Abstract

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Title of diploma thesis: Design, synthesis and evaluation of pyrazinamide derivatives as potential antimicrobial compounds II

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* complex and is currently one of the most common causes of death from an infectious disease. Treatment of tuberculosis is long-term, combined and controlled to prevent resistance. Resistance is very serious and therefore treatment is always performed with more antituberculars at the same time. Finding new drugs and improving existing ones is a constant part of research.

In the theoretical part I tried to summarize information about tuberculosis, its causative agent, diagnostics, possible prevention and treatment strategy. I have described the most commonly used antituberculars, especially the first-line antituberculars – pyrazinamide, from which the derivatives synthesized in my work are based.

In the experimental part I described the procedures and reactions used for synthesis of the new compounds, which were formed by combining pyrazinamide with various amino acids. In this thesis I dealt with 23 prepared derivatives. These compounds were measured for melting point, ^{1}H, ^{13}C NMR, IR and MS spectrometry. All derivatives were tested for antimycobacterial, antibacterial and antifungal activity. None of these compounds showed significant antifungal or antibacterial activity. Six substances showed antimycobacterial activity (*M. tuberculosis* H37Ra) – PC-L-Ala-Et (MIC = 3,91 μg/ml), PC-L-Glu-diEt (MIC = 31,25 μg/ml), PC-L-Met-Me (MIC <3,91 μg/ml), PC-D/L-Pgl-Me

(MIC <1,95 μg/ml), PC-L-*O*Bn-Ser-Me (MIC = 7,81 μg/ml) and PC-L-Tyr-Et (MIC = 7,81 μg/ml). Most derivatives showed higher antimycobacterial activity in a mildly acidic environment – pH 6. The activity was bound to compounds with higher lipophilicity and mostly to compounds with the amino acid fragment in L-configuration. Cytotoxic effects were also found for the active substances, the best cytotoxic profile was shown by PC-L-Ala-Et, PC-D/L-Pgl-Me and PC-L-*O*Bn-Ser-Me.