Introduction

Tuberculosis (TB) is a specific contagious bacterial disease caused by *Mycobacterium tuberculosis*. This small, aerobic, non-motile bacillus typically affects the lungs (Pulmonary TB) and is capable of affecting any organ or tissue of the body (Extra-pulmonary TB). It is transmitted via infectious sputum aerosol droplets from the throat and lungs of patients with active TB.¹

Scientific evidences suggest that *Tuberculosis* has affected the mankind for at least 9,000 years. Skeletal remains show that prehistoric humans (4000 BC) had TB, and even researchers have found tubercular decay in the spines of Egyptian mummies dating from 3000–2400 BC.² Tuberculosis is known to Indian since ancient age, and in Indian literature there are passages on TB from around 1500 BC. The Sanskrit literatures describe the disease as yaksman (consumption) or rajayaksman (kindly consumption). In March 1882, Prussian physician Heinrich Hermann Robert Koch, first time identified *Mycobacterium tuberculosis* in the sputum of TB patients and proved it as the causative organism for Tuberculosis.³

Tuberculosis is the second leading cause of death from an infectious disease worldwide. In 2011, WHO has reported 8.7 million new cases of TB with 1.4 million deaths due to TB.⁴ Though the incidence of TB predominates in adults, it is estimated that even 4,70,000 to 5,10,000 children are suffering from TB throughout the world. India remains the global leader in number of TB incidences (2.2 million, 2011)⁴ and accountable for 26% of global TB burden. Public survey suggests that approximately 40% of the Indian population is infected with TB bacillus⁵ and nearly one person dies every minute by TB in India.

The campaign to reduce TB infections is seriously jeopardized by MDR-TB (Multi Drug Resistant Tuberculosis) and XDR-TB (Extremely Drug Resistant Tuberculosis). Globally 3.5% new TB cases and 20% old TB cases are detected with Multi Drug Resistant (MDR) TB. Recently, 84 countries worldwide have reported XDR TB cases and it is figured that MDR cases with XDR are 9%. Even few Total Drug Resistant (TDR) TB cases have also been emerged in the recent past to make the condition more challenging.⁶

In addition to these entire adversaries, the co-infection of TB with HIV has made it an unstoppable global threat. HIV makes TB more contagious by converting the latent TB to its transferable form and TB helps in the progress of HIV infection. Around 48% of the TB patients are living with HIV worldwide and 4,30,000 HIV patients have died with TB in 2011.⁴
If not controlled, it is estimated that 1 billion people will newly be infected, 150 million people will get sick and 36 million will die from Tuberculosis by 2020.

WHO recommended regimen for the treatment of Drug Susceptible TB is 50 years old. These first line drugs (combination of Isoniazid, Pyrazinamide, Rifampicin and Ethambutol) take six months to cure Drug Susceptible TB. Usually second line drugs (Capreomycin, Kanamycin, Para Amino Salicylic Acid, Ethionamide and Cycloserine) are used for the treatment of MDR TB and it takes 20 months of rigorous treatment. Unfortunately, they are associated with many lethal side effects and low cure rates. Treatment by cocktail of existing antitubercular agents (DOTS) for a long period leads to patient noncompliance and this is anticipated to be the prime reason for drug resistance. Existing therapy for the treatment of HIV-TB Co-infection and TB in immunosuppressed patients is also very complicated and not free from drug incompatibility.

In spite of the deep knowledge on epidemiology of tuberculosis, this malady is still harder to treat and it is gaining ground day by day. Despite of the life threatening lacunas, complex combination therapy is inevitable in the current scenario as non-replicating state of the pathogen maintains metabolically dormant state to survive long periods of treatment. Lack of chance in commercial success and unusual behavior of the microbe has made the effort towards the discovery of new AntiTB agents very much sluggish.

In recent past, few organizations have come forward to conduct clinical trials of existing anti-infective agents like Gatifloxacin, Moxifloxacin, Levofloxacin, Linezolid, and Metronidazole for antitubercular activity through multipartnership consortia. In December 2012, FDA and Janssen Therapeutics announced the approval of Diarylquinoline based AntiTB drug (Bedaquiline, TMC-207) for the treatment of multidrug-resistant pulmonary tuberculosis. Though this drug has broken the 50 years of silence of antitubercular drug discovery, it carries black box warning for cardiac arrhythmia and some other life threatening features. Potential clinical candidates like PA-824 (GATB, Phase-III), OPC-67683 (Otsuka, Phase-II), SQ-109 (Sequella, Phase-II), LL-3858 (Lupin, Phase-I), are still under clinical trial.

Looking in to the less efficacious existing TB therapy, co-morbidity, patient incompliance, drug resistance and uncertain future of current clinical trial candidates, it is evident that there is an unmet need to discover potential antitubercular agents which can retreat TB through an alternate target to avoid drug resistance and simplify the current therapeutic regimen.