

Flavonoids down regulate the CYP1A1 gene expression Ystimulated by TCDD

*K. E. Joung, Mm K.N., Bang S.R., and Y.Y. Sheen.**

College of Pharmacy, Ewha University, Seoul 120-750, Korea

We have examined the effect of natural estrogen, phytoestrogens and environmental estrogens on the regulation of CYP1A1 gene expression. pCYP1A1 -luc reporter gene was transfected into MCF-7 or PC3 cells. After these cells were treated with various chemicals, luciferase assay and RTPCR were carried out to measure both CYP1A1 mRNA levels. 17beta-Estradiol significantly inhibited TCDD stimulated luciferase activity dose dependently and this inhibition was partially recovered by concomitant treatment of tamoxifen. 17beta-Estradiol(E2) metabolites, 2-OH-E2 and 16alpha-estriol resulted in less potent inhibitory effect than E2 and synthetic estrogen, diethylstilbestrol (DES) showed no effect on CYP1A1 gene expression. Some flavonoids such as genistein, morin, naringenin, chrysin, kaempferol, daidzein, octylphenol and nonylphenol, resveratrol exhibited inhibitory effect on TCDD induced luciferase activity. CYP1A1 mRNA was increased by 5-fold in MCF7 cells and 2-fold in PC3 cells with TCDD treatment. Estrogen inhibited these TCDD-induced CYP1A1 mRNA expression and this inhibition was recovered by tamoxifen treatment. This study demonstrated that estrogen downregulated TCDD stimulated CYP1A1 mRNA expression via estrogen receptor mediation. And we have found out that several flavonoids such as genistein, kaempferol, daidzein, naringenin, and alkylphenols such as nonylphenol, 4-octylphenol and resveratrol also inhibited TCDD-induced CYP1A1 mRNA expression like estrogen. [Supported by grants from the Korean Ministry of Human Health and welfare]