ABSTRACT

Charles University in Prague, Faculty of Pharmacy in Hradec Králové
Department of Organic and Inorganic Chemistry
Candidate: Mgr. Eva Petrlíková
Supervisor: Prof. RNDr. Karel Waisser, DrSc.
Title of Doctoral Thesis: Antituberculosis Agents and Their Antimicrobial Effects.

The dissertation focuses on the preparation of antimycobacterially active compounds. Some of the prepared compounds were also screened for the in vitro antibacterial and antifungal activity.

The prepared compounds included sulfur derivatives of 3-benzyl-2*H*-1,3-benzoxazine-2,4(3*H*)-diones, *N*-(pyridylmethyl)salicylamides, sulfur derivatives of 3-(4-alkylphenyl)-2*H*-1,3-benzoxazine-2,4(3*H*)-diones, *N*-benzylthiosalicylamides, benzaldehyde-*S*benzylisothiosemicarbazones, salicylaldehyde-S-benzylisothiosemicarbazones, derivatives of 1,2-bis(9*H*-fluoren-9-ylidene)-*N*,*N*′-diarylethane-1,2-diamine, and hybrid molecules of cholesterol and terpenes.

The highest antimycobacterial activity was exerted by 3-benzyl-2*H*-1,3-benzoxazine-2,4(3*H*)-dithione and 3-(3,4-dichlorobenzyl)-2*H*-1,3-benzoxazine-2,4(3*H*)-dithione, 3-(4-secbutylphenyl)-7-methyl-4-thioxo-2*H*-1,3-benzoxazine-2(3*H*)-one, *N*-(4-methylbenzyl) thiosalicylamide and 4-methyl-*N*-(4-methylbenzyl)thiosalicylamide. Salicylaldehyde-*S*-(4-chlorobenzyl)isothiosemicarbazone was the most active derivative in the group of *S*-benzylisothiosemicarbazones. [Endo-(1*S*)-(1,7,7-trimethylbicyclo[2.2.1]heptane-2-yloxy)-6-oxohexyl]isochinolin-2-ium-bromide showed the highest antimycobacterial activity among the hybrid molecules of cholesterol and terpenes. The derivatives of *N*-(pyridylmethyl)salicylamide showed moderate to low activity against mycobacteria. Phenyl-4-methoxysalicylate was the most active among the phenylesters of salicylic acid.

The sulfur derivatives of 3-(4-alkylphenyl)-2*H*-1,3-benzoxazine-2,4(3*H*)-dione and *N*-benzylthiosalicylamide were found to be antibacterially active. *N*-benzylthiosalicylamides also show effectivity against fungi.

3-Benzyl-4-thioxo-2*H*-1,3-benzoxazine-2(3*H*)-ones, 3-benzyl-2*H*-1,3-benzoxazine-2,4(3*H*)-dithiones and *N*-benzylthiosalicylamides were screened for antiproliferative activity and cytotoxity. 3-(3,4-Dichlorobenzyl)-4-thioxo-2*H*-1,3-benzoxazine-2(3*H*)-one, 3-(3,4-dichlorobenzyl)-2*H*-1,3-benzoxazine-2(3*H*)-dithione, 4-methyl-*N*-(4-methylbenzyl) thiosalicylamide and *N*-(4-methylbenzyl)thiosalicylamide exerted high antimycobacterial activity and their antiproliferative activity and cytotoxicity were found to be moderate among the tested compounds.

The lipophilicity of *N*-(pyridylmethyl)salicylamides, sulfur derivatives of 3-(4-alkylphenyl)-2*H*-1,3-benzoxazine-2,4(3*H*)-diones, *N*-benzylthiosalicylamides and phenyl salicylates was measured by thin layer chromatography on silica gel impregnated with trioctadecylsilane.