

**MOLECULAR DOCKING STUDIES OF NOVEL 1,2,4-TRIAZOLE
DERIVATIVES WITH 5BK8 AND 9EHA PROTEIN TARGETS**

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Currently, heterocyclic compounds, particularly 1,2,4-triazole derivatives, are of considerable importance in the search for biologically active compounds and the development of promising pharmaceutical agents. Since compounds containing a 1,2,4-triazole ring exhibit a broad spectrum of biological activities, the synthesis of new derivatives and the investigation of the relationship between their structures and biological properties represent one of the relevant areas of modern scientific research.

During the study, molecular docking investigations were carried out to theoretically evaluate the interactions of the synthesized compounds, N-(4-(6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl)phenyl)acetamide, N-(4-(6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl)phenyl)propionamide, and N-(4-(6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl)phenyl)benzamide, with biological targets. Macromolecules with the identifiers 5BK8 and 9EHA, obtained from the Protein Data Bank, were selected as biological targets for the molecular docking studies.

According to the molecular docking results, the binding energies of N-(4-(6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl)phenyl)acetamide with the 5BK8 and 9EHA macromolecules were –8.7 and –8.0 kcal/mol, respectively. For N-(4-(6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl)phenyl)propionamide, the corresponding binding energies were –8.4 and –7.6 kcal/mol, whereas for N-(4-(6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl)phenyl)benzamide, they were –10.4 and –8.1 kcal/mol, respectively. Among the obtained results, the benzamide derivative exhibited the highest affinity toward the 5BK8 macromolecule, with a binding energy of –10.4 kcal/mol.

Analysis of the interactions between the ligands and the active site of the protein revealed the formation of various non-covalent interactions involving amino acid residues, including hydrogen bonds, π -anion, π -alkyl, and van der Waals interactions. In particular, the amino acid residues ARG220, ASN217, GLU315, ASP489, LYS492, and MET496 located in the active site of the 5BK8 macromolecule were found to participate in the formation and stabilization of the ligand–protein complexes.

The obtained results demonstrate that the synthesized 1,2,4-triazole derivatives are capable of forming stable complexes with the selected biological targets. In particular, the high binding affinity of N-(4-(6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-3-yl)phenyl)benzamide indicates that this compound may be considered a promising candidate for further biological and pharmacological investigations.

The docking results showed that modification of the amide fragment influenced the binding affinity of the synthesized compounds. In particular, the benzamide derivative demonstrated stronger interaction with the 5BK8 target, indicating its potential for further biological studies. This work was supported by the Academy of Sciences of the Republic of Uzbekistan.