

Abstract

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Title of diploma thesis: Derivatives combining the fragment of pyrazinamide and 4-aminosalicylic acid as antimycobacterial compounds

According to WHO, tuberculosis (TB) is the leading cause of death from a single infectious organism worldwide and the number of cases with drug resistant TB is still increasing, creating the need for new antitubercotics. Therefore, we report design, synthesis and antimicrobial evaluation of a series of hybrid compounds combining different pyrazinamide derivatives and *p*-aminosalicylic acid as potential antitubercotic agents. The compounds were prepared by mixing different pyrazinecarboxylic acids, after activation by 1,1'-carbonyldiimidazole, with *p*-aminosalicylic acid in dimethylsulfoxide as a solvent. Obtained compounds were *in vitro* tested for their antimycobacterial activity against *M. tuberculosis* H37Rv, *M. tuberculosis* H37Ra and four other mycobacterial strains. Prepared compounds were also *in vitro* screened for antibacterial, antifungal, and cytotoxic (HepG2) activity. Most compounds showed antimycobacterial activity in range of minimum inhibitory concentration (MIC) from 3.13–12.5 µg/ml against *M. tuberculosis* H37Rv. The most active compound was 4-(6-chloropyrazine-2-carboxamido)-2-hydroxybenzoic acid with MIC against *M. tuberculosis* H37Rv = 3.13 µg/ml (10,7 µmol.l⁻¹). None of the prepared compounds exerted antibacterial, antifungal or cytotoxic activity.

