

## Abstract

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Title of Thesis: Synthesis and evaluation of compounds active against resistant Gram-positive cocci

The topic of this diploma thesis are compounds with potential activity against resistant Gram-positive cocci. It deals with currently existing antibiotics and compounds that are at various stages of research or development. Those are potential drug candidates, which could bring a substantial progress in a solution of the recent antibiotic resistance phenomenon.

The theoretical part deals with the classification of Gram-positive cocci based on the different characteristics of each group. The following part focuses on antibiotic resistance, its mechanisms and mechanisms of transmission between organisms. Then, the representatives and their laboratory diagnostics, virulence factors, and specific diseases they are causing are discussed. The last but not least chapter covers new strategies against resistant strains, which include new molecules, modifications of established drugs, new use for pre-existing drugs, phage therapy, prevention of resistance by the use of probiotics, virulence elimination, and finally, international and national strategies to combat resistance are mentioned as well.

The experimental part deals with the synthesis of sixteen compounds derived from 4'-cyclohexylacetophenone and 4'-piperidinoacetophenone. These reagents were chosen for their proven antimicrobial activity. Twelve compounds were prepared by Claisen-Schmidt condensation of acetophenones with 2-methoxybenzaldehydes and remaining four compounds were synthesized by the formation of hydrazone-hydrazones from the aforementioned precursors with the corresponding hydrazides. All compounds were obtained in sufficient quantities

(yields in the range of 32-91 %). They were characterized and subjected to biological activity assays to identify potential structure-activity relationship. Activities tested were antibacterial, antifungal and antimycobacterial action. Prepared compounds did not show any significant activity on bacteria or fungi. However, in the case of mycobacteria, the activity of some compounds was interesting. In particular, it was related to hydroxylated hydrazones against *Mycobacterium kansasii* and *M. avium*.

*Keywords*

Antibiotics, antimicrobial activity, chalcones, hydrazide-hydrazones, methicilin-resistant staphylococci, resistance, synthesis, vankomycin-resistant enterococci, vankomycin-resistant staphylococci