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In order to examine if alkylphenols and other chemicals such as curcumin derivaties have estrogenic activities we have studied uterotrophic assay, Escreening and ERE-Luc reporter assay with chemicals. Based on OEDC guideline, immature rats were administered with diethylstilbestreol as a positive control, tamoxifen as a control of antiestrogen, and various chemicals daily for three days. Rats were sacrificied and uteri were taken out and wet and dry weights were weighted. Estrogen showed uterine weight increse ten-fold over control and tamoxifen alone treatment showed minmal increse. And tamoxifen and estrogen concommitant treatment showed inhibition on estrogen stimulated uterine weight increase. Nonylphenol showed two to three-fold increase in uterine weight and phthalate showed one and half-fold increse in uterine weight. pERE-Luc was stably trasfected into MCF-7 cells and used for estrogenicity assay. 10pM Estradiol showed maximal stimulation on luciferase activity and tamoxifen showed no stimulation with alone treatment and inhibit estrogen stimulated luciferase activity when it was added into cells concommitantly. Among the tested curcumine derivatives, 10uM LV1154 showed minimal stimulation and SB118 showed moderate stimulation and SB100 showed antiestrogenic activity.[This study was supported from the grants of the ministry of environment]

[PA3-18] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Evaluation of estrogenic activities of several pyrethroid insecticides in human breast cancer cell line

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Synthetic pyrethroids are analogs of a natural chemical moiety, pyrethrin, derived from the pyrethrum plant Chrysanthemum. The natural pyrethrin structure has been modified to be highly lipophilic and photostable, creating an effective pesticide and resulting in an increased presence in the environment. Worldwide, they are commonly used insecticides against ticks, mites, mosquitoes, and as treatment for human head lice and scabies. Therefore, human exposure to their compounds in extensive. Several studies on the effects of pyrethroids on thyroid hormone regulation, estrogen and androgen function have been reported and yet little has been done to assess their potential hormonal activities.
We examined estrogenic/antiestrogenic potential of three pyrethroid insecticides, that is permethrin, allethrin and fenvalerate in human breast cancer cell(MCF7-BUS, MCF-7, T47D) and action mechanism mediated by the estrogen receptor.

[PA3-19] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Antiestrogenicity of school waste incinerator residues

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Incinerator residues samples collected from combustion of school inciner -ator contains several PACs includuing polycyclic aromatic hydrocarbons -(PAHs), polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans(PCDFs). These toxic organic chemicals may disrupt repro -ductive system by acting as estrogens or antiestrogens. In the case of PACs, they are not only ubiquitous and persistent in the environment, being primarily released from incomplete combustion process, solid wastes, and waste water but also can cause cancer.
Incinerator residues is extracted with toluene in a Soxhlet system using glass fiber thimbles. Clean-up method of incinerator residues is used in the fractionation. In this method, basic alumina binds neutral, planar aromatic compounds, which can be eluted from the colum with solvent mixtures. Fractions -(fraction I :Aliphatic hydrocarbons, nonplanar aromatic compounds -most

PCBs, fraction II :Planar aromatic compounds-PAHs, PCDDs and PCDFs, so-called "TCDD-equivalents" ) obtained from the fly ash is screened for their estrogenicity and antiestrogenicity in the E-screen assay.

[PA3-20] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Induction of Apoptosis by A Novel Intestinal Metabolite of Ginseng Saponin via Cytochrome c Mediated Activation of Caspase-3 Protease

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Ginseng saponins exert various important pharmacological effects with regard to the control of many diseases including cancer. The novel intestinal bacterial metabolites of ginseng protopanaxadiol saponins have been recently found and isolated after the oral administration of ginseng extract in human and rats. 20-O-(?-D-Glucopyranosyl)-20(S)-protopanaxadiol (IH-901) formed from ginsenosides Rb1, Rb2 and Rc is of particular interest in cancer chemoprevention and treatment. We investigated the effects of IH-901 on human myeloid leukemia cell line HL-60, in terms of inhibition of proliferation and induction of apoptosis. IH-901 showed a significant cytotoxic activity in HL-60 cells (IC50 =24.3 ?M) following a 96 hr incubation. Treatment of HL-60 cells with IH-901 resulted in the formation of internucleosomal DNA fragments. The dose- and time-dependent induction of apoptosis by IH-901 was demonstrated in the sandwich enzyme immunoassay and the results were confirmed by flow cytometric analysis. Morphological examination of IH-901 treated samples showed cells with chromatin condensation, cell shrinkage and nuclear fragmentation, which are typical characteristics of apoptotic cells. The treatment of HL-60 cells with IH-901 caused activation of caspase-3 protease and subsequent proteolytic cleavage of poly(ADP-ribose) polymerase. IH-901 did not affect the expression of antiapoptotic protein Bcl-2 but caused a release of mitochondrial cytochrome c into cytosol. In conclusion, our results demonstrate that IH-901 dramatically suppresses HL-60 cell growth by inducing programmed cell death through activation of caspase-3 protease, which occurs via mitochondiral cytochrome c release independently of Bcl-2 modulation. These results may provide a pivotal mechanism for the use of IH-901 in the prevention and treatment of leukemia.

[PA4-1] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Excretion of optical fenfluramine in the rat at various dosages.

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Fenfluramine, a substituted amphetamine derivative which lacks the psychostimulant effect of amphetamine, is abused as diet pill in Korea because it is freely marketed in China. Fenfluramine is administered orally as the racemic mixture, but it's optical isomers have different actions ; d-Fenfluramine is an anoretic agent, while l-isomer is a neuroleptic agent. An anorectic effect of racemic fenfluramine is due to its d-isomer and it's N-dealkylated metabolite d-norfenfluramine. The metabolism and excretion of fenfluramine isomers were studied in the rat following oral administration of 5, 25 and 40mg/kg of racemic fenfluramine. The enantiomeric separation of fenfluramine was performed on achiral column by gas chromatography using (S)-N-(trichloroacetyl)-L-propyl chloride (TFP-Cl) as a derivatizing agent. Urinary recoveries of l- and d-fenfluramine in urine specimens collected during first 24hr after oral dosing of racemic fenfluramine in rat were 0.72-2.72% & 1.30-5.58% and 4.20-8.17% & 11.53-20.01% in 5mg/kg and 40mg/kg dose respectively. The comparison in the levels of isomers showed that d-fenfluramine were higher than l-form, while d-norfenfluramine were lower than l-form in all doses. The metabolite to parent drug ratio declined on dosage. This indicates that high dose of femfluramine result in transient