Abstract

Isoniazid is a first-line drug used against tuberculosis. It is a bactericidal drug with a selectivity for *Mycobacterium tuberculosis* (*Mtb*.). The mechanism of action is primarily based on the blockade of mycolic acid synthesis and thus cell wall synthesis. The development of resistance is limiting the therapeutic potential of isoniazid and that is the reason for the development of its new structural modifications.

This diploma thesis is focused on synthesis and evaluation of novel isoniazid analogues based on a hydrazone obtained from isoniazid and glyoxalic acid. The free carboxyl group was further modified by various amines to form amides. A total of sixteen substituted 2-(2-isonicotinoylhydrazono)-*N*-phenylacetamides were prepared and tested for their *in vitro* antimycobacterial activity on selected strains of mycobacteria – *Mtb.*, *M. avium* and *M. kansasii*. The best activity against *Mtb*. was shown by (*E*)-2-(2-isonicotinoylhydrazineylidene)-*N*-(4-propylphenyl)acetamide and (*E*)-*N*-(4-butylphenyl)-2-(2-isonicotinoylhydrazineylidene)acetamide, their minimal inhibitory concentration (MIC) is 0.125 μM compared to isoniazid's MIC of 0.5 μM. They were also active against nontuberculous mycobacterium *M. kansasii* (MIC from 2 μM). Their activity against multidrug-resistant strains was lower due to cross-resistance with parent isoniazid.