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SYNTHESIS AND PROPERTIES OF S-DERIVATIVES OF 5-(2-BROMO-4-FLUOROPHENYL)-4-PHENYL-1,2,4-TRIAZOLE-3-THIOL

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Introduction. In recent years, the chemistry of nitrogen-containing heterocyclic compounds has attracted increasing attention from researchers. This is primarily due to the fact that over the past decades, many pharmaceutical agents containing a 1,2,4-triazole core have been widely used in medicine. This structural fragment is characterized by diverse biological activity and relatively low toxicity. Studies have shown that the combination of a 1,2,4-triazole ring with a dihalophenyl fragment may result in the appearance of new promising properties that warrant further investigation. Therefore, this area of research remains highly relevant.

The **objective** of this study is to synthesize new S-derivatives of 5-(2-bromo-4-fluorophenyl)-4-phenyl-1,2,4-triazole-3-thiol and to evaluate their potential biological activity *in silico*.

Materials and methods. The starting compound for the synthesis was 5-(2-bromo-4-fluorophenyl)-4-phenyl-1,2,4-triazole-3-thiol. It was subjected to alkylation reactions with haloalkanes, halogenocarboxylic acids and their corresponding esters and amides. The reactions were carried out in an alkaline-alcoholic medium. The resulting products were crystallized from a water–methanol mixture. The structures of the synthesized compounds were confirmed using a set of modern physicochemical analysis methods with instruments available at ZSMPhU.

To identify potentially biologically active compounds and their possible mechanisms of action, *in silico* screening methods were applied, including the SwissADME/Tox platform, molecular docking (AutoDock) and the Toxicity Estimation Software Tool (TEST). Based on the analysis of the obtained data, it was determined that the synthesized compounds are highly likely to exhibit antimicrobial, antifungal, anti-inflammatory, analgesic, antihypoxic and antioxidant activities, while showing virtually low levels of toxicity and mutagenicity, as well as an overall favorable pharmacological profile. These results formed the basis for further investigation of the biological properties of the studied series of compounds using *in vitro* and *in vivo* methods.

Results. The study encompasses the synthesis of 12 new compounds, optimization of their structures and elucidation of their chemical composition, excluding intermediate products. Preliminary *in silico* prescreening studies indicated that the synthesized compounds are likely to exhibit antimicrobial, antifungal, anti-inflammatory, analgesic, antihypoxic and antioxidant activities.

The **conclusions** state that, within the framework of the conducted study, a series of alkyl derivatives of 5-(2-bromo-4-fluorophenyl)-4-phenyl-1,2,4-triazole-3-thiol, as well as a series of 2-(5-(2-bromo-4-fluorophenyl)-4-phenyl-1,2,4-triazole-3-thio)alkanoic acids, their esters and amides were successfully synthesized. The synthesized compounds were evaluated for their potential biological activity and the results indicate the feasibility and relevance of further investigation of their biological properties.

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ANTIRADICAL ACTIVITY OF A SERIES OF NOVEL 6-SUBSTITUTED 3-R-2H-[1,2,4]TRIAZINO[2,3-C]QUINAZOLIN-2-ONES

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The investigation of the antiradical activity of compounds constitutes an integral part of a comprehensive assessment of their potential as biologically active agents. This approach is justified by the accessibility of the corresponding analytical techniques and by the wide range of biological activities that are closely associated with antiradical and antioxidant properties. Compounds exhibiting pronounced antioxidant and antiradical effects are considered promising candidates for further studies aimed at the development of anti-ischemic, cardioprotective, hepatoprotective, and anti-inflammatory pharmaceutical agents. Among the numerous methods used to evaluate antiradical activity, one of the most widely applied is based on the interaction with the 2,2-diphenyl-1-(2,4,6-trinitrophenyl)hydrazin-1-yl radical (DPPH) [1]. This method has gained extensive application for determining the antiradical activity of both natural and synthetic compounds due to its high accessibility, procedural simplicity, and reproducibility of the obtained results.

This particular method was selected for the preliminary evaluation of the pharmacological potential of a series of previously unknown 6-substituted 3-R-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones (compounds **1–6**, Fig. 1), which were synthesized by Assoc. Prof. K. P. Shabelnyk and Ph.D. O. A. Hrytsak at the Department of Pharmaceutical, Organic and Bioorganic Chemistry, Zaporizhzhia State Medical and Pharmaceutical University.

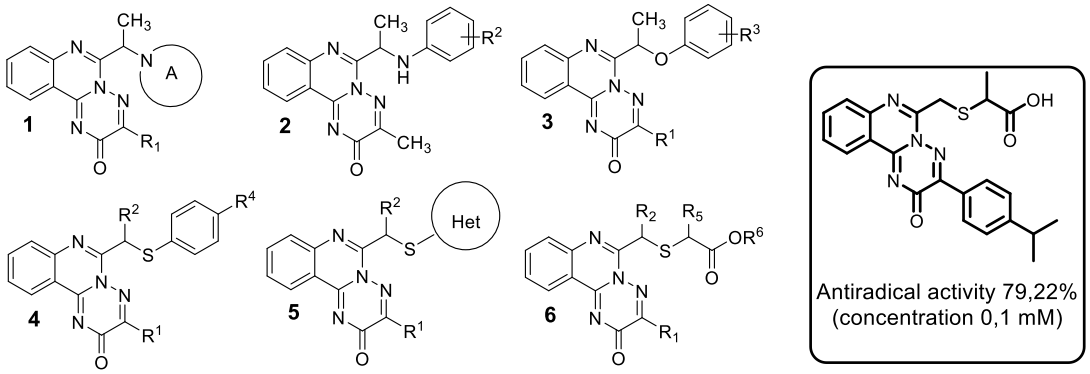

Fig. 1 The structure of the studied compounds.

The obtained results demonstrated that compounds **1**, **3**, and **4** exhibited no antiradical activity, whereas certain representatives of class **2** showed moderate activity. Compounds of series **5** displayed considerable variation in antiradical properties depending on the structure of the heterocyclic substituent at position 6 of the [1,2,4]triazino[2,3-*c*]quinazoline core. The most active compound, 2-(((3-(4-isopropylphenyl)-2-oxo-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-6-yl)methyl)thio)propanoic acid (Fig. 1), demonstrated a higher antiradical effect than the reference compound (ascorbic acid). It was established that within the investigated series, compounds containing a thiomethyl fragment exhibited superior antiradical activity. The obtained results indicate the promise of several studied compounds as potential biologically active agents. In future research, these compounds are planned to be investigated for pharmacological activities associated with their antiradical properties.

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