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Effects of o,p'-DDT on the 2,3,7,8-tetrachlorodibenzo-*p*-dioxin-inducible CYP1A1 expression in murine Hepa-1c1c7 cells

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Cultured mouse hepatoma Hepa-1c1c7 cells were treated with either o,p'-DDT or 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) or in combination to assess the role of o,p'-DDT on CYP1A1 expression. o,p'-DDT alone did not affect CYP1A1-specific 7-ethoxyresorufin *O*-deethylase (EROD) activity. In contrast, the TCDD-inducible EROD activities were markedly reduced upon concomitant treatment with TCDD and o,p'-DDT in a dose dependent manner. Treatment with ICI 182.780, an estrogen-receptor antagonist, did not affect the suppressive effects of o,p'-DDT cn TCDD-inducible EROD activity. The TCDD-inducible CYP1A1 mRNA levels were markedly suppressed upon concomitant treatment with TCDD and o,p'-DDT that is consistent with their effects on EROD activity. A transient transfection assay using dioxin-response element (DRE)-linked luciferase and electrophoretic mobility shift assay revealed that o,p'-DDT 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 that the down regulation of CYP1A1 gene expression by o,p'-DDT in Hepa-1c1c7 cells might be an antagonism of the DRE binding potential of the nuclear Ah receptor but is not mediated through the estradiol receptor.

Keywords : CYP1A1, o,p'-DDT, DRE, Hepa-1c1c7