Biotechnology and Applied Biochemistry. Vol. 72 (2), 2025, pages 1184 - 1194

Potential anti-filarial molecules against atp binding site of mure enzyme: A molecular docking and dynamics approach to combat lymphatic filariasis

Abstract

Lymphatic filariasis (LF) is a mosquito-borne disease caused by parasitic nematodes Brugia malayi, Brugia timori, and Wuchereria bancrofti. The drugs available are effective in several cases, and the absence of vaccination is the crucial factor hindering the elimination of LF. The UDP-N-acetylmuramoyl-L-alanyl-D-glutamate-2,6-diaminopimelate ligase (MurE) plays an important role in the peptidoglycan biosynthesis of Wolbachia endosymbiont B. malayi, which are reported to be a vital drug target for bacterial and endosymbiotic hosts. Thus, we selected the ATP binding cavity of MurE as the potential site to screen inhibitors. The MurE structure was modeled using AlphaFold due to the absence of an experimental structure. Structure-based screening identified five potent phytochemicals targeting the ATP binding site with higher Glide scores and affinity. The top five phytochemicals CID 311, CID 445713, CID 441626, CID 39077, and CID 10814 showed a docking score of −16.812, −16.117, −15.668, −15.324, and −13.442 kcal/mol, respectively. Further, the molecular dynamics simulations depicted the binding stability of the phytochemical inhibitors bound to the MurE complex. Moreover, ADME assessment and Density Functional Theory analyses of the predicted compounds have shown acceptable pharmacokinetic properties and high reactivity with the drug target of MurE.

Keywords

ATP; Brugia malayi; enzyme ligase; molecular docking; phytochemical