

ABSTRACT

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Title of diploma thesis: *In vitro* assessment of cytotoxic action of novel potencial nitro group-containing antitubercular agents

More than 10 million new cases of tuberculosis occur every year. Lack of efficient antitubercular drugs and their unavailability, poor diagnostic and especially inappropriate treatment are drawbacks complicating and even precluding eradication of tuberculosis. An already serious disorder has become even more serious in the last years, especially because of the occurrence of drug-resistant tuberculosis, especially MDR-TB and XDR-TB. Due to chromosomal mutations that make bacteria resistant to drugs it is still necessary to develop new effective drugs to replace those in current use, which are often toxic and associated with the occurrence of side effects.

The research group at the Department of Organic and Bioorganic Chemistry, Faculty of Pharmacy in Hradec Králové, Charles University, which has been researching new antitubercular agents for many years, has created new structures of aromatic nitrocompounds with very high antimycobacterial effect. The aim of this diploma thesis was to *in vitro* evaluate the cytotoxicity of nine new compounds from this group.

Assessment of cytotoxicity was performed on non-malignant 3T3 and HaCaT cell lines. Using the neutral red uptake assay the cells viability was determined. Microphotographs of the cells labeled with specific fluorescence probes MitoTracker Red CMXRos, Hoechst 33342 and ActinGreen 488 were taken using confocal microscopy to assess changes on mitochondria, nuclei and actin fibers, respectively.

Due to cytotoxicity experiments we found that the compounds have shown negligible or very low cytotoxicity up to the limit of their solubility in cell culture medium. Photographic documentation has shown absence of morphological changes of the cells which further confirmed non-toxic effect of studied antituberculosic drugs. All studied compounds appear to be very promising candidates for further pre-clinical evaluation of potential antitubercular agents.

Key words: antitubercular agents, *in vitro* cytotoxicity assessment, aromatic nitrocompounds, substituted oxadiazoles, cytotoxicity, neutral red uptake test, fluorescent microscopy