Abstract

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Název diplomové práce: Study on cytotoxicity of compounds *in vitro*

The subject of this diploma thesis was to assess the effect of newly synthesized antimycobacterial substances on the viability of human hepatocellular carcinoma (HepG2) cells. The tested substances were esters (HE-nMe, HE-4PHOPH, HE-KARVA, HE-2NAFT, HE-METRO, HE-CH2PY, HE-8CHIN) and thioesters (HES-4H, HES-nETH) of antituberculotic isoniazid. Experiments performed with these substances have shown, that like isoniazid, the substances inhibit InhA enzyme in mycobacteria and therefore interfere with cell wall biosynthesis. Isoniazid is a drug standardly used in the first line of TB treatment. Together with other first-line antituberculotics, some hepatotoxic potential has been reported during treatment. To assess the possible cytotoxic effect of the tested isoniazid derivatives, the standard human hepatocyte cell line HepG2 was chosen as the cell model. Cell viability was assessed by a colorimetric method that measures the metabolic activity of cells based on the reduction of the tetrazolium compound MTS. Obtained values were quantitatively compared using the toxicological parameter IC50.

The measured values show that all newly synthesized substances show very low toxicity to the selected cell line. IC_{50} values for all substances are > 100 μM. The substance tested under the name HES-4H has turned out to be the most hepatotoxic. The substances HE-CH2PY, HE-METRO, HE-nETH, HE-nMe did not show any toxic effects. In terms of liver toxicity, they therefore appear to be very promising compounds for further development.