ABSTRACT

Charles University in Prague, Faculty of Pharmacy in Hradec Králové
Department of Inorganic and Organic Chemistry
Candidate: Mgr. Lucie Tichotová
Supervisor: Prof. Milan Pour
Title of Doctoral Thesis: Coincidence of antifungal and cytostatic activity of coruscanone A derivatives and analogues of natural lactones

This Thesis was focused on the synthesis and biological evaluation of novel analogues of a natural antifungal compound, coruscanone A. For this purpose, a catalytic version of Knoevenagel condensation of cyclopent-4-ene-1,3-dione with aldehydes was developed. Evaluation of antifungal and cytostatic activity of the new derivatives revealed that antifungal activity of many compounds is accompanied by a cytostatic effect against certain tumour cell lines (CCRF-CEM). Subsequent examination of these arylidene analogues uncovered their decomposition in water medium under the conditions of *in vitro* testing. Therefore, stable analogues based on maleinimide were prepared by the Mitsunobu reaction. In these compounds, antifungal and antiproliferative effects occur simultaneously as well. *N*-2-indanylmaleinimide displayed the highest antifungal activity against *A. fumigatus*, while *N*-benzylmaleinimide had an excellent effect against HT-29 cells (IC_{50} = 0.6 μmol.l^{-1}).

Furthermore, cytostatic activity of various analogues of natural lactones was evaluated against the resistant colorectal carcinoma cell line HT-29. Since the in vitro activity of some 6-membered lactones exceeded that of clinically used antineoplastics, their structures could be used as potential leads in anticancer drug development.