

via progesterone related mechanism.  
Supported by NITR/Korea FDA Grant ED2001-19

[PA4-21] [ 10/18/2002 (Fri) 09:30 - 12:30 / Hall C ]

#### Estrogenic Activities of Pyrethroid Compounds in MCF-7 BUS cells

Han SoonYoung<sup>O</sup>, Shin Jae-Ho, Kang IlHyun, Kim InYoung, Kim HyungSik, Lee SuJung, Moon HyunJu, Kim TaeSung, Moon Aree \*, Choi KwangSik

Endocrine Toxicology Division, National Institute of Toxicological Research, Korea FDA: \*Department of Pharmacy, Duksung Woman's University

Pyrethroids are extensively used as insecticide in agriculture and home. Several studies have reported that pyrethroids are relatively safe to humans and wildlife. However, some studies have suggested that pyrethroids possess estrogen-like activity. Thus, the purpose of this study was to investigate the effects of pyrethroid compounds on cell proliferation, and expression of ERs and pS2 using estrogen receptor positive human breast cancer cell line (MCF-7 BUS cells). Seven pyrethroids (bioallethrin, cypermethrin, deltamethrin, fenvalerate, permethrin, sumithrin, and tetramethrin) were tested with 17 $\beta$ -estradiol as a positive control. Among the pyrethroid compounds tested, only sumithrin increased the MCF-7 BUS cell proliferation in a dose-dependent manner, maximum induction of cell proliferation was observed at dose of 10<sup>-5</sup>M. In ER expression, 17 $\beta$ -estradiol (10<sup>-10</sup>M) decreased the level of cytosolic ER $\alpha$  and ER $\beta$  protein expression compared with the vehicle control, and sumithrin significantly decreased the expression of ER $\alpha$  and ER $\beta$  protein at high concentrations, 10<sup>-7</sup> ~ 10<sup>-5</sup>M, in a dose-dependent manner. Similarly to 17 $\beta$ -estradiol, sumithrin dose-dependently increased pS2 mRNA expression. The other six test compounds used in the present study did not show any estrogenic effect at all concentrations (from 10<sup>-11</sup> to 10<sup>-5</sup>M). These findings suggest that sumithrin could be considered to induce weak estrogenic activity via ER related pathways.  
Supported by NITR/Korea FDA Grant ED 2001-19.

[PA4-22] [ 10/18/2002 (Fri) 09:30 - 12:30 / Hall C ]

#### Down-regulation of inducible nitric oxide synthase and tumor necrosis factor- $\alpha$ expression by Bisphenol A via nuclear factor- $\kappa$ B inactivation in macrophages

Kim JiYoung<sup>O</sup>, Jeong HyeGwang

Department of Pharmacy and Research Center for Proteineous Materials, Chosun University, Kwangju, Korea

Bisphenol A [BPA, 2,2-bis(4-hydroxyphenyl)propane] is reported to have estrogenic activity; however, its influence on cytokine production or immune system function remains unclear. In this study, we investigated the effects of BPA on the production of nitric oxide (NO) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and on the level of inducible nitric oxide synthase (iNOS) and TNF- $\alpha$  gene expression in mouse macrophages. BPA alone did not affect NO or TNF- $\alpha$  production. In contrast, BPA inhibited lipopolysaccharide (LPS)-induced NO and TNF- $\alpha$  production, and the levels of iNOS and TNF- $\alpha$  mRNA in a dose-dependent manner. Treatment with ICI 162,780, an estrogen-receptor antagonist, inhibited the suppressive effects of BPA. Transient expression and electrophoretic mobility shift assays with NF- $\kappa$ B binding sites revealed that BPA reduced the levels of the LPS-induced NF- $\kappa$ B transcription factor complex. These results demonstrate that BPA may affect the regulation of the immune system function by reducing NO and TNF- $\alpha$  production via the inhibition of NF- $\kappa$ B transactivation mediated through the estradiol receptor.

[PA4-23] [ 10/18/2002 (Fri) 09:30 - 12:30 / Hall C ]

#### Aluminium increase Iron uptake into Glial cells

Cheong Jae Hoon<sup>O</sup>, Lim Sung Sup, Lee Choong Jae