Abstract

Charles University
Faculty of Pharmacy in Hradec Králové
Department of Pharmacology and Toxicology
Student: Bc. Marie Zádrapová
Supervisor: RNDr. Jana Maixnerová, Ph.D.
Title of diploma thesis: Determination of renal toxicity of antineoplastics *in vitro*

BRAF inhibitors are important antineoplastics. They work on the principle of inhibition of certain types of protein kinases and turned out to be very efficient for the treatment of melanoma. One of their disadvantages is relatively early onset of resistance; thus, it is important to look for new combinations of drugs that are already in use or work on the development of new structures with similar inhibition efficacy on melanoma cells. Encorafenib and its combination with binimetinib have been shown to be very promising drugs from the group of BRAF inhibitors, however, potential renal toxicity may be a therapeutic limitation.

This thesis was focused on the determination of *in vitro* cytotoxicity of encorafenib on different types of renal cells in three time intervals and on its comparison with two drug standards - amphotericin B and paracetamol. Three types of morphologically and functionally different kidney cells (PODO / TERT256, HK-2 and HEK293) were used for this purpose. The cytotoxic potential was measured by colorimetric method CellTiter 96® AQueous One Solution Cell Proliferation Assay, which is based on reduction of MTS reagent and cell viability was subsequently determined by the reduction rate. The obtained results are presented as IC_{50} values determined by analysis of the inhibition curves. The toxicity rate of the drug increased in the following order: HK2 **<** HEK293 < PODO/TERT256. This shows encorafenib to be the most toxic to podocyte cells, which may be related to the fact that BRAF is highly expressed in glomerular podocytes. As can be seen from the obtained data, encorafenib is also toxic to the other studied renal lines. Even so, encorafenib is a promising drug with good efficacy against several malignancies.