Abstract

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Clinical research is constantly progressing, new, missing drugs are being searched for, more effective substances are being synthesized, adverse effects are being minimized.

The aim of this thesis was to determine the effect of ten substances (JZ195, JZ186, MH17, JZ178, MH9, MH18, JZ177, JZ170, JZ172, JZ174) in the HepG2 cell line and evaluate their cytotoxic potential. The tested substances were derived from the structure of pyrazine-2-carboxamide and synthesized within the Department of Organic and Bioorganic Chemistry at the Faculty of Pharmacy in Hradec Králové, Charles University and developed for the purpose of having promising effect on mycobacterial strains. Cytotoxicity was evaluated *in vitro* by CellTiter96® AQueous One Solution Cell Proliferation Assay, commercially available colorimetric method based on reduction of the tetrazolium salt to a violet-coloured formazan which directly reflects the number of viable cells. We assessed the hepatotoxic effect using the IC_{50} values obtained from the analysis of the inhibition curves and compared acquired data with the chosen drug standard – amphotericin B, representing a negative hepatotoxic control and tamoxifen as a representative of positive hepatotoxicity.

The highest IC_{50} range above the value of 100 μM was detected for substance JZ177 and MH18. Based on the results, we can draw a conclusion that each of the tested substances has a toxic effect on liver cells. Due to the precipitation of substances in higher concentrations, these values were determined only in the initial concentrations and therefore, we cannot consider the results to be specific enough. To assess the valid cytotoxic effect, further suitably adjusted studies are needed to qualify the chance of their potential use in a clinical practice more precisely.