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SYNTHESIS AND BIOLOGICAL POTENTIAL OF 1,2,4-TRIAZOLE DERIVATIVES WITH A 2-BROMO-5-METHOXYPHENYL FRAGMENT

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Derivatives of 1,2,4-triazole currently occupy leading positions among various biologically active substances. This class of heterocyclic compounds has attracted the attention of specialists not only in the field of pharmacy, but also scientists from various fields for many decades. It is known that the compounds formed with the participation of the 1,2,4-triazole nucleus and various functional substituents have high biological activity. Their low toxicity and high reactivity make this class of compounds particularly attractive.

During the last five years, numerous new medicines and fertilizers have been registered in the world, the active ingredients of which are based on 1,2,4-triazole derivatives. All these factors point to the prospects of further studies of new substituted 1,2,4-triazole both theoretically and practically.

The purpose of the work is the purposeful synthesis of new promising substances - derivatives of 1,2,4-triazole-3-thiones containing an aromatic substituent in their structure, the study of biological activity, as well as the establishment of regularities between the chemical structure and pharmacological action of the synthesized compounds.

Materials and methods. The primary stage was the bibliosemantic analysis of scientific literature. After drawing certain conclusions from scientific sources, the synthesis was started. The synthetic part consisted in the synthesis of initial thiols. 2-bromo-5-methoxybenzoic acid was used as the key compound. Through a series of successive chemical transformations, namely, reactions of esterification, hydrazinolysis, nucleophilic addition of substituted isothiocyanates (methyl, ethyl, phenyl) and subsequent intramolecular alkaline heterocyclization, the original thiols were obtained.

The structure of the synthesized compounds was confirmed by a modern physicochemical complex (^{1}H-NMR, IR spectroscopy), and their individuality was confirmed by chromatography-mass spectrometry.

To expand the library of compounds, S-alkyl derivatives were synthesized as a result of alkylation reactions of halogens with alkanes (from iodo methane to bromodecane).

The next stage was the prediction of possible biological activity using the SwissTargetPrediction online service. According to the results, it was established that the derivatives of this group are highly likely to exhibit anti-inflammatory, antioxidant, hypoglycemic, antihypoxic, antimicrobial and antifungal activity.

To confirm the screening data, molecular docking was performed for anti-inflammatory, antimicrobial and antifungal activity.

The results. As a result of the work, 13 new compounds were synthesized, the structure and individuality of these substances were confirmed. Based on the results of biological activity prediction and docking studies, the number of compounds for more in-depth studies is outlined.

Conclusions. Therefore, in silico studies of the biological activity of 1,2,4-triazole derivatives with a 2-bromo-5-methoxyphenyl fragment indicate the prospect of conducting pharmacological tests of all tested compounds for the presence of anti-inflammatory, antimicrobial and antifungal activity.