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MEETING ABSTRACTS

SYNTHESIS OF PYRIMIDINE DERIVATIVES WITH ANTITUBERCULAR ACTIVITY

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Tuberculosis (TB) is a transmissible infectious disease caused by the intracellular bacteria, *Mycobacterium tuberculosis* (*MtB*), (1) which is currently one of the top 10 leading causes of death in low and middle-income countries (2). During 2020, 5.8 million patients were diagnosed with TB, 1.5 million of them died. In that year, 150 thousand patients were infected with drug-resistant TB strain.1 M. tuberculosis can quickly develop resistance against anti-TB regimens, and if not cured adequately, it can evolve into MDR-TB (multidrug resistant TB) and XDR-TB (extensive-drug resistant TB) (1). Therefore, there is a critical need to develop new chemotherapeutic agents with new mechanism of action to fight against a growing public health menace caused by cross-resistant TB strains (3).

We screened our in-house library of small molecules for their potential antimycobacterial properties identifying compound K1827 with excellent antimycobacterial *in vitro* activity against *M. Kansasii* (MIC_{99} = 0.25 μM, which is more than 100 times more efficient that INH) and moderate activity against *M. tuberculosis* H37Rv (MIC_{99} = 32 - 64 μM, for comparison MIC_{99} of INH = 0.5 μM). This core scaffold of K1827 is pyrimidine that was functionalized to develop derivatives with higher activity against *M. tuberculosis*, better safety profile, and to determine the structure-activity relationships in the series. The effect of individual structural fragments on *in vitro* antimycobacterial activity, toxicity and selectivity of action have been evaluated and will be discussed within our contribution.

Keywords: Tuberculosis; pyrimidine; resistance

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