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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