ABSTRACT

The topic of this bachelor thesis is an alarming global problem of acquired resistance of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Staphylococcus aureus*, vancomycin-intermediate susceptible *Staphylococcus aureus* and vancomycin-resistant enterococci strains, their limited current treatment options for infections caused by these pathogens, synthesis and evaluation of potential antimicrobial compounds active also against these resistant Gram-positive strains.

The development of novel drugs against drug-resistant pathogens is challenging. Designed compounds are based on sulfa drug mafenide, which is used in the treatment of topical infections caused by Gram-positive and Gram-negative bacteria. The targeted imines were prepared from mafenide acetate and carbonyl compounds in one step. Most of these novel compounds are derivatives of salicylaldehyde, furthermore, derivates of 5-nitrothiophene-2-carbaldehyde and isatin were also synthesized. Thirteen compounds were prepared with good yields (50-95%). All these compounds were tested against Gram-positive (including MRSA) and Gram-negative bacteria, mycobacteria, and fungi by the broth microdilution method. The lowest minimum inhibitory concentration (MIC) values against bacteria, fungi as well as the highest antimycobacterial activity were found for (*E*)-4-{[(2-hydroxy-3,5-diiodobenzylidene)amino]methyl}benzenesulfonamide, (*E*)-4-{[(5-chloro-2-hydroxy-3-iodobenzylidene)amino]methyl}benzenesulfonamide and (*E*)-4-({[(5-nitrothiophene-2-yl)methylene]amino}methyl)benzenesulfonamide. The lowest MIC values reached were 7.8 μmol/L for bacteria including MRSA, 3.9 μmol/L for fungi and 3.9 μg/mL for mycobacteria, respectively. The substitution by heavier halogens as well as halogen disubstitution are beneficial. In general, all the novel derivatives showed a higher *in vitro* antimicrobial effect than the parent molecule of mafenide and some of the were comparable or even superior to standards used for a comparison.