Abstract

Charles University, Faculty of Pharmacy in Hradec Králové

Department of Pharmaceutical Chemistry and Pharmaceutical Analysis

Candidate Daria Nawrot

Supervisor Prof. PharmDr. Martin Doležal, Ph.D.

Title of Doctoral Thesis *Study of pyridine derivatives as potential antimycobacterial active drugs.*

Besides the period when COVID-19 was the biggest threat to health systems efficiency worldwide, tuberculosis remains the most important cause of death by an infectious disease. This, coupled with a rise in antibacterial resistance, remains a substantial challenge for the new drug research pipeline.

The theoretical part of this commentary briefly highlights issues related to tuberculosis, specifically antimicrobial resistance. In the experimental part, the design, synthesis, and biological evaluation of novel compounds investigated during the doctoral program are discussed. In total, three publications are addressed.

The designed compounds were prepared and screened for their *in vitro* activity against selected mycobacterial strains (*M. avium*, *M. aurum*, *M. kansasii*, *M. smegmatis* were used alongside strains of main interest - *Mtb* H37Ra and *Mtb* H37Rv), eight fungal strains (*Candida albicans*, *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis*, *Aspergillus fumigatus*, *Aspergillus flavus*, *Absidia corymbifera*, and *Trichophyton interdigitale*) and eight bacterial strains (*Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus spp*., *Klebsiella pneumonia*, and *Acinetobacter baumannii*). The compounds were tested *in vitro* for their cytotoxicity against the HepG2 cancer cell line and where applicable on the *Galleria mellonella in vivo* model. Some selected compounds were tested for their *in vitro* antiproliferative activity against human epithelial kidney cancer cell line A498, human prostate cancer cell line PC-3 and human glioblastoma cell line U-87MG. The more advanced *in vivo* testing in a murine tuberculosis model was also performed where justified.

Unpublished work is briefly summarized at the end of this commentary.