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