determined even at the maximal administrable dosage, 4mL/kg, due to the high viscosity of chemical and there was no significant change in body weight, hematological and serum biochemical analysis, organ weight, and histopathological examination compared with that of Cremophor EL. For the repeated dose toxicity test, male and female mice were given the dosage of 0, 1.6mL Cremophor EL/kg body weight/day, and 1.6mL Aceporol 460/kg body weight/day for 2 weeks. Results of repeated dose toxicity tests for 2 weeks suggested that Aceporol 460 treated group show no significant toxicological findings with body weight, hematological and serum biochemical analysis, organ weight, urinalysis, and ophthalmoscopic and histopathological examination compared with that of Cremophor EL. These results indicate that Aceporol 460 have higher paclitaxel-loading capacity than Aceporol 330 and less toxic effects than Cremophor EL in male and female mice.

[PA4-9] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Effects of aqueous extract isolated from Platycodon grandiflorum against oxidative stress in rat primary hepatocytes

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Herbal medicines are increasingly being utilized to treat a wide variety of disease processes. The aim of this study was to evaluate the ability of aqueous extract from the roots of Platycodon grandiflorum A. DC (Campanulaceae), Changkil (CK), to affect cellular response in primary cultures of rat hepatocytes to t-butyl hydroperoxide (t-BHP) induced oxidative stress and hepatotoxicity. CK-treated cells showed an increased resistance to oxidative challenge, as revealed by a higher percent of survival capacity in respect to control cells. CK added prior or simultaneously with t-BHP reduced enhanced lipid peroxidation measured as production of malondialdehyde and enhanced intracellular reduced glutathione depletion by t-BHP. Furthermore, CK protected from the t-BHP-induced intracellular generation of reactive oxygen species assessed by monitoring dichlorodihydrofluorescein fluorescence. It can be concluded that CK exerts an antioxidant action inside the cell, responsible for the observed modulation of the cellular response to oxidative challenge, and CK have a marked antioxidative and hepatoprotective potency.

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

Effects of Platycodi Radix on dimethylnitrosamine-induced hepatic fibrosis in rats

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Herbal medicines are increasingly being utilized to treat a wide variety of disease processes. We previously reported that aqueous extract from the roots of Platycodon grandiflorum A. DC (Campanulaceae), Changkil (CK), had hepatoprotective effects against acetaminophen induced liver injury. In the present study, we assayed the preventive and therapeutic effects of CK on experimental hepatic fibrosis induced by dimethylnitrosamine (DMN) in rats. Rats were given a single intraperitoneal injection of 20 mg/kg DMN twice weekly for 4 weeks. CK was given orally at 10-200 mg/kg daily for 4 weeks after the first injection of DMN. CK reduced the hepatic levels of malondialdehyde, a production of lipid peroxidation and partially prevented the marked decrease in body weight and reduced the mortality rate. The degree of fibrosis was evaluated by image analysis and also by measurements of collagen and hydroxyproline content in the liver. The expression of a-smooth muscle actin (a-SMA) in the liver was also evaluated. CK treatment significantly decreased the occurrence of DMN-induced hepatic fibrosis and reduced the collagen and hydroxyproline content and a-SMA expression in the liver. These findings indicate that CK suppress the induction of hepatic fibrosis and suggest that CK might be useful therapeutically in hepatic fibrosis/cirrhosis.

[PA4-11] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Protective effect of Platycodon grandiflorum against t-butyl hydroperoxide-induced hepatic toxicity in rats

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Increasing evidence regarding free radical generating agents and inflammatory processes suggests that accumulation of reactive oxygen species can cause hepatotoxicity. A short-chain analog of lipid hydroperoxide, t-butyl hydroperoxide (t-BHP), can be metabolized to free radical intermediates by cytochrome P-450 in hepatocytes, which in turn can initiate lipid peroxidation, affect cell integrity and result in cell injury. In this study, we used t-BHP to induce hepatotoxicity and determined the antioxidative bioactivity of aqueous extract from the roots of Platycodon grandiflorum A. DC (Campanulaceae), Changkil (CK). Pretreatment with CK prior to the administration of t-BHP significantly prevented the increase in serum alanine aminotransferase and aspartate aminotransferase activity and hepatic lipid peroxidation in a dose-dependent manner. Hepatic glutathione level was not affected by treatment with CK alone, but pretreatment with CK protected the t-BHP-induced depletion of hepatic glutathione levels. Histopathological evaluation of the rat livers revealed that CK reduced the incidence of liver lesions induced by t-BHP, including hepatocyte swelling, leukocyte infiltration, and necrosis. Based on the results described above, we speculate that CK may play a hepatoprotective effects via reducing oxidative stress in living systems.

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

The flavonoid quercetin inhibits dimethylnitrosamine-induced hepatic fibrosis in rats

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Quercetin, one of the most abundant flavonoids in human diet has been reported to exhibit a wide range of pharmacological properties. In this study, we investigated the protective effect of quercetin on hepatic fibrosis induced by dimethylnitrosamine (DMN) in rats. Treatment with DMN caused a significant decrease in body and liver weight. Oral administration of quercetin (10 mg/kg daily for 4 weeks) remarkably prevented this DMN-induced loss in body and liver weight and inhibited the elevation of serum alanine transaminase, aspartate transaminase, and bilirubin levels. Quercetin also increased serum albumin and hepatic glutathione levels and reduced the hepatic level of malondialdehyde. Furthermore, DMN-induced elevation of hydroxyproline content was reduced in the quercetin treated animals, the result of which was consistent with histological analysis of liver tissue stained with Sirius red. A reduction in hepatic stellate cell activation, as assessed by 깱-smooth muscle actin staining, was associated with quercetin treatment as well as a reduction in transforming growth factor-깱1 expression. In conclusion, these results demonstrate that quercetin exhibited in vivo hepatoprotective and anti-fibrogenic effects against DMN-induced liver injuries and suggest that quercetin may be useful in the prevention of hepatic fibrosis development.

[PA4-13] [10/18/2002 (Fri) 09:30 - 12:30 / Hall C]

Toxicological Evaluation of Oriental Herbal Medicine Kamijadowhan Preparations

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Choi group reported that Kamijadowhan (KMD), an oriental herbal medicine, has anti-angiogenic effects and it may be a potential agent for clinical chemoprevention since it inhibits angiogenesis. Objectives of this experiment are to investigate acute, genetic and reproductive/developmental toxicities of KMD preparations. Acute toxicity was performed after single administration of KMD (200~500 mg/kg) to mice. Supravital staining micronucleus assay was conducted using peripheral reticulocytes in mice. Thymidine kinase (tk+/-) gene forward mutation was tested in mouse lymphoma L5178Y cell line, and *Salmonella*/histidine reversion assay was tested using TA 98 and TA 100. Reproductive/developmental toxicity was performed in pregnant rats treated with two different dose of KMD. MTT-based cytotoxicity in Neuro-2A cell line was measured. In acute toxicity test using mice given KMD intraperitoneally (200~5000 mg/kg), LD_{50} value was decided to be >5000 mg/kg. The tk+/- forward gene