ABSTRACT

Charles University Faculty of Pharmacy in Hradec Králové Department of Biochemical Sciences

Candidate: Martin Hupák

Supervisor: doc. PharmDr. Iva Boušová, Ph.D. Advisor: PharmDr. Martin Ambrož, Ph.D. Title of diploma thesis: Cytotoxicity of semisynthetic derivatives of prenylflavonoids in breast carcinoma cells

Cancer is a cause of a significant portion of death in the human population. In the Czech Republic, breast cancer is the most common type of cancer in women. Pharmacological treatment of cancer is often accompanied by resistance development, so new treatment options are still searched for and natural compounds are one of the sources of new structures. Prenylflavonoids present in common hop (Humulus lupulus, Cannabaceae), for example, xanthohumol, isoxanthohumol, 8-prenylnaringenin, 6prenylnaringenin, possess a wide spectrum of biological effects. One of them is an anticancer effect. This diploma thesis dealt with the determination of the cytotoxic potential of semisynthetic prenylated derivatives of flavonoid naringenin in breast carcinoma cell line MCF-7. Methods used included the determination of cytotoxicity using neutral red uptake assay, analysis of apoptosis and necrosis using flow cytometry, determination of mitochondrial membrane potential using JC-1 probe, and analysis of morphological changes of cells using confocal microscopy. Firstly, an initial cytotoxicity screening of all eight studied substances was performed. Substances A, B, C, and E showed the highest effect in the cytotoxicity test and were selected for further testing. The values of halfmaximal inhibitory concentration (IC₅₀) for these substances were determined to be 21.2μM (A), 45.7 μM (B), 47.3 μM (C), and 53.4 μM (E). A decrease in mitochondrial membrane potential was detected for all four substances, but this decrease wasn't statistically significant. Neither morphological changes nor changes in the ratio of apoptotic/necrotic cells were detected.