ORIGINAL RESEARCH ARTICLES

EXPLORING NOVEL NCEs TARGETING InhA AS PROSPECTIVE KEY COMPOUNDS TO TREAT TUBERCULAR INFECTIONS: A COMPUTATIONAL APPROACH

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ABSTRACT

The main goal of this research was to investigate unique molecules for potential anti-tubercular properties. These NCEs are targeted as inhibitors of InhA, a pivotal mediator in tubercular infections. This exploration was carried out through computational molecular docking. In lieu of prior research, we conducted an *in silico* analysis of various potential and reported anti-tubercular and anti-bacterial molecules. The objective was to determine their interaction patterns with InhA (PDB ID: 4TRN) using the AutoDock Vina software. Simulations of molecular docking were carried out using a grid cell with dimensions of 49.4839, 47.3457, and 49.1114 Å, centered at coordinates 3.4082, -36.9200, and 18.0223 Å, respectively. Additionally, the BIOVIA Discovery Studio visualizer software was employed to evaluate two-dimensional (2D) and three-dimensional (3D) interactions between the ligands and specific amino acid residues in the target protein. Lipinski's rule and the SwissADME database were utilized to analyze physicochemical properties and further support the *in silico* findings. During this investigation encompassing various novel chemical entities, over 1500 compounds were subjected to screening against the InhA receptor protein. The binding scores varied from –9.9 to –7.3 kcal mol^{-1}. Notably, 40 ligands exhibited strong binding affinities. Furthermore, the ADMET profiles of these compounds fell within acceptable ranges, as observed *in silico*. Based on our initial findings, it can be concluded that the chosen novel chemical entities possess promising potential as effective anti-tubercular and anti-bacterial candidates due to their inhibition of the InhA receptor target. These compounds warrant further optimization and validation, potentially serving as novel therapeutic elements for the development of enhanced and safe anti-tubercular molecules.