2. The structure of the synthesized compounds was proved with the help of the elemental analysis, the NMR spectroscopy data.

3. The hypocholesterolemic activity of the obtained compounds were studied. Priorities for further research of biologically active compounds have been outlined.

THE DESIGN OF NEW ANTIBACTERIAL AGENTS OF DERIVATIVES QUINOLINE-4-ONES

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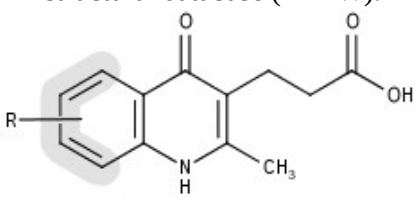
Introduction. One of the greatest challenges to global public health today is antimicrobial resistance. Antimicrobial resistance is the ability of a microbe to resist the effects of medication that once could successfully treat the microbe. Antimicrobial resistance is currently responsible for over 700,000 deaths annually around the world and has been predicted to exponentially rise o above 10 million deaths annually by 2050, with an estimated economic cost of $100 trillion [1]. As antimicrobial resistance continues to rise, the effective treatment of an ever increasing range of infectious diseases caused by drug resistant parasites, viruses, fungi and bacteria will be threatened [2,3]. The medical need for novel antimicrobial treatment options globally is undeniable, and efforts to discover and develop novel antimicrobial drugs should be intensified.

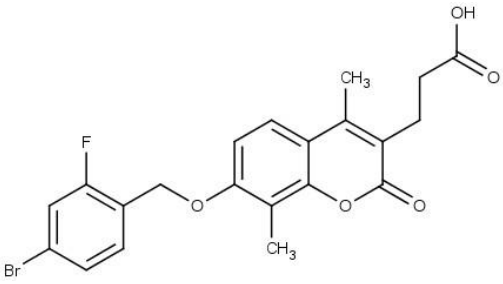
The increasing prevalence of drug-resistant bacterial infections demands the development of new antibacterials that are not subject to existing mechanisms of resistance. Recently, a special interest of researchers as new targets has attracted special proteins called helicases. Helicases are a class of enzymes vital to all living organisms. Their main function is to unpackage an organism's genes. Several features of enzymes of bacterias, such as, the *B. anthracis* and *S.aureus* replicative DNA helicase make them particularly attractive as targets for the discovery of new antibacterial therapeutics for biodefense. First, they are members of a drug-validated pathway. While gyrase, topoisomerase IV, and DNA polymerase III have been targeted successfully, helicase remains an untapped vulnerability in the mechanism of bacterial DNA replication. Second, they are multifunctional proteins, providing multiple opportunities for antibacterial intervention. Third, helicase activity is essential to bacteria. Fourth, the primary structures of the *B. anthracis* and *S. aureus* replicative helicases differ significantly from those of their eukaryotic counterparts, indicating that bacterial-specific inhibitors of helicase may be identified.

Aim. Earlier, at the Department of Medical Chemistry NUPH, it was found that the 3-(4-oxo-2-methylquinoline-3-yl)propanoic acids (I) are a promising scaffold to research of new antimicrobial medicines. At the same time, it is known that some coumarin-based inhibitors (II, III) that are ligands to an underexploited bacterial target, namely, replicative helicase. The main purpose of this work was to conduct the selection of possible substituents in the benzene ring of the quinolone cycle for the 3-(4-oxo-2-methylquinoline-3-yl)propanoic acids as possible inhibitors of helicase using the methods of computer-aided drug design (CADD).

Materials and methods. Common methods of chemoinformatics, were carried out using the computer platform ChemAxon: calculation of molecular descriptors, the definition of 2D molecular similarity; optimization of the geometry of molecules and the search conformers by molecular mechanics force fields, the alignment of 3D molecules and the determination of 3D molecular similarity. The docking studies were carried out by helping the Autodock 4.2.6 program. The targets, B. subtilis helicase structure, were taken from the RSCB PDB structural database (4M4W).



I



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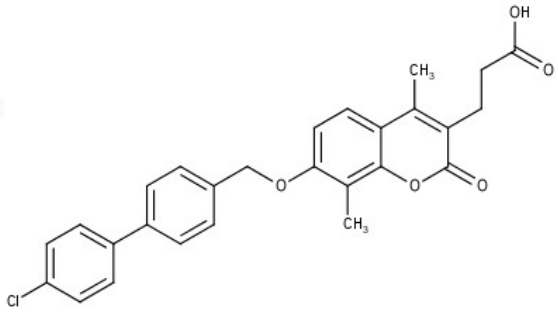

III

Results and discussion. As a result of the research, a large-scale variation of various electron density substituents in the benzene ring of the quinolone heterocycle was carried out. Substitution groups were also ranked by the number of rotating bonds, and parameters such as lipophilicity, topological polar surface areas, molecular volume, etc. The variation of the substituents was carried out at the C-7 position of the quinolone heterocycle. Molecular docking studies have shown the ability to interact with minimal binding energy between helicase enzyme and derivatives of 3-(4-oxo-2-methylquinoline-3-yl) propanoic acids.

Conclusions. Carried out studies using CADD methods did not disprove our assumption about the possibility of antimicrobial activity of the derivatives of 3-(4-oxo-2-methylquinoline-3-yl) propanoic acids as inhibitors of replicative DNA helicases, in particular, DnaB type.

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THE USE OF THE IN SILICO STUDIES WITH PURPOSE OF SEARCHING POTENTIAL ANTIMICROBIAL DRUGS

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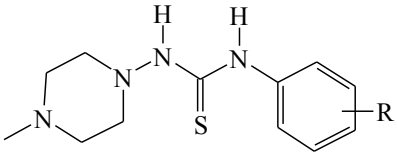
Introduction. The problem of finding new biologically active compounds with a specific biological activity and low toxicity is one of the most important tasks of pharmaceutical chemistry. Pre-experimental studies *in silico* successfully used at various stages of the search and optimization of the structures of biologically active compounds.

Purpose of our work is *in silico* studies of biological activity, adverse effects and acute toxicity of thiourea derivatives**.** It allows us to eliminate the potentially toxic substances as unpromising objects for experimental pharmacological screening.

Materials and methods. The objects of our study – 1-(N-methylpiperazin-1-yl)-3-(R-phenyl)thioureas *I (a-i)* of general formula:



I (a-i)

where, a) R=H, b) R=2-CH_3, c) R=3-CH_3, d) R=2,3-diCH_3, e) R=4-C_2H_5, f) R=4-OCH_3, g) R=3,6-diOCH_3, h) R=4-OC_2H_5, i) R=4-Br.