Abstract

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Thesis title: Design, synthesis and biological evaluation of aminothiazole and aminooxazole derivatives as antimicrobial compounds

Tuberculosis (TB) is currently the second most fatal infectious disease, after COVID-19, still requiring new effective drugs. The aim of our work was thus to synthesize and investigate new potential antimycobacterial agents based on 2-aminothiazole and 2-aminooxazole. The design of the compounds was based on the recently described inhibitors of the serine acetyltransferase (SAT), an essential enzyme in the cysteine biosynthesis pathway. Reduced synthesis of cysteine in bacteria has been shown to lead to a reduced virulence and drug resistance, the SAT thus represents a promising target.

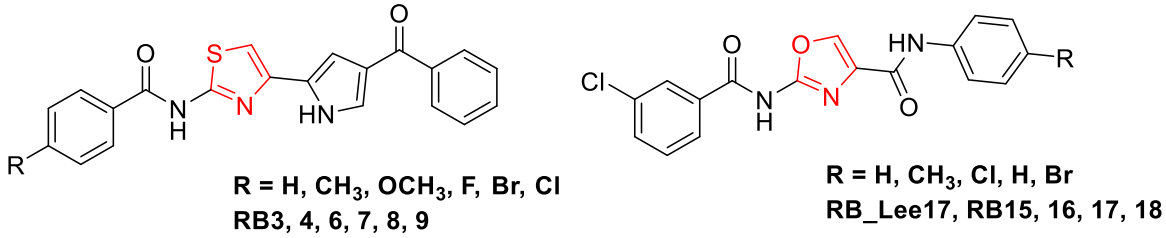

Figure 1 General structure of the synthesized compounds

In total, 11 derivatives of the structures seen in **Figure 1** were prepared and screened for activity against different species of mycobacteria, including *Mycobacterium tuberculosis*. Higher activity was seen in aminothiazole derivatives (X = S), but poor solubility hindered more advanced screening. The highest activity was observed in RB6 (MIC = 3.91 µg/mL) bearing 4-methoxybenzamide core (R = OCH_3), and RB3 (MIC = 7.81 µg/mL) with the non-substituted benzamide (R = H) moiety.