ABSTRACT

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Title of the Diploma thesis: Study of the expression and toxicity of catechol derivatives in MCF-7 cell line

Estrogens perform many important functions in the human body. They act by binding to estrogen receptors (ER) and thus regulate reproduction, the menstrual cycle, bone density, cholesterol metabolism or brain function. They also play an important role in the development and onset of breast cancer, where the amount of ER expressed is used as a very important biomarker in patients suffering from this disease. Despite ongoing research, breast cancer is considered to have the highest mortality rate.

Catechols are organic compounds. In the human body, they can occur as metabolites in the degradation of benzene and estrogens or other endogenous compounds such as neurotransmitters and their precursors. Catechols are known to be involved in redox processes in the body, to exert antioxidant and toxic effects, to interfere with protein function and to cause DNA strand breaks. Their positive effect on breast cancer therapy is the subject of research, but it has not yet been fully explored.

The subject of this thesis is to study the cytotoxic activity of thirteen selected catechol derivatives in the breast cancer cell line MCF-7/S0.5. In the second part of the experiment, the effect of these compounds at a concentration of 10 μM on the gene expression of estrogen responsive genes Estrogen Receptor 1 (ESR1) and Trefoil Factor 1 (TFF1) was tested.

The results show that the selected catechol derivatives are not toxic at the relevant concentrations at which they might be present in the body. The lowest cytotoxic activity was exhibited by 2-aminophenol (2-APh). This substance showed proliferative effects at all concentrations, which were highest at concentrations of 100 μM and 50 μM, where

the initial values increased by up to 60 % compared with the control (DMSO 0.1 %). Other derivatives were also proliferative at these concentrations. The cytotoxic activity increased with decreasing concentration of the derivative solutions. At the lowest concentrations of 10 μM and 1 μM, only 4-MC and 3-MOC were cytotoxic.

The gene expression study showed that most of the substances at the tested concentration of 10 μM were able to activate the ER and thus increase the activity of target genes by direct and indirect interaction of each substance with the estrogen receptor. In particular, the derivative pyrocatechol (PC) proved to be a potent activator of the ESR1 gene, showing several times higher activity compared to estradiol (which was repressive). The TFF1 gene was then expressed at similar levels compared to estradiol.

Catechol derivatives may have a place, after more careful study, both in cancer prevention and in the development of new potential agents useful in anticancer therapy.