Abstract

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Title of diploma thesis: *In vitro* testing of cytotoxicity and hematotoxicity of drugs in development

Preclinical drug evaluation is an important stage in development of new drug, it describes testing substances before they may be carried out in humans. This work is focused on the experimental measurement of cytotoxicity and hematotoxicity, which are parts of preclinical research. *In vitro* cytotoxicity tests are one of the first methods used for investigating novel drugs. Viability was monitored in the HepG2 model cell line. The viability evaluation was performed by obtaining parameter IC_{50}, the concentration of substance at which half of the cultured cells lose their viability. We studied the stability of rat red blood cells after administration of the tested substances, so we observed *in vitro* hemolysis, which is a good indicator of substances effect and safety. The EC_{50} value is monitored to determine the hemolytic effect. The EC_{50} concentration causes a hemolytic effect on 50% of tested erythrocytes. The no observed effective concentration parameter was also observed, when the 10% limit of positive control´s hemolytic activity was not exceeded. The hemolytic effect was determined on basis of structural similarity to sulfonamides. Antibacterial sulfonamides are structural analogues of our investigated substances. The test substances, as well as sulphonamides, are chemically defined as *p*-aminobenzoic acid derivatives, there are eleven potential substances with antimicrobial activity. Most of the tested substances showed a hemolytic effect comparable to HEPES buffer, a non-hemolytic standard. Three of substances appear to have hemolytic effect. HEPES buffer is needed for reading of the background absorbance. All test substances showed a negative effect on the viability of the HepG2 cell line with increasing concentration, but IC_{50} values were always above 100 μM. However, in a large number of clinically used drugs, the effective concentration is in the range of units up to tens of μM. This implies that the substances can be considered suitable for further testing.