Abstract

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Title of diploma thesis: Activity of novel acridine dyes – *in vitro* study

Acridine derivatives are being investigated for their potential in the treatment of many diseases, such as cancer, bacterial infections, and malaria. For example, amsakrin, acting as a topoisomerase poison that interacts with both DNA and human topoisomerase II, is used in clinical practice in conventional antitumor chemotherapy. Derivatives of 9-aminoacridine-4-carboxidoamide act similarly. The master's thesis investigates the *in vitro* activity of the newly synthesized 9-aminoacridine-4-carboxidoamide derivatives and other derivatives of acridine.

The purpose of the thesis was to determine whether the studied compounds FK-8-HCl, FK-20-HCl, FK-27-HCl, FK-36-HCl, FK-42-HCl, FK-46-HCl, FK-48, FK-78-HCl, FK-97-HCl and FK-106 are cytotoxic, what concentration induce inhibition of proliferation, what type of cell death is triggered and whether they inhibit the human topoisomerase II.

The human epithelial cell line HeLa was used for cytotoxicity experiments. The neutral red uptake assay was used to determine the cell viability. Cells were exposed to different concentrations of studied compounds for 24 hours at 37 °C. The IC_{50} was selected as a parameter to evaluate the cytotoxicity. Inhibition of human topoisomerase II was evaluated by gel electrophoresis and kDNA decatenation assay. The identification of apoptosis or necrosis on the HeLa cell line was determined using a luminescence method. The cells were exposed to the studied compounds for 24 hours with continuous measurement of luminescence and fluorescence.

The results show that all studied acridine derivatives inhibit the proliferation of the HeLa cell line. The highest cytotoxicity was shown by the FK-78-HCl with $IC_{50} = 1{,}06 \pm 0{,}22$ μM. Except for FK-106, all substances caused inhibition of topoisomerase II. Except for FK-27-HCl, FK-36-HCl and FK-106, all substances induce apoptosis.