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# Design, synthesis and antitubercular assessment of 1, 2, 3-triazole incorporated thiazolylcarboxylate derivatives

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## Highlights

- A library of 1, 2, 3-triazole incorporated thiazolylcarboxylate derivatives was synthesized.
- The compounds were evaluated for their *in vitro* antitubercular activity against Mycobacterium tuberculosis.
- Two compounds were displayed potent antitubercular activity with MIC values of 1.56 and 3.12 μg/mL.
- Whereas, the four compounds were displayed noticeable antitubercular activity with a MIC value of 6.25μg/mL.

## Abstract

A library of 1, 2, 3-triazole incorporated thiazolylcarboxylate derivatives (**7a-q**) and (**8a-j**) were synthesized and evaluated for their *in-vitro* antitubercular activity against Mycobacterium tuberculosis H37Rv. The two compounds **7h** and **8h** have displayed excellent antitubercular activity with MIC values of 3.12 and 1.56μg/mL respectively (MIC values of standard drugs; Ciprofloxacin 1.56μg/mL & Ethambutol 3.12μg/mL). Whereas, the four compounds **7i**, **7n**, **7p** and **8i** displayed noticeable antitubercular activity with a MIC value of 6.25μg/mL. The active compounds of the series were further studied for their cytotoxicity against RAW264.7 cell line using MTT assay. Furthermore, to study the probable mechanism of antitubercular action, physicochemical property profiling, DFT calculation and molecular docking study were executed on mycobacterial cell wall target *Decaprenylphosphoryl-β-D-ribose 2′-epimerase 1* (DprE1). Among all the compounds, **7h** (-10kcal/mol) and **8h** (-10.1 kcal/mol) exerted the highest negative binding affinity against the targeted DprE1 (PDB: 4NCR) protein.

## Graphical abstract