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Structure-Based Virtual Screening and in Silico Toxicity Test of Compounds against Mycobacterium tuberculosis 7,8-Diaminopelargonic Acid Aminotransferase (MtbBioA)

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Abstract : One of the major interferences in the Philippines' tuberculosis control program is the widespread prevalence of Mtb strains that are resistant to known drugs, such as the MDR-TB (Multi Drug Resistant Tuberculosis) and XDR-TB (Extensively Drug Resistant Tuberculosis). Therefore, there is a pressing need to search for novel Mtb drug targets in order to be able to combat these drug resistant strains. The enzyme 7,8-diaminopelargonic acid aminotransferase enzyme, or more commonly known as BioA, is one such ideal target, as it is known that humans do not possess this enzyme. BioA primarily plays a key role in Mtb's lipid biosynthesis pathway; more specifically in the synthesis of the enzyme cofactor biotin. In this study, structure-based pharmacophore screening, docking, and ADMET evaluation of compounds obtained from the DrugBank chemical database were performed against the MtbBioA enzyme. Results of the screening, docking, ADMET, and TOPKAT calculations revealed that out of the 6,516 compounds in the library, only 7 compounds indicated more favorable binding energies as compared to the enzyme's known inhibitor, amiclenomycin (ACM), as well as good solubility and toxicity properties. Moreover, out of these 7 compounds, Molecule 6 exhibited the best solubility and toxicity properties. In the future, these lead compounds may then be subjected to bioactivity assays in vitro or in vivo for further evaluation of its therapeutic efficacy.

Keywords : 7,8-diaminopelargonic acid aminotransferase, BioA, pharmacophore, molecular docking, ADMET, TOPKAT
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