Abstract

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Title of candidate thesis: Derivatives of pyrazine as potential antituberculotic drugs

The aim of this thesis was a preparation of derivatives of pyrazine-2-carboxylic acid (POA), namely substituted anilides of 5-chloropyrazine-2-carboxylic acid with potential antituberculotic activity. In the theoretical part of this thesis, there is a short description of tuberculosis (TB) as an infectious disease. The main topic of this part are: etiology and pathogenesis of TB, epidemiology of TB, a both common and resistant TB form and a big problems with the co-infection between TB and HIV. Next part of the theory includes a therapy of TB, first and second line antituberculars as well some drugs in clinical trials. More detailed data are giving only to pyrazinamide (PZA), because its analogues are the basic topic of this thesis. There is a summary of simple structural modifications of pyrazine (in testing from 50´s years of 20th century to present) and recent theories about pyrazinamide´s mechanism of action.

In the practical part of this thesis is presented preparation of 12 new, in the literature so far not mentioned substances, namely anilides 5-chloropyrazine-2-carboxylic acid. Prepared substances are characterized by melting point, IR, ^{1}H and ^{13}C NMR spectra and elementary analysis. All prepared compounds were subjected to *in vitro* testing for their potential antimycobacterial activity against *M. tuberculosis* H37Rv, *M. kansasii* and two different strains of *M. avium*. Most of the prepared compounds showed activity against *M. tuberculosis* in the range of MIC = 0,78-6,25 μg/ml. The best substance (5-chloro-N-4-hydroxyphenyl-pyrazine—carboxamide), showed almost 20x higher activity against *M. tuberculosis* compared to PZA, after conversion to molar concentracion (μmol/l). Additionally, the substances were subjected to testing for the antifungal and antibacterial activity, in which there were no significant results against the tested strains.