

## **ESTABLISHMENT OF BIOASSAY TO DETECT ESTROGENIC FLAVONOIDS USING STABLE MCF-7-ERE CELL AND MCF-7 CELL PROLIFERATION ASSAY**

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Stable MCF-7-ERE cells, in which pERE-Luc reporter gene has been stably integrated into the genome of the MCF-7 cells, were used to detect the estrogenic activity of various dietary flavonoids in either pure chemical or mixtures. Estradiol (E2) induced luciferase activity in dose dependent manner and this activity was inhibited by tamoxifen (Tam) concomitant treatment. A large series of flavonoids showed estrogenic activities, corresponding to EC50 values between 0.2 and 9 microM and their mixtures didn't show additive or synergistic effects. And we could find some structure and activity relationship. First, 4-methoxylation and catechol structure decreased estrogenic activities. Second, hydroxylation of 3 position reduced estrogenic effect. Third, glycosides of flavonoids showed weak estrogenic activity or no activity. Interestingly, when tested at high concentrations, genistein, kaempferol, biochanin A and chrysin elicited luciferase induction higher than that of the maximum induction by estradiol. And these effects of genistein and kaempferol could not be fully inhibited with tamoxifen

The estrogenic activity of the dietary flavonoids was further investigated using MCF-7 cell proliferation assay. In this system, several flavonoids were capable of mimicking natural estrogens and thereby induced cell proliferation. Among the investigated flavonoids, 7 compounds elicited the significant cell proliferation. whereas remaining flavonoids were weak estrogenic or devoid of estrogenic activity