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Inhibition effects of murine CYP1A1 in mouse hepatoma hepa-1c1c7 cells by formononetin

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Isoflavone phytoestrogen, formononetin, is 4'-O-methyl derivatives of daidzein. In the present study, we investigated the effect of formononetin on 2,3,7,8-Tetrachlorodibenzo-p-dioxine (TCDD)-inducible P450 1A1 gene expression in mouse hepatoma Hepa-1c1c7 cells. TCDD-induced cytochrome CYP1A1-specific 7-ethoxyresorufin O-deethylase (EROD) activity was markedly reduced in the concomitant treatment of TCDD and formononetin in a dose dependent manner. TCDD-induced CYP1A1 mRNA level was alsomarkedly suppressed in the concomitant treatment of TCDD and formononetin. A transient transfection assay using dioxin-response element (DRE)-linked luciferase and electrophoretic mobility shift assay revealed that formononetin reduced transformation of the aryl hydrocarbons (Ah) receptor to a form capable of specifically binding to the DRE sequence in the promoter of the CYP1A1 gene. These results suggest the down regulation of the CYP1A1 gene expression by formononetin in Hepa-1c1c7 cells might be antagonism of the DRE binding potential of nuclear Ah receptor.

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