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IN SILICO STUDY OF THE TOXICITY AND BIOLOGICAL ACTIVITY OF 1,2,4-TRIAZOLE DERIVATIVES CONTAINING A HETEROCYCLIC SUBSTITUENT

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A complex mechanism of testing new compound begins, before a new substance becomes a medicine and begins to be sold in pharmacies. First of all, it is necessary to prove that the compound is low-toxic and pharmacologically active. Even 20 years ago, it was an alternative study of pharmacological activity using *in vitro* or *in vivo* methods. Now, when science and computer technology are advanced, primary research can be realized based on the prediction of various computer programs. These methods help to save animals and, based on the forecast, conduct a targeted search for a highly active substance.

The aim of the work was to study the toxicity parameters and Docking analysis of pharmacological activity data of already synthesized substances in order to obtain more extensive information about the benefits of the substances for modern society.

To study various parameters of toxicity was used the Toxicity Estimation Software Tool (TEST), an open-source application developed by the US EPA. Toxicity Estimation Software Tool (ver. 5.1.2). The TEST software is trained on the endpoint from the EPA ECOTOX database (US EPA 2022). Each cross-reading model or regression model has a specific application. The application of the software allows the calculation of an approximate threshold LD_{50} value based on the prediction of each model and the combined average value of the component models. The DockingPie plugin was used to analyze the possible pharmacological activity and study the docking data of ligands and protein.

As a result of the study, 35 compounds of 1,2,4-triazole derivatives containing pyridin-2-yl, pyridin-3-yl, and pyridin-4-yl substituents at the 5th position were analyzed (Fig. 1). Analysis of toxicity in silico showed that the compounds belong to the III-th toxicity class (low-toxic substances) and are not mutagenic. The bond of compounds with the following enzymes were also investigated: Peroxiredoxin (peroxidase) (PDB: 3MNG); NO synthase (PDB: :6NGJ); NAD(F)H-oxidase (PDB: 2CDU); Tyrosinase: (PDB: 3NM8); NMDA receptor (PDB: 4KFQ); Hemoxygenase, (PDB: 1N3U).

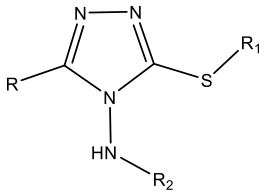

Fig. 1. Analyzed 1,2,4-triazole derivatives

This study allows to correctly orient yourself in the further pharmacological analysis already *in vitro* or *in vivo* methods. The search for compounds with high pharmacological activity and low toxicity continues.