allied academies
25th Anniversary of scientific services

6th International Conference on
Pharmaceutical Science and Advanced Drug Delivery Systems

April 28, 2022 | Webinar

Discovery of a highly potent novel Rifampicin analog by preparing a hybrid of the precursors of the antibiotic drugs Rifampicin and Clofazimine

Pasupathy Saravanan
ICMR-National Institute for Research in Tuberculosis, Chennai, INDIA

Introduction: Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis (Mtb). The present work reports the design and synthesis of a hybrid of the precursors of rifampicin and clofazimine, which led to the discovery of a novel Rifaphenazine (RPZ) molecule with potent anti-TB activity.

Methods: The synthesized novel molecule was characterized using high-resolution mass spectroscopy and NMR spectroscopy. The efficacy of RPZ was evaluated in-vitro using the reference strain Mtb H37Rv. Herein, 2,3 diamino phenazine, a precursor of an anti-TB drug clofazimine, was tethered to the rifampicin core. This 2,3 diamino phenazine did not have an inherent anti-TB activity even at a concentration of up to 2 µg/mL, while rifampicin did not exhibit any activity against Mtb at a concentration of 0.1 µg/mL.

Results: The synthesized novel Rifaphenzine (RPZ) inhibited 78% of the Mtb colonies at a drug concentration of 0.1 µg/mL, while 93% of the bacterial colonies were killed at 0.5 µg/mL of the drug. Furthermore, the Minimum Inhibitory Concentration (MIC) value for RPZ was 1 µg/mL. Time-kill studies revealed that all bacterial colonies were killed within a period of 24 h. Cytotoxicity studies (IC50) were performed on human monocytic cell line THP-1, and the determined IC50 value was 96 µg/mL, which is non-cytotoxic.

Conclusion: These data suggested that Rifaphenazine (RPZ) is a promising pre-clinical candidate for the treatment of drug-susceptible tuberculosis (DS-TB). The results of the in-vitro analysis suggest that the efficacy of Mtb inhibition demonstrated by RPZ at a lower drug concentration has a prospect of shortening the TB treatment duration. The significance of the present work is that, even at a one-tenth concentration of rifampicin MIC, the drug candidate Rifaphenazine (RPZ) was able to kill 78% of Mtb, while rifampicin could kill zero percent Mtb at the same concentration.

e: saran2k5@gmail.com