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Discovery of novel bicyclic derivatives to stop the growth of mycobacterium tuberculosis by Inhibiting MenA

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Abstract

Tuberculosis (TB) is the second largest infection in number of deaths around the world. Importantly, about one third of world population has latent tuberculosis. However, HIV-TB is growing fast, especially HIV is stimulating latent TB to form active TB infection. In addition drug resistant TB is also a challenge for researchers. In this order novel drugs are necessary to eradicate TB. Most of the TB drugs were based on inhibiting the process of cell wall and protein synthesis, therefore a novel method is important for drug discovery and development. Interestingly, Bacilli require electron transport chain components and ATP synthesis for survival. The lipoquinones involved in the respiratory chains of bacteria consists of menaquinones and ubiquinones where else, mammals require only ubiquinone, which makes more specific to Bacilli. In relation, menaquinone is an essential component in the electron transfer process, similarly, MenA is an essential enzyme involved in the synthesis of menaquinone. In addition menaquinones are the major lipoquinones of mycobacteria and other Gram Positive bacteria. Hence MenAa promising drug target is explored in determining the inhibitor. While Screening and designing inhibitors we observed that bicyclic derivatives showed high coordinating complexes with enzymes in transition state and interrupted the growth of M. Tb. Especially, alkylamino bicyclic complexes showed extensive inhibition towards M. Tb. The quantitative structure activity relationship was carried out for the alkyl amino bicyclic complex and tested against Gram Positive bacteria. After optimizing the inhibitors we observed promising MIC and IC_{50}values to encounter the infection.

Biography

Dr. Prabagaran Narayanasamy is a faculty member in the Department of Pharmacology and Experimental Neurosciences at the University of Nebraska Medical Center. He received his Ph. D at IIT in Organic Chemistry and did his postdoctoral studies at North Dakota State University, Harvard University and University of Illinois Urbana-champaign. Later, he joined as a Research Scientist at Colorado State University to explore drug discovery. He has been a faculty at University of Nebraska Medical Center since 2012. Dr. Narayanasamy's research interests are on development, delivering and discovering drug for anti-mycobacterial medicine and antiretroviral therapy. Conventional drugs and new inhibitors are used in nanoformulation to generate active nanomedicine. For antibacterial drug discovery - glyoxalase, quorum sensing, MEP and menaquinone pathway are utilized. Additionally, development of exosomes as drug delivering agent is initiated for infectious disease. In addition, metabolites are evaluated in the infected brain for characterizing neurodegenerative disorders.