【P-69】

Resveratrol, an Antioxidant in Red Wine, Inhibits Metabolic Formation of Catechol Estrogens and Their Induction of Oxidative Dna Damage and Cell Death

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cResveratrol (3,5,4'-trihydroxystilbene), a naturally occurring phytoalexin present in grapes and other foods, has been well documented for chemopreventive effects in different systems based on its striking inhibition of diverse cellular events associated with tumor initiation, promotion and progression. In the present study, we found that resveratrol inhibited 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced cytochrome P450 1A1 (CYP1A1) and 1B1 (CYP1B1) expression in human breast MCF-10A cells and formation of catechol estrogens from 17β-estradiol in the presence of recombinant human CYP1A1 and CYP1B1. Both 2-hydroxyestradiol (2-OHE_2) and 4-hydroxyestradiol (4-OHE_2) caused intracellular reactive oxygen species (ROS) accumulation, oxidative DNA damage and apoptosis in MCF-10A cells. In contrast to the previous report that 4-OHE_2 is more carcinogenic due to its oxidative product 3,4-quinone that may cause depurinated DNA adducts, our result indicates that 2-OHE_2 is more active than 4-OHE_2 in terms of ROS accumulation, oxidative DNA damage and cytotoxicity in MCF10A cells. Resveratrol significantly attenuated intracellular ROS accumulation, 8-OH-deoxyguanosine formation induced by these catechol estrogens. Resveratrol exerted antiproliferative activity as determined by the [3H]-thymidine incorporation assay. Further studies are necessary to determine the effect of resveratrol on metabolic formation of catechol estrogens in TCDD-stimulated MCF-10A cells and its possible chemopreventive potential in mammary carcinogenesis.

Keyword : Resveratrol, TCDD, Catechol estrogens, Reactive Oxygen Species, Human breast epithelial cells