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obtained through the stage of formation of ethyl 5-methylpyrazole-3-carboxylate and 5-methylpyrazole carbohydrazide. The synthesis of 5-(3-(indol-3-yl)propyl)-4-phenyl-1,2,4-triazole-3-thiol was previously accompanied by the interaction of the potassium salt of indole-3-butanoic acid with bromoethane, which made it possible to obtain the corresponding ester . The next stages of chemical transformation included reactions of hydrazinolysis, addition of phenylisothiocyanate and alkaline cyclization. Subsequently, S-alkylation reactions were implemented. Ethanol turned out to be the optimal medium for their implementation. The reaction was carried out with the participation of potassium hydroxide.

The structure of the obtained compounds was confirmed by the data of elemental analysis, ^{1}H NMR spectroscopy and IR spectrophotometry. The individuality of substances is established using high-performance liquid chromatography with electrospray ionization mass spectrometry.

The results. Synthesized S-alkyl derivatives of 5-(3-(indol-3-yl)propyl)-4-phenyl-1,2,4-triazol-3-thiol and 4-phenyl-5-(pyrrol-2-yl)-1,2,4-triazole-3-thiol, their structure was proven and their physical properties were investigated.

The biological potential of the synthesized compounds was previously determined using docking studies. A possible effect on anaplastic lymphoma kinase was obtained using the 2XP2 model, lanosterol 14α-demethylase using the 3LD6 model and cyclooxygenase-2 using the 4Z0L model, which were obtained from the Protein Data Bank.

Conclusions. Conducted *in silico* studies on a number of S-alkyl derivatives of 5-(3-(indol-3-yl)propyl)-4-phenyl-1,2,4-triazole-3-thiol and 4-phenyl-5-(pyrrole-2-yl)-1,2,4-triazole-3-thiol demonstrated the possibility of creating biologically active compounds that can affect the activity of anaplastic lymphoma kinase, lanosterol 14α-demethylase and cyclooxygenase-2.

CREATION OF PROMISING DIURETICS BASED ON THE XANTHINE CORE

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An important problem of modern pharmacology, nephrology and pharmacy is the search for new pharmacological agents for the correction of homeostasis and vital functions of the body.

A change in the water-electrolyte composition of intracellular and extracellular fluids can cause various pathological conditions. Violation of renal excretion of electrolytes plays a significant role in the development of hypertensive conditions.

Renal transport of electrolytes and water is a complex multicomponent process that is implemented at various levels and is under the control of numerous regulatory factors: nervous, hormonal, humoral, physicochemical, etc. Diuretic drugs can affect the leveling of the water-electrolyte balance in the body.

Despite the high therapeutic effectiveness of diuretic drugs: hydrochlorothiazide, furosemide, clopamide, ethacrynic acid, etc. can cause unwanted side effects: hypokalemia, dizziness, headache, metabolic acidosis, hyperlipidemia, hyperglycemia, and others, which limit their practical use.

For the treatment of hypertensive conditions, combined pharmacotherapy is used, which includes the diuretic hydrochlorothiazide and the hypotensive drug losartan, valsartan, irbesartan, which affects the cardiovascular system and kidney function.

Thus, the search for new compounds that have diuretic activity is a relevant and promising direction in the development of original domestic drugs.

The purpose of this work is the synthesis of undescribed in the literature 8-aminosubstituted of 7-(2-hydroxy-3-p-methoxyphenoxy-)propyl-3-methylxanthine and to study their physical, chemical and biological properties.

The melting point was determined by the open capillary method on the PTP-M device. Elemental analysis was performed on the Elementar Vario L cube device, the NMR spectra were taken on the Bruker SF-400 spectrometer (operating frequency 400 MHz, DMSO solvent, TMS internal standard). Molecular descriptors were calculated using the ALOGPS and DRAGON computer programs. Biological properties of synthesized compounds were calculated using the GUSAR and ACD/Percepta Platform. The study of the diuretic effect of the obtained compounds was carried out according to the method of E. B. Berkhin. Hydrochlorothiazide was used as a comparison standard.

Continuing the synthetic research of Professor M. I. Romanenko, the library of 8-aminosubstituted 7-β-hydroxy-γ-aryloxypropylxanthines was expanded. The reaction of 8-bromo-3-methylxanthine with p-methoxyphenoxymethyloxyrane in a dioxane environment results in formation of the 8-bromo-7-(2-hydroxy-3-p-methoxyphenoxy-)propyl-3-methylxanthine, which interaction with primary and heterocyclic amines leads to the synthesis of corresponding 8-aminoderivatives.

The structure of synthesized compounds has been definitely proved by the data of elemental analysis and NMR-spectroscopy.

Further properties of the synthesized compounds were calculated. It has been found that all aminotheophyllines satisfy to the Rule of five. Assisted by computer programs GUSAR and ACD / Percepta Platform, further on there has been calculated the acute toxicity rate for rats and mice. According to the data synthesized substances belong to Class IV of the toxicity. Thus the findings have shown the feasibility of further studies in vitro and in vivo.

Research of the diuretic activity of synthesized compounds showed that, according to the diuretic activity indexes, there were identified compounds that are not inferior to, and in some cases, are more active than the comparison standards.

The above facts clearly demonstrate reasonability and prospects for further search of antioxidant agents in the series of xanthines, especially among their 8-aminosubstituted 7-β-hydroxy-γ-aryloxypropylxanthines. For final conclusions it is necessary to significantly expand the number of the compounds synthesized.

STAGES OF DEVELOPMENT OF PHARMACEUTICAL TECHNOLOGIES

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Introduction. Modern pharmaceutical technology includes different areas of development of pharmaceutical production. Against the backdrop of the development of science and technology, pharmaceutical technology has developed significantly. As in other industries, pharmacy is characterized by a change in product generations, the evolution of which directly depends on the market needs to improve the quality of drug research and development to provide more guarantees for human health [1]. Traditional dosage forms have been replaced by drugs with a prolonged effect. Further, because of biopharmaceutical and biotechnological research, dosage forms with controlled release have been created [2]. And with the active introduction of nanotechnologies into pharmacy, gene therapy appeared.

Materials and methods. Pharmaceutical technology development stages in search of improving the quality of drug research and development, validation and verification of all production and control processes, involving related industries in the development of new drugs, in order to create a wider space for the development of the pharmaceutical process.

Results and discussion. Traditional dosage forms are the first generation of drugs. Poor bioavailability and a short therapeutic optimum increase the frequency of use of these drugs. Long-acting dosage forms have reduced the frequency of drug use and have become the next stage in the