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In-silico identification of lead compounds for pseudomonas aeruginosa PqsA enzyme: computational study to block biofilm formation.

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Pseudomonas aeruginosa is an opportunistic gram-negative bacterium implicated in acute and chronic nosocomial infections and a leading cause of patient mortality. Infections caused by Pseudomonas aeruginosa are often linked to the formation of biofilms, which gives the bacteria increased resistance to multiple drugs and makes them more virulent. The purpose of this study was to inhibit the quorum signaling system of P. aeruginosa through a rational drug design strategy by designing potent inhibitory lead molecules against Anthranilate-CoA ligase enzyme encoded by the pqsA gene. This enzyme produces auto inducers for cell-to-cell communication, which result in biofilm formation, and thus plays a pivotal role in the virulence of P. aeruginosa. A library of commercially available was used by performing pharmacophore based virtual screening using an available enzyme inhibitor. The most promising hits obtained during virtual screening (VS) were put through molecular docking with the help of MOE. The virtual screening yielded and 7/160 and 10/249 hits (ZINC and Chembridge). Finally, 2/7 hits (ZINC database), and 2/10 hits (ChemBridge database) were chosen as potent lead compounds using various scaffolds due to their considerable binding affinity with pqsA enzyme. The outcomes of PBVS were then validated using an analysis based on molecular dynamics simulation (MDS). The complexes' stability was tested using MDS and post-MDS. The most promising candidates were found to exhibit a high capacity for fitting into the protein-binding pocket and interacting with the catalytic dyad. At least one of the scaffolds selected will possibly prove useful for future research. However, further scientific confirmation in the form of preclinical and clinical research is required before implementation.

Biography

Muhammad Shahab working in State key laboratories of chemical Resources Engineering and also working as faculty Beijing University of chemical technology..