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Effects of xenoestrogen on Cyp1a-1 gene expression

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4-Nonylphenol (NP) is a degradation product of a widely used non-ionic surfactant group, alkylphenol polyethoxylates that are mainly found as an intermediate in the chemical manufacturing industry. 4,4'-isopropylidenediphenol (BPA) is a monomer in polycarbonate plastics and a constituent of epoxy and polystyrene resins that are used extensively in the food-packaging industry and it has been shown to possess estrogenic properties. Cultured mouse hepatoma Hepa-1c1c7 cells were treated with either xenoestrogen (nonylphenol, Bisphenol A) or 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) or in combination to assess the role of xenoestrogen in the process of cytochrome P450 1A1 (Cyp1a-1) induction. Treatment of Hepa-1c1c7 cultures with TCDD induced Cyp1a-1, as indicated by analysis of 7-ethoxyresorufin O-deethylase (EROD) activities. Xenoestrogen alone did not affected the activity of Cyp1a-1-specific EROD; in contrast, TCDD-induced EROD activities were markedly reduced in the concomitant treatment of TCDD and xenoestrogen in a dose dependent manner. Treatment with tamoxifen, an antiestrogen that acts through the estrogen receptor did not affect the suppressive effects of Xenoestrogen on TCDD-induced EROD activity. TCDD-induced Cyp1a-1 mRNA levels were markedly suppressed in the concomitant treatment of TCDD and Xenoestrogen consistent with EROD activity. Transient transfection assay using dioxin-response element (DRE)-linked luciferase revealed that nonylphenol reduced transformation of the aryl hydrocarbons (Ah) receptor. These results suggest the down regulation of the Cyp1a-1 gene expression by xenoestrogen in Hepa-1c1c7 cells might be antagonism of the DRE binding potential of nuclear Ah receptor but not through estradiol receptor [This work was supported by KFDA Grant and RCPM from KOSEF].

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Effect of 17β-estradiol and o.p'-DDT on iNOS and proinflammatory cytokines in murine macrophages

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In this study, we investigated the effects of 17β-estradiol and o.p'-DDT on the regulation of iNOS and proinflammatory cytokines, such as, IL-1βand IL-6 in murine macrophages. 17β-estradiol, o.p'-DDT alone did not affect the expression of iNOS and proinflammatory cytokines; in contrast, treatment of 17β-estradiol and o.p'-DDT suppressed the LPS-induced gene expression of IL-1β, IL-6 and iNOS in a low dose manner, but 17β-estradiol and o.p'-DDT recovered the gene expression of IL-1β,IL-6 and iNOS in a high dose manner as determined by RT-PCR analysis. NO production was assessed by measurement of nitrites in the medium. The level of NO was found to correlate well with in transcripts of iNOS. Since the promoter in IL-1βand iNOS gene contains binding motifs for NF-kB, the effect of these on the inactivation of this transcripts factor was determined by transient transfection assay. Employing a transfection and reporter gene expression system with p(NF-kB)3-Luciferase, the treatment of 17β-estradiol produced a inhibition of luciferase activity in RAW 264.7 murine macrophage cell line; in contrast, o.p'-DDT was not effect the luciferase activity. These results suggest that 17β-estradiol and o.p'-DDT suppressed the LPS-induced gene expression of IL-1β, IL-6 and iNOS mediated by NF-kB activation site in a low dose manner, but 17β-estradiol and o.p'-DDT recovered the gene expression of IL-1β,IL-6, and iNOS in a high dose manner [This work was supported by KFDA Grant and RCPM from KOSEF].