# 10 Souhrn v anglickém jazyce

Author participated during his doctoral thesis on theme with long history in Pharmaceutical Faculty research program, which is search for new antimycobacterial active compounds. An approach that had been chosen to develop such compounds is structure analogy of pyrazinamide, first-line agent in treatment of tuberculosis. This pathway have been set up in late 80's and early 90's of last century by doc. Jiří Hartl, CSc. and followed by doc. Martin Doležal, Ph.D. until nowadays. In summary there was prepared over 800 compounds that were screened on their antimycobacterial activity.

This thesis deals with structure-activity relationships of some pyrazinamide analogues rather structures derived from arylsulphanylpyrazine-2-carboxamide, arylsulphanylpyrazine-2-carbonitrile, *N*-aryl or *N*-thiazolylpyrazine-2-carboxamide, arylaminopyrazine-2,5-dicarbonitrile respectively.

The first step of the whole study was chemical synthesis of new analogues which was done by the author of this thesis. Chemical synthesis was followed by structure elucidation and lipophilicity determination. After synthetic and analytical part were completed, biological evaluation begun. Biological analysis comprised antimycobacterial activity screening as a main task. Current knowledge that some antimycobacterials are active antifungals as well gave good reason to evaluate even antifungal activity. Lastly, because all prepared compounds absorbed in the visible range of electomagnetic spectrum some of them were evaluated for their potential photosynthetic inhibitory activity.

Some of prepared compounds exhibited relatively high antimycobacterial activity, namely *N*-(3,5-dibromo-4-hydroxyphenyl)pyrazine-2-carboxamide, *N*-(3-trifluoromethylphenyl)pyrazine-2-carboxamide and 3-{[3-(trifluormethyl)phenyl]amino}pyrazine-2,5-dicarbonitrile respectively. These structures exhibited activity units of $\mu g.ml^{-1}$. These compounds were released to higher levels of TAACF antimycobacterial screening. In these levels the nitrilic compound exhibited unacceptable toxicity but one of amidic compounds showed good selectivity index and is evaluated further. Published

results give good view onto structure-activity relationships of these analogues and promise even better activity after some structure optimization experiments.

In case of activity only poor or moderate activities were found thus no relevant conclusions on structure activity relationships can be done. Inhibition of photosynthetic activity was an additional experiment, because prepared compounds of were. On the other hand, some of them exhibited good photosynthesis inhibiting activity.