

ABSTRACT

Charles University in Prague
Faculty of Pharmacy in Hradec Králové
Department of Inorganic and Organic Chemistry

Candidate: Marek Kolenič

Consultant: PharmDr. Marcel Špulák, Ph.D.

Title of Thesis: Synthesis and biological evaluation of dimeflurone and benflurone derivatives

Benflurone is an original Czechoslovak cytostatic drug developed at Research Institute of Pharmacy and Biochemistry (VÚFB). Due to its unfavorable pharmacokinetic properties it has not been used for human therapy of cancer. Dimeflurone, developed with aim to improve pharmacokinetics of benflurone, was discontinued either at the phase of preclinical trials. Disadvantageous properties of both drugs is caused by rapid deactivation leading to formation of nearly inactive 7-hydroxyderivatives.

In my diploma thesis, I concern about synthesis, *in vivo* and *in vitro* biological evaluation of C₇-derivatives of both compounds. We assume lower deactivation rate and also longer and more potent effect. Firstly, sufficient amount of dimeflurone had to be synthesized, this process was improved and scaled-up.

Although all the derivatives are more cytotoxic on cell lines MCF-7, BT-549 and MDA-MB-231 and they are also less toxic in mice after p.o. administration, they do not reduce weight of solid Ehrlich tumor neither prolong time of survival.