A Study on Endocrine Disruptors: E-Screen Assay of Newly Synthesized Plasticizer

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It is well known that environmental estrogens may play an important role in the increasing incidence of breast cancer, testicular cancer, and another problems of the reproductive systems. We tested newly synthesized plasticizer by E-screen assay. E-screen assay is suitable for large-scale screening of suspected endocrine disrupting chemicals. The method introduced by Soto *et al.* is based on proliferative activity of MCF-7 estrogen sensitive human breast cancer cell line. This quantitative cell proliferation assay of MCF-7 cells was performed in the absence and presence of 17β-estradiol (negative and positive controls), and at the range of various concentrations (10^{-14}~10^{-5} M) of newly synthesized plasticizer. Cell proliferation yields in the positive control increased up to six-eight fold over those of negative control cells after 144 hr incubation. Among the newly synthesized plasticizer, KH005(10^{-11}~10^{-9} M), KH008(10^{-13}~10^{-5} M), KH010(10^{-14}~10^{-6} M) and KH011(10^{-9}~10^{-5} M) appear to possess estrogenic activity about 2~6 fold. And KH001(10^{-7}~10^{-5} M) showed week estrogenicity (1~2 fold). The most potent estrogenic chemical was KH 008(10^{-13}~10^{-5} M), which was able to stimulate these biological responses to the similar extent as 17β-estradiol itself, albeit at a 10^{-5} M fold greater concentration than 17β-estradiol. KH001(10^{-14}~10^{-5} M) exihibited very week estrogenicity. Futher study such as molding capacity for the development of new plasticizer is undergoing.

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Cytokine-mediated Induction of Metallothionein by α-Hederin in Macrophages

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α-Hederin, a triterpenoid saponin which exists in some oriental herbs, was known to decreased the hepatotoxicity of cadmium by inducing expression of the metallothionein. However, the mechanism(s) by which α-Hederin induces metallothionein is not well investigated. In the present study, we investigate the role of inflammatory cytokines in α-Hederin-induced up-regulation of the metallothionein in murine peritoneal macrophages. The induced expression of metallothionein in α-Hederin-treated cells was accompanied by increase of productions and transcripts for IL-1β, IL-6, and TNF-α in a dose-dependent manner by immunoassay and RT-PCR analysis, respectively. Since the promoter in IL-1β, and TNF-αgene contains binding motifs for NF-kB, the effect of α-Hederin on the activation of this transcription factor where determined. Using DNA fragments containing the NF-kB binding sequence, α-Hederin was shown to activate the protein/DNA binding of NF-kB to its cognate site as measured by electrophoretic mobility shift assay. Collectively, the results of these experiments indicate that expression of IL-1β, IL-6, and TNF-α were induced by α-Hederin and these results show that the inflammatory cytokines that are induced by α-Hederin may play an important role in the α-Hederin-induced up-regulation of metallothionein. [Supported by KOSEF Grant 1999-2-214-001-5]