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Solanum lyratum (Solanaceae) has been used as a traditional analgesic, antipyretic and hepatoprotective agents in Korea. In this study, we investigated the hepatoprotective effect of ethylacetate extract of *Solanum lyratum* (SL) on the dimethylnitrosamine (DMN)-induced liver damage in rats. Oral administration of SL (150, 300 mg/kg daily for 4 weeks) into the DMN-treated rats remarkably prevented the elevation of serum alanine transaminase, aspartate transaminase and alkaline phosphatase levels. SL also increased serum protein level and reduced the hepatic level of malondialdehyde in DMN-treated rats. Furthermore, DMN-induced elevation of hydroxyproline content was reduced by the treatment of SL. In conclusion, these results demonstrated that SL exhibited *in vivo* hepatoprotective effect against DMN-induced liver injury, and suggest that SL may be useful in the prevention of liver damage.

[PA4-26] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effect of Proanthocyanidins on Dimethylnitrosamine-Induced Liver Damage in Rats

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Proanthocyanidins, one of the major natural polyphenolic compounds of grape has been reported to exhibit a wide range of pharmacological properties. In this study, we investigated the hepatoprotective effect of proanthocyanidins on the dimethylnitrosamine (DMN)-induced liver damage in rats. Oral administration of proanthocyanidins (20, 50mg/kg daily for 4 weeks) into the DMN-treated rats remarkably prevented the elevation of serum alanine transaminase, aspartate transaminase and alkaline phosphatase, and bilirubin levels. Proanthocyanidins also increased serum protein level and reduced the hepatic level of malondialdehyde in DMN-treated rats. Furthermore, DMN-induced elevation of hydroxyproline content was reduced by the treatment of proanthocyanidins and which result was consistent with a histochemical analysis of liver tissue stained with Sirius red. In conclusion, these results demonstrate that the *in vivo* hepatoprotective effect of proanthocyanidins against DMN-induced liver injury, and suggest that proanthocyanidins may be useful in the prevention of liver damage.

[PA4-27] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Inhibition of capsaicin on pulmonary metastasis of B16-F10 melanoma cells

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Capsaicin (8-methyl-N-vanillyl-6-nonenamide), a pungent ingredient of hot chili peppers, has been reported to possess substantial anticarcinogenic and antimutagenic activities. In the

present study, we investigated the effects of capsaicin on pulmonary metastasis of B16-F10 murine melanoma cells, as well as its mechanism of action. Capsaicin (i.p., 2.5mg/kg) suppressed the number of lung colonies (58%) in experimental lung metastasis assay. We studied the effects of capsaicin on B16-F10 melanoma cells growth, apoptosis and expression of VEGF and iNOS using western blot and immunohistochemistry. We found that capsaicin (i.p., 1.25, 2.5 mg/kg) inhibited the expression of iNOS and VEGF in the tumor lesions. DNA fragmentation, Caspase-3 activation and cleavage of PARP were observed after treatment with capsaicin dose- and time- dependent manner. We also observed in situ DNA fragmentation in the tumor lesions using the TUNEL method in animal model. TUNEL-positive cells were rarely found in tumor lesions of control mice, whereas many positive cells with marked fragmented nuclei were present in the tumor lesions