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STRUCTURE-BASED VIRTUAL SCREENING OF NEW SELECTIVE INHIBITORS OF IMIDAZOLEGLYCEROL-PHOSPHATE DEHYDRATASE FROM MYCOBACTERIUM TUBERCULOSIS

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Imidazoleglycerol-phosphate dehydratase from Mycobacterium tuberculosis (IGPD Mt), which catalyzes the conversion of imidazoleglycerolphosphate (IGP) to imidazoleacetol-phosphate (IAP) in the histidine biosynthesis pathway, is present only in bacteria, fungi and plants. Moreover animals and microorganisms, plants need amino acid histidine for their growth and development [1]. There is possibility of usage enzyme IGPD as target for selective drug-design because IGPD is not synthesized in mammals.

In this work we carried out searching for new inhibitors of protein IGPD by method of virtual screening with Internet-service Mcule [2]. Protein IGPD in complex with its substrate was chosen for screening (PDB ID: 4LOM). Once this is done model of active site of IGPD was created. It is formed by three subunits where coordinates of atoms of phosphate group of substrate were selected as center of docking field.

The amount of potential ligands was 974, of which were adopted only four with reference to the scoring docking function and the Lipinski`s rules. Refinements of location of the inhibitors in the field of active site were made by program package GROMACS [3]. Also we identified amino acid residues, which are responsible for bind between the chosen ligands and the active site of protein.

The achieved data will be used in future for further searching of inhibitors of IGPD as potential tuberculosis drugs.

This work was done by usage of high-performance computing of federal center of shared use in the Kurchatov Institute [4].

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