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Modulationg effects of chrysoeriol, a methoxyflavonoid, on development of breast cancer.

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Recent epidemiologic studies showed that women working night shifts have a significantly increased risk of breast cancer. This may be due to their potential increased exposure to light at night. Now we have 24-hour societies, which make us stressful. The purpose of this study has focused on prevention of breast cancer.

17β-Estradiol (E2) plays an important role in breast cancer development. E2 is metabolized to catechol estrogens (CEs, i.e., 2- and 4-hydroxy-E2) catalyzed by cytochrome P450 (CYP) enzymes in humans. In extrahepatic tissues, 2-hydroxy-E2 is mainly catalyzed by CYP1A1, however, 4-hydroxy-E2 is formed by CYP1B1 which is highly expressed in estrogen target tissues including mammary, ovary, and uterus. And 4-hydroxy-E2 has been reported to cause hormonal carcinogenesis. Selective inhibition of CYP1B1 enzyme activity could be chemopreventive for E2-related tumor formation.

In this study, we examined the modulating effects of methoxyflavonoids on a 7-ethoxyresorufin-*o*-deethylation (EROD) activity and the 2- and 4-hydroxylation of E2 catalyzed by human recombinant CYP1A1/1B1 microsomes, respectively, and their metabolic formation in MCF-7 human breast cancer cells. We found that chrysoeriol, a natural methoxyflavonoid found in perilla seed, significantly inhibited EROD activity and 4-hydroxy-E2 formation by human recombinant CYP1B1 microsome under 0.1 μM but not for CYP1A1, and inhibited the formation of 4-methoxy-E2 but not 2-methoxy-E2 in MCF-7 cells. On the other hand, It was shown by ^{32}P-postlabeling method that chrysoeriol inhibited benzo(a)pyrene-DNA adduct formation. Chrysoeriol may be a potent chemoprotectant in human mammary carcinogenesis by selectively inhibiting the enzymatic activity of CYP1B1.