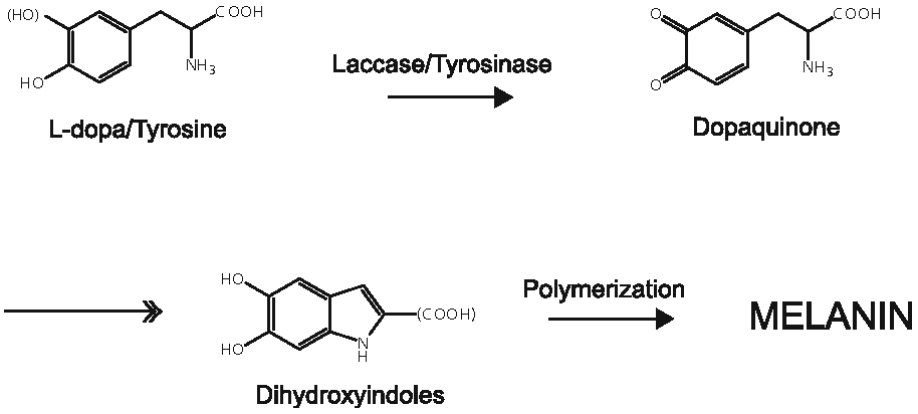
Deviation from the melanin content causes freckles, chloasms, lentigo, vitiligo, birthmarks and age spots. Melanin synthesis disorders can be eliminated only after its causes have been identified

The macromolecular complex of tyrosine and serine transformations by successive oxidation reactions leads to the synthesis of a heterocyclic polymer – melanin.The first two stages of the process take place with the active involvement of the tyrosinase enzyme:



For the correction of the content of melanin in the tissues use three groups of agents. The first is irreversible inactivators that form covalent bonds with tyrosinase (arbutin, coic acid). The second group of inhibitors include substances that inhibit melanin synthesis. They form temporary bonds with tyrosinase (the "gold standard" is hydroquinone, azelaic acid, niacinamide, ascorbic acid and its derivatives). TThe third group includes preventive agents ("ANA" acids - α-hydroxy acids). They are used for chemical peels, fluffy of the epidermis. Good results are achieved only by a competent combination of substances.

Conclutions. For the correction of pigmentation is used a wide arsenal of different mechanism of action of organic compounds. These include: phenols and their glycosides (hydroquinone, arbutin), dicarboxylic acids (azelaic), α-hydroxy acids (glycolic, malic, citric, salicylic, almond), heterocyclic compounds (koy, ascorbic acids).

GOLD IN MEDICAL AND BIOLOGICAL RESEARCHES, IN MEDICINE AND PHARMACY

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Introduction. The role of gold in human history, its content in the environment and element value for the human body. The use of gold and its compounds in pharmacology, traditional therapy and modern electronics is considered.

Aim. The use of nanogold, its chemical compounds and radioactive nuclides in various fields of biomedicine is explained by high chemical stability, low toxicity, relative simplicity of the synthesis and modification of the obtained products, economic and environmental safety, rapid excretion of the ^{198}Au radionuclide from the body, and action selectivity.

Materials and methods. In the 20s of the last century researchers found that gold chlorides have a bactericidal effect. Some gold compounds exhibit antibacterial effects against Helicobacter pylory as well as antifungal activity. Gold compounds such as aurothioglucose, sodium aurothiomalate, triethylphosphine have also been tried to treat syphilis, alcoholism, morphine addiction, nephritis, anemia, neurasthenia and premature aging. A more effective and less toxic compound was gold sodium thiosulfate $AuNaS_2O_3$ which has successfully proved itself in the treatment of lupus. Since the middle of the last

century complex compounds of gold with organic ligands have been used in medical practice for example krizolgan, trifol, auranofin, aurootioprol, etc. Crysolgan was widely used in Europe to fight tuberculosis, and trifol less toxic and more effective than sodium gold thiosulfate - as a cure for erythematous lupus. Later a highly active drug cryzanol $(Au\text{-}S\text{-}CH_2\text{-}CHOH\text{-}CH_2SO_3)_2Ca$ was synthesized and used to treat tuberculosis, lupus, and leprosy. The interaction of tetrachloroaurate acid $H[AuCl_4]$ with glycine, histidine and tryptophan yielded substances with high antimicrobial activity. The resulting substances are tested as part of medical drugs for the treatment of rheumatoid and psoriatic arthritis, pulmonary tuberculosis and larynx, erythematous lupus, epilepsy, syphilis.

There are great prospects in the use of gold due to the rapid developing of nanotechnology. They make it possible to synthesize gold nanoparticles (NPs), modify them with molecules of biologically active substances and use them for early diagnosis and treatment of many diseases.

NPs are synthesized by two methods: dispersion and condensation. The disadvantage of the dispersion method is the formation of particles that are inhomogeneous in size. The condensation method makes it possible to obtain gold nanoparticles uniform in size with a diameter of 8-120 nm by chemical reduction of ions with various reducing agents. Sodium citrate or borohydride, ascorbic and isoascorbic acids, EDTA, an alkaline solution of hydrogen peroxide and potassium thiocyanate are used as reducing agents. The rate of NPs formation depends on the concentration of reagents and the chemical nature of the reducing agent and the size of the NPs depends on the rate of nucleation and the rate of condensation.

