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In silico studies of novel naphthalene hydrazone derivatives as enoyl acyl carrier protein reductase inhibitors

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ABSTRACT Tuberculosis (TB), caused by mycobacterial strains, remains a global threat, especially due to multidrug-resistant forms. Enoyl acyl carrier protein reductase (InhA) mutations contribute to resistance in 20–25% of clinical isolates, highlighting the need for novel inhibitors. The present study involves *in silico* analysis of eighty-one naphthalene-based hydrazone derivatives against InhA (**PDB ID: 2X22**). Compounds **78** and **79** showed strong binding affinities (−11.61 to −11.69 kcal/mol) as compared to the reference drug Isoniazid (binding energy = −5.28 kcal/mol) and favorable pharmacokinetic profiles. Compound **78** has shown high thermodynamic stability throughout 100 ns MD simulation without any major fluctuation, while DFT analysis confirmed the electronic stability of compounds **78** and **79** (ΔE = 0.159 eV and 0.149 eV, respectively). Therefore, compounds **78** and **79** may act as lead molecules in the development of potent antitubercular agents for the successful clinical management of resistant TB.

KEYWORDS Antimycobacterial, Enoyl acyl carrier protein reductase inhibitor, Density functional theory, Molecular docking, Molecular dynamics simulation, 2-Naphthoxyacetic acid hydrazide/hydrazone.

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