The neuronal nitric oxide synthase (nNOS) specific inhibitor, 7-nitroindazole (7-NI), and the nitric oxide (NO) donor (S-nitroso-N-acetylpenicillamine: SNAP) were used to study the role of NO in polychlorinated biphenyl (PCB: Aroclor 1254)-induced cytotoxicity in the immortalized dopaminergic cell line (CATH.a cells), derived from the central nervous system of mice.
Treatment of the CATH.a cells with various concentrations of Aroclor 1254 (0.5-10 μg/ml), a commercial PCB mixture, showed significant cytotoxicity as evaluated by LDH release and assessment of cell viability, depending on the concentrations used. We also observed that Aroclor 1254 treatment reduced the level of nNOS expression and activities. Furthermore, the cytotoxicity of Aroclor 1254 was augmented by 10μM of 7-NI, which alone did not produce cytotoxicity, while it was protected by treatment with SNAP. Therefore, these results suggest that PCBs have the potential for dopaminergic neurotoxicity, which may be related with the PCBs-mediated alteration of NO production originating from nNOS. Depending on the concentrations of Aroclor 1254 used, intracellular dopamine concentrations were significantly decreased. Also, the metabolic pathway of dopamine to dihydroxyphenylacetic acid (DOPAC) was not altered by Aroclor 1254 treatment.
Thus, we suggest that Aroclor 1254 alters NO-mediated control of intracellular dopamine, which is a possible mechanism of the Aroclor 1254-induced cytotoxicity, at least in part.

[PA4-11] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

CCl4-induced Lipid Peroxidation and Acute Liver Fibrosis in the Rat

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Oxidative stress and its consequent lipid peroxidation exert harmful effects, which have been currently involved in the generation of carbon tetrachloride-induced cirrhosis. In this study, we investigated whether lipid peroxidation can be associated with liver fibrosis(cirrhosis) in CCl4-induced rats, and CCl4-induced model used in this study is suitable as screening of lipid peroxidation and liver fibrosis(cirrhosis). The female Sprague-Dawley rats were divided in 2 groups(Normal, CCl4) and were observed in 3 weeks. Except for normal, the rats rendered fibrotic(cirrhotic) by CCl4 administration(0.6㎖/rat/week) for 3 weeks. In the result, the hepatomegaly appeared in CCl4 group, and significantly higher liver weight and liver/body weight ratio were observed in CCl4 group compared with in normal group($p<0.001$). The value of clinical parameters in sera were significantly increased in CCl4-induced rats($p<0.001$). Especially, the value of MDA and the content of hyp in CCl4 group significantly increased 1.3~1.7 times than in normal group($p<0.05$, $p<0.001$). Our data indicate that lipid peroxidation and liver fibrosis(cirrhosis) can be observed in liver fibrosis-induced rats by CCl4 administration for 3 weeks. Furthermore, we suggest that lipid peroxidation may be a link between tissue injury and fibrosis in CCl4-induced rats, and CCl4-induced rat model used in this study can eliminate problem of already well known CCl4-induced experimental model.

[PA4-12] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Effect of all trans retinoic acid and 9-cis-retinoic acid on human breast cancer MCF-7 cell proliferation.

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We have examine the effect of all trans retinoic acid and 9-cis-retinoic acid on human breast cancer cell proliferation using SRB assay and cell cycle analysis. 1)In MCF-7 cells, in the presence of phenol red, either all trans retinoic acid or 9-cis-retinoic acid treatment showed the inhibition of the cell proliferation over control cells and also inhibit the estrogen stimulated cell proliferation when it was given together with estrogen. When either all trans retinoic acid or 9-cis-retinoic acid treatment in the presence of tamoxifen, it did not affect the effect of tamoxifen. 2) In MCF-7 cells, in the absence of phenol red, all trans retinoic acid alone treatment showed slight increase in cell proliferation over control cells and inhibit the estrogen stimulated cell proliferation when it was given together with estrogen. 9-Cis-retinoic acid alone treatment did not affect the cell proliferation but inhibit the estrogen stimulated cell proliferation when it was given together with estrogen. When either all trans retinoic acid or 9-cis-retinoic acid treatment in the presence of

tamoxifen, it did not affect the effect of tamoxifen. 3) The cell cycle analysis results showed that either all trans retinoic acid or 9-cis-retinoic acid treatment showed increase in G2-M phase and When either all trans retinoic acid or 9-cis-retinoic acid treatment in the presence of estrogen, it did not affect the effect of estrogen. When either all trans retinoic acid or 9-cis-retinoic acid treatment in the presence of tamoxifen, it did not affect the effect of tamoxifen. 4) The mRNA of cycline D1 was increased by either all trans retinoic acid or 9-cis-retinoic acid treatment both in the phenol red + and - medium.

[PA4-13] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Protective effects of paeonol on cultured rat hepatocytes exposed to chemical toxicants.

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Br-A23187 (Ca+2 inophore) and t-BuOOH (oxidative stressor) are frequently used as models of cell killing as Br-A23187 and t-BuOOH induce both necrotic and apoptotic cell death, respectively. The aim of this study was to evaluate the protective effects of paeonol isolated from Paeonia Moutan on cultured rat hepatocytes exposed to Br-A23187 and t-BuOOH. Cell killing was assessed by propidium iodide fluorometry. Br-A23187 and t-BuOOH caused dose-dependent cell killing. Br-A23187 and t-BuOOH-induced cell killings of hepatocytes were decreased in the presence of paeonol (20, 50, 100 uM). On the other hand, Paeonol decreased intracellular [Ca+2] level of hepatocytes in a dose-dependent manner. Therefore, the present results indicate that paeonol has protective effects against Br-A2187 and t-BuOOH-induced hepatocytotoxicity in rat, indicating paeonol decreases intracellular [Ca+2] level of hepatocytes.

[PA4-14] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Determination of 5α-Reductase Activity in Glial Cells and Rat Tissues by Gas Chromatography/Mass Selective Detector

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The steroid enzyme 5α-reductase (5AR) catalyzes the conversion of testosterone to dihydrotestosterone. Generally, 5AR activity was measured from ^{3}H- or ^{14}C- labelled testosterone as substrate by TLC or HPLC separation of its product. Radiolabelled substrate is expensive and requires the caution in its treatment. TLC and HPLC separation for the identification of the enzyme product is also the additional step. In our study, we tested to develope the new method for measurement of 5AR activity by GC/MSD without using a radiolabelled substrate. Testosterone as substrate was used for 5AR assay in brain homogenate and this reaction was started by the addition of NADPH (0.5 mM) and terminated by the addition of cold ethyl acetate. The organic layer after extraction was evaporated and the residue was derivatized with silylating agent before injection to GC/MSD. Retention times of testosterone and dihydrotestosterone were 7.2 and 6.8 min, respectivity. Calibration curve of dihydrotestosterone showed good linearity (r=0.9997). When compared specificity of substrate of dihydrotestosterone with androstenedione, specificity to these substrates were similar (1.288 ± 0.096 nmol/hr/mg protein for androstenedione vs 1.160 ± 0.087 nmol/hr/mg protein for dihydrotestosterone). Optimal incubation time and substrate concentration were decided to be 30 min and 0.1 mM, respectively. This assay was applied to measure 5AR activity in glial cells and the frontal cortex of rat brain. 5AR activity in male rat brain was about 13-fold higher compared to that in female. This method is suitable for measurement of 5AR activity in cells or tissues.

[PA4-15] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Estimation of Methamphetamine Consumption History by the Sectional Analysis of Hair