Results and discussion. The opinions of experts on gold compounds are mixed. Of course they help the patient but they have distinct side effects and have many contraindications. Gold compounds are toxic, they accumulate in the liver, kidneys, spleen, hypothalamus that leads to adverse reactions such as dermatoses, proteinuria, diarrhea, less often to more serious organic complications: pulmonary fibrosis, enterocolitis, nephrotic syndrome, aplastic anemia, thrombocytopenia, leukopenia and others. The appropriateness of using gold compounds in medicine is controversial since they exacerbate morphofunctional changes caused by the underlying disease. These facts indicate that gold is not the best agent for creating dosage forms. Nowadays gold therapy is one of the most effective methods of treating rheumatoid arthritis. The mechanism of therapeutic and toxic effects of Au compounds is associated with inhibition of thiol enzymes that is confirmed by studies on the interaction of gold compounds with blood proteins, enzymes, immunoglobulins and hormones. It is based on the ability of Au to inhibit macrophages as a result of which the development of subsequent pathological immune reactions of the body is inhibited. An important advantage of gold preparations in comparison with other immunosuppressants is the possibility of prescribing them to patients with concomitant chronic infections or oncological diseases.

Modern medicine uses various forms of gold. For the cancer diagnosis and treatment colloidal solutions containing the ions of the synthetic radioactive isotope ^{198}Au are used. An isotope is synthesized by neutron irradiation of natural ^{197}Au. The half-life of ^{198}Au is 2.8 days. The presence of β- and γ-radiation contributes to the creation of high tissue doses and the determination of isotope dislocation sites. Colloidal solutions of radioactive nanogold selectively accumulate in the cells of the reticuloendothelial system and on the structures of the connective tissue which allows them to be used for the diagnosis and treatment of cancer tumors. In biomedicine modern methods are being developed for introducing gold nanocapsules into the tumor tissue followed by heating them with infrared rays, as a result cancer cells die and healthy ones are not damaged.

Conclusions. Drug based on gold compounds in many cases have a positive therapeutic effect but pronounced body toxic reactions appear due to their use. Therefore, their use is limited. The situation is changing with the development of nanotechnology which makes it possible to obtain gold NPs with a diameter of 1 to 100 nm or more. They are used in the diagnosis and therapy of malignant tumors and in biomedical research for the delivery of drugs directly to the area of the cancer tumor.

An independent branch of knowledge has now been formed which includes the use of gold NPs in biomedical researches, diagnostics, biosensors, photothermal and photodynamic therapy and targeted delivery of drugs and genetic materials. Great importance for biomedicine are the developed methods for

the synthesis of gold NPs as well as the simplicity and reliability of methods for modifying their surface by attaching oligonucleotides, peptides, polyethylene glycol and other biologically active components to them. Modified particles circulate longer in the bloodstream and are less affected by cellular components of the immune system. Today it is generally accepted that gold NPs conjugates are excellent labels for the diagnosis of cancer, Alzheimer's disease, AIDS, hepatitis, tuberculosis, diabetes mellitus and other diseases.

PREDICTION OF THE ANTI-INFLAMMATORY ACTIVITY OF NEW S-ALKYL DERIVATIVES OF 1,2,4-TRIAZOL-3-THIONES USING THE PASS COMPUTER PROGRAM AND MOLECULAR DOCKING

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Introduction. Scientists refer the heterocyclic system of 1,2,4-triazole to the privileged structure since most of the derivatives of this heterocycle synthesized exhibit some pharmacological activity, including the anti-inflammatory one. A careful study of the literature data on the spectrum of pharmacological properties of the heterocyclic system of 1,2,4-triazole allows us to confidently assert that the presence of this cycle in the structure of substances determines the manifestation of the anti-inflammatory activity. Moreover, some studies suggest that the presence of the 1,2,4-triazole cycle causes selective inhibition of cyclooxygenase-2 (COX-2). Our analysis of the scientific literature has shown that despite a large number of publications devoted to functional derivatives of 1,2,4-triazole the pharmacological potential of this class of compounds at the present stage is not exhausted.

Aim. Search for selective COX-2 inhibitors based on the basic structure of 4-amino-3-thio-1,2,4-triazole. Modification of the base molecule and creation of a virtual library of S-derivatives of 5-substituted 4-amino(pyrol)-3-thio-4H-1,2,4-triazoles in an amount of 100 compounds (ten groups). Selection of six groups of promising compounds for further synthesis based on the analysis of the results of PASS-prediction and molecular docking.

Materials and methods. The introduction of different pharmacophore fragments into the molecule by modifying the thio group and obtaining S-derivatives of 5-substituted 4-amino(pyrrol)3-thio-4H-1,2,4-triazoles. The following ways of modification have been planned: alkylation of 5-pyridine-4-amino(pyrrol)3-thio-1,2,4- triazole derivatives by haloalkanes (**I**); introduction of the arylideneaniline fragment (**II**) to alkyl derivatives of group (**I**) ; oxidation of 5-(pyridine-4)-4-amino-3-thio-1,2,4-triazole derivatives to alkylsulfonyl derivatives (**III**); introduction of the 5-(pyridine-4)-4-amino-3-thio-1,2,4-triazole fragment of alkylurea (**IV**) into the basic structure; alkylation of 5-(pyridine-4(2,3))-4-amino-3-thio-1,2,4-triazoles (**V-VI)** by α-chloroacetamides; alkylation of 5-(furyl-2)-amino-3-thio-1,2,4-triazoles (**VII)** by α-chloroacetamides; replacement of the amino group in S-alkyl derivatives of 5-(pyridine-2,4)-4-amino-3-thio-*4H*-1,2,4-triazoles (**VIII-IX)** and 5-(furyl-2)-4-amino-3-thio-*4H*-1,2,4-triazoles (**X)** on the pyrrol residue.

The logical and structural assessment of the possible biological effect was performed using the PASS computer system *online*. In order to optimize the targeted search for COX-2 inhibitors as potential anti-inflammatory agents and substantiate the feasibility of the experimental screening for the anti-inflammatory activity the docking studies were also conducted. The docking studies of hypothetical compounds were conducted using a SCIGRESS software package (Fujitsu, Fukuoka, Japan (license 742F6852C191)).