Abstract:

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Title of the diploma thesis: Study of the influence of natural drugs on estrogen receptor and confirmation of their influence in cell culture

Estrogens are one of the main reproductive hormones in women. Their function in the human organism is mediated by the estrogen receptor (ER). Estrogens are involved in important physiological processes such as reproduction, bone metabolism and cardiovascular function. Long term elevated levels of these hormones may also lead to breast cancer development.

Phytoestrogens are natural ligands of estrogen receptor widely found in dietary products. These compounds have beneficial properties in treatment of menopausal symptoms thank to their estrogenic activities but are able to function as antiestrogenic agents too. In addition, they may play a role in the development of other illnesses (breast cancer etc.). Therefore, they can be considered as a potential pharmacological tool for the treatment of estrogen-related conditions.

Within this master thesis, a total of six compounds, two phytoestrogens and four of their more relevant metabolites, were chosen (genistein, daidzein, S equol, O desmethylangolensin, 2- (R, S)-2-(4-hydroxyfenyl) propionic acid, 4 ethylphenol) and their interaction with estrogen receptor was studied by polymerase chain reaction (PCR). Cytotoxicity of the compounds was also stablished. For these purposes, we used ER expressing cell lines MCF7/S0.5 and their fulvestrant resistant derivates MCF7/182R-6.

Toxicity was tested at different concentrations. The highest toxicity was presented by S-equol in both cell lines at concentration 100 μM, which reached 50 % viability and was decreasing at lower concentrations. The remaining drugs did not report significant toxicity at all. Genetic expression results show an overall high expression of estrogen receptor target genes (TFF1 and ESR1), but at the same time differences according to concentration and cell line type. In general, results were higher in MCF7/S0.5 cell line for all phytoestrogens tested. The highest estrogenic activity was observed for daidzein, and for that reason it was chosen

for further experimentation. Results show that ER fold activation is concentration dependent. The results here presented confirm the strong estrogenic activity of the compounds. However, they indicate that the activation can be exerted also through indirect interaction with the receptor.