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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

development of pharmaceutical technologies. The frequency of administration decreased, but the concentration of active substances in the systemic circulation was not regulated and often differed from the therapeutic optimum.

With the active development of biopharmaceutical research, the third generation of drugs with controlled release of active substances has been developed, which made it possible to control the therapeutic optimum of active substances in the systemic circulation. Solid dispersed systems increased the bioavailability of tablets and reduced the frequency of administration, while macromolecular systems increased the bioavailability of other routes of drug administration into the body. The third generation of drugs guarantees a stable intake of the drug into the body, reduces side effects, ensures dosing accuracy, safety, a wide spectrum of action and convenience for the patient. The fourth generation of pharmaceutical technology is already targeting and delivering active ingredients to target cells. These are magnetically controlled therapeutic systems and liposomes. The fifth generation is gene therapy drugs that deliver active substances to cell organelles. These include: iRNA, shRNA, antisense oligonucleotide, CRISPR/Cas9 system, plasmid DNA and miRNA have shown great potential in biomedical applications.

Conclusions.

1. As a result of the study, five stages in the development of pharmaceutical technologies have been established.

2. Traditional drugs have been replaced by controlled release drugs.

3. Research in the field of targeted delivery of active substances to targets and cell organelles is relevant.

References

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SYNTHESIS OF ANTISEPTIC SOLUTIONS OF N-CHLOROTAURINE BY ACTIVATION OF CHLORINE-ACTIVE POLYMERS

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Recent events related to the COVID-19 pandemic have demonstrated the urgent need for the search and implementation of new drugs and technologies for disinfection and antiseptic treatment of various surfaces as the most rational and economically feasible part of the infectious disease prevention system. Various derivatives of active chlorine are effective and available chemical reagents for this purpose, among which N-chlorotaurine, the substance with a wide spectrum of biological activity and extremely high tolerability, occupies a special place [1]. It has been proven that its solutions can be used for the treatment of chronic ulcers, dermatitis, psoriasis, and when used internally – for respiratory tract infections and for detoxification.

Synthesis of N-chlorotaurine solutions from taurine and trivial chlorinating agents such as sodium hypochlorite is possible in many ways and is not difficult in the laboratory, but this does not allow achieving sufficiently high purity; obtaining its sodium salt in crystalline form is also possible, but this process is much more complicated, and the product itself must be stored at a temperature of -20°C. The main problem limiting the medical use of N-chlorotaurine is the inevitable instability of its solutions, especially at elevated temperatures, due to dehydrohalogenation and subsequent deamination. Therefore, it is topical to develop methods for obtaining such drugs *in situ* for their immediate use.