ABSTRACT

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Title of diploma thesis: Mycobacterial resistance against currently used antimycobacterial drugs

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The successful treatment of mycobacterial diseases is nowadays often confronted with the declining effect of antituberculotics and other antimicrobial agents, which are often used in the therapy of mycobacterial diseases. The goal of the theoretical part of the thesis was to focus on a comprehensive assessment of the issue of resistance to the current therapeutics used in the fight against resistant mycobacterial strains, to summarize the basic characteristics of the genus *Mycobacterium*, to address resistant TBC and NTM, and to describe the mechanisms of action and resistance known so far for individual therapeutics, which are often interrelated. The emergence of highly resistant mycobacterial strains is constantly increasing the risk of serious, life-threatening infections. The mechanisms of resistance either arise from the natural properties of the cell or develop gradually as a result of external stimuli, which is the more common and therapeutically more problematic option. The basis of resistance may be the production of inactivating enzymes, increased expression of efflux pumps, alteration of target structures due to mutation, the presence of porins or a very resistant cell wall.

The experimental part is focused on testing new, potentially effective molecules against five different mycobacterial strains. It describes the testing procedure using the microdilution broth method, information about the equipment used, the tested substances and the mycobacterial testing strains. A total of 71 substances were tested, more than half showed significant efficacy. The heterocyclic coordination compounds, where the central atom was silver or gold, showed the best results, followed by pyrazine-2-carboxamide derivatives with MIC ranging between 1.98-3.91 μg/ml. Measurement results are also included and summarised in the final evaluation.