

Genotoxic evaluation of *Gryllus bimaculatus* in 3 sets of mutagenicity tests

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The mutagenic potential of *Gryllus bimaculatus* was evaluated using the short-term genotoxicity tests including Ames, chromosome aberration and micronuclei tests. In salmonella typhimurium assay, *G. bimaculatus* did not show any mutagenic response in the absence or presence of S9 mix with TA98, TA100, TA1535, and TA1537. In chromosome aberration test, *G. bimaculatus* did not show any significant effect on Chinese Hamster Ovary (CHO) cells compared with control. In mouse micronucleus test, no significant increase in occurrence of micronucleated polychromatic erythrocytes was observed in ICR male mice intraperitoneally administered with *G. bimaculatus* at a dose of 15, 150 and 1500 mg/kg. These results indicate that *G. bimaculatus* has no mutagenic potential in these in vitro and in vivo systems.

[PA4-24] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Cytochrome P-450 3A4 proximal promoter activity by histone deacetylase inhibitor in HepG2 cell.

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Cytochrome P-450 3A4 (CYP3A4) is major enzyme in human liver, the role of this is detoxification and metabolizing more than 50% clinical drugs in use. Expression of CYP3A4 is transcriptionally regulated by the Pregnenolone X receptor (PXR), of which human form is Steroid and Xenobiotics receptor (SXR). SXR is activated by wide range of endogenous and exogenous compounds, and then induces CYP3A4 gene expression. In the previous study, it has been known that proximal promoter (-864 to +64) does not response to chemical inducers such as pregnenolone 16 α -carbonitrile (PCN), Rifampicin, Estrogen in terms of transcription of CYP 3A4 in cultured cells. Here, we developed luciferase reporter gene assay system to detect SXR-based CYP 3A4 transcriptional activity. We have used CYP3A4-Luc plasmid that contains proximal promoter of human CYP3A4 gene upstream of the luciferase gene. We did transient transfection of 3A4-luciferase gene and SXR. In the HepG2 cells transfected with CYP3A4-Luc, when rifampicin treatment was combined with histone deacetylase inhibitor (HDAC Inhibitor), such as Trichostatin A, Hc-toxin and IN 2001 of the luciferase activity was induced 10-20 fold over control.

[PA4-25] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Induction of apoptosis by dihydro-N-caffeoyltyramine on human leukemia cells

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Lycii Radicis Cortex, the root bark of *Lycium chinense* Miller (Solanaceae) is used in oriental medicine as a tonic and is reported to exhibit hypotensive, hypoglycemic, and antipyretic activity. Recently, we have isolated dihydro-N-caffeoyltyramine, a phenolic amide, from the Lycii Radicis Cortex. Treatment with dihydro-N-caffeoyltyramine significantly inhibited the proliferation of human leukemia cell lines HL-60 in a dose-dependent manner. We found also that the growth inhibition of HL-60 by dihydro-N-caffeoyltyramine is associated with induction of apoptosis of cells. Dihydro-N-caffeoyltyramine induced the apoptosis of HL-60 such as apoptotic body and DNA fragmentation. In addition, the flow cytometric analysis revealed dihydro-N-caffeoyltyramine dose-dependently increased apoptotic cells with hypodiploid DNA contents. These results indicate that 4372 can control growth of leukemic HL-60 cells through apoptosis and may have a possibility of

potential anticancer activities.

[PA4-26] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Antioxidative Effect of *Houttuynia cordata* Thunb in TCDD-Damaged Rats

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Houttuynia cordata Thunb (HCT) is a herbal plant growing in China, Japan and Korea. According to the records of the Chinese medicine, this plant has been used as folk medicine for analgesics, beriberi, edema, hepatitis, icterus, etc. TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin), one of the notorious toxic environmental pollutants, damages various organs including liver and is regarded as an endocrine disrupter. After 7 days from TCDD (1 $\mu\text{g}/\text{kg}$) injection, HCT (200 mg/kg) was administered into rats intraperitoneally for 4 weeks. In this study, the effect of antioxidative enzymatic activity on HCT was investigated. This antioxidative effects of HCT on TCDD-damaged rats were measured through that the activity of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) in serum and Superoxide dismutase (SOD), Catalase (CAT), Glutathione reduced form (GSH), Glutathione oxidized form (GSSG), Glutathione peroxidase (GPx) in liver tissue. HCT administered and TCDD-damaged (HTD) group showed inhibitory effect in AST and ALT activity compared to TCDD-damaged abnormal (TDA) group. GSH, GSSG and GPx of HTD group were significantly higher than those of TDA group. SOD and CAT in HTD administered group were increased compared to those of TDA group.

[PA4-27] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

Up-regulation of inducible nitric oxide synthase expression and inflammatory cytokines by collagen and gelatin in murine macrophages

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Synthetic polymers, biological polymer such as collagen and gelatin are employed extensively as backbones in the construction of hydrogels or cell/tissue scaffoldings for various biomedical applications. In the present study, we investigated the effect of collagen and gelatin on the inducible nitric oxide synthase (iNOS) gene expression in the mouse macrophage cell line RAW 264.7. The production of nitric oxide and expression level of iNOS mRNA were induced by both of collagen and gelatin in dose-dependent manner. The production of TNF- α , IL-1 β and IL-6 and their mRNA levels of cytokines were also increased in dose-dependent manner similarly with nitric oxide and expression level of iNOS mRNA. The effects of collagen and gelatin on the transcriptional activity of NF-kB were examined, since the transcriptional regulation of iNOS has been shown to be under the control of the NF-kB. Transient expression assay with the luciferase reporter vector containing three-copies of NF-kB binding site revealed that the increased level of iNOS mRNA induced by collagen or gelatin could be mediated by the NF-kB transcription factor complex. Furthermore, collagen and gelatin activates the DNA binding ability of NF-kB, in the result of electrophoretic mobility shift analyses using the NF-kB binding sequence within iNOS promoter as a probe. These results demonstrated that nitric oxide, TNF- α , IL-1 β and IL-6 production in the collagen- and gelatin-stimulated macrophages might be induced by the up-regulation of these genes expression through NF-kB transactivation.

[PA4-28] [2003-10-10 09:00 - 13:00 / Grand Ballroom Pre-function]

A Fatal Case Involving Venlafaxine Intoxication

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