Design, Synthesis, and Molecular Docking of Novel Benzothiazinone Derivatives as DprE1 Inhibitors with Potential Antitubercular Activities

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Abstract

Objective: As a possible antitubercular agent, we disclose in this study the design and synthesis of a novel series of benzothiazinone derivatives (**Va–Vi**), contributing to the worldwide fight to eradicate TB, one of the deadliest infectious killers in the world. **Methods:** The newly synthesized benzothiazinone derivatives were characterized using various spectroscopic and elemental analysis techniques. The antituberculosis activity of the synthesized benzothiazinone derivatives was evaluated against drug-sensitive *Mtb* H37Rv and MDR-TB strains. To explain their inhibitory qualities, potent compounds underwent molecular docking studies. The synthetic molecules' ability to function as lead-like molecules and the drug-likeness of the compounds were computed using the SwissADME online tool. **Results and Discussion:** With a MIC of 0.01 and 0.21 µM, respectively, compound (**Vi**) showed the most promising antitubercular efficacy against drug-sensitive *Mtb* H37Rv and MDR-TB strains. Four of the nine studied compounds had strong DprE1 inhibitory action, with IC_{50} values ranging from 0.02 to 0.79 μ M. The molecular docking findings indicated that these compounds had a high docking score and