ABSTRACT

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Title of the diploma thesis: Study of the expression and toxicity of catechol derivates in breast cancer cell lines

Estrogens have several important functions in the human organism and are also involved in the formation and development of breast cancer. These effects are mediated by binding to estrogen receptors (ER) and show complex spectrum of effects such as regulation of reproduction, menstrual cycle, brain function, bone density or mobilization of cholesterol. In addition the presence and quantification of ER in breast cancer is currently used as one of the most important predictive biomarkers in patients suffering from this disease. The occurence and activity of ER correlates with the response of breast cancer to hormonal treatment and with the patient's prognosis. Despite intensive research, breast cancer is still ranked among the cancers with the highest lethality.

Catechols are organic compounds that are naturally present in food as pollutants, but also can be found in the human body, where they play an important role as precursors of neurotransmitters. Due to the presence of phenolic groups in their structure, catechols are structurally similar to polyphenols. Polyphenol-type compounds are known to have positive effects in reducing the incidence of breast cancer. However, their potential effect in the development and progression of breast cancer has not yet been completely explored.

The aim of this thesis was to study the cytotoxic activity of nine selected substances derived from the basic structure of catechol in breast tumour cell line MCF7/S0.5 and its fulvestrant-resistant derivative MCF7/182R-6. Subsequently, the level of influence of these substances on the gene expression of the estrogen-

responsive genes trefoil factor 1 (TFF1) and estrogen receptor 1 (ESR1) was tested. The results show that the test substances are well tolerated in both cell lines, even at the highest concentration tested. The study of gene expression indicated the ability of these derivatives to activate ER and increase the activity of the target genes by direct interaction with the receptor, but probably also by indirect activity. In particular, the substance 4-chloropyrocatechol (4-CPC) showed a strongly increased expression of TFF1 and similar activity for ESR1 in the MCF7/S0.5 cell line when compared to estradiol. Therefore, it was selected for more detailed study at six different concentrations. In the MCF7/182R-6 cell line, catechol activity was quite different. Compared to the parenteral cell line, TFF1 expression was significantly reduced, but for ESR1, expression results were similar. These results prove that the tested substances are able to interact with ER. Considering these results, catechol derivates may be studied in more depth as promising agents in ER-mediated physiological processes and may serve as scaffolds for the development of new active molecules.