ABSTRACT

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Title of diploma thesis: Structure-antimycobacterial activity relationships in the series of dinitrophenyl-substituted heterocycles

Tuberculosis is an infectious disease with an increasing number of cases each year. Resistance of the pathogen, namely *Mycobacterium tuberculosis*, to the treatment, even against combined therapy keeps increasing. In 2020, tuberculosis was the second most common cause of death by infectious disease after COVID-19 (it claimed 1.5 million lives) and it is also estimated that with COVID-19 weakening the population, these numbers will only grow.

The aim of this work was to develop derivatives of previously studied 1*H*-tetrazoles and 1,3,4-oxadiazoles, with a sterically hindered sulfur atom (*Fig. I*), which may protect them from metabolic oxidation and therefore possibly increase their activity against resistant strains of *M. tuberculosis* as well as other mycobacterial strains and to increase biological halftime of these potential antituberculosis drugs. We prepared two test series, namely 1*H*-tetrazole series and 1,3,4-oxadiazole series both containing 4 compounds, whose antimycobacterial activities were evaluated and the results were compared with their non-sterically shielded parent compounds.

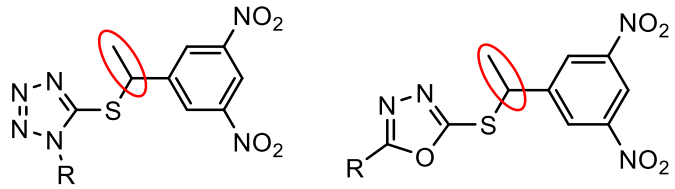

Fig. I – Derivates of 1H-tetrazoles (left) and 1,3,4-oxadiazoles (right) with marked steric hinderance

As up next, we synthetized a third series, the analogs of the 3,5-dinitrophenyloxadiazole series, in which we have made a substitution of one nitro group for a halogen group (*Fig. II*). The impact of this substitution on antimycobacterial effectivity, biological half-life and other important properties will be evaluated and the results will be compared those of their parent compounds.

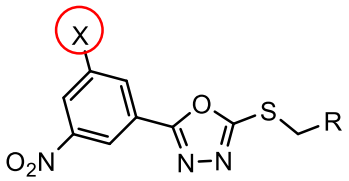

Fig. II – Analogues of the 3,5-dinitrophenyloxadiazoles with marked substitution of one nitro group for a halogen group