

## Benzothiazole-based amide derivatives: Microwave-assisted synthesis, biological screening, and *in silico* validation against multidrug-resistant tuberculosis

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**ABSTRACT** A series of benzothiazole-based amide derivatives (**S1-S15**) was synthesized through a rapid and efficient three-step protocol involving carboxylic acid formation, the carboxylic acid was then converted into the corresponding acid chloride intermediate using thionyl chloride, and microwave-assisted coupling with various aromatic amines, amino acids, and aromatic acids, yielding the target compounds in good-to-excellent purity and yield, evaluated for anti-tubercular activity using both *in vitro* and *in silico* approaches. *In vitro* activity was assessed via the microplate alamar blue assay against *Mycobacterium tuberculosis* H37Rv (ATCC 27294), with compounds **S8**, **S9**, **S13**, and **S14** showing significant inhibition (minimum inhibitory concentration: 1.6 µg/mL). Molecular docking against glutamine synthetase (PDB ID:2BVC), glutamyl-tRNA synthetase (PDB ID:2JA2), and InhA (PDB ID:6R9W) identified **S4**, **S5**, and **S7** as top binders. Absorption, distribution, metabolism, excretion, and toxicity predictions supported the drug-likeness of **S1**, **S4**, **S7**, and **S15** with favorable pharmacokinetic profiles. Overall, the *in vitro* and *in silico* studies highlight **S8**, **S9**, **S14**, **S15**, and **S4**, **S5**, **S7** as promising multi-target lead candidates for further pre-clinical development against resistant tuberculosis.

**KEYWORDS** Benzothiazole derivatives, *In vitro*, Microplate alamar blue assay, Anti-tubercular activity, Docking, PyRx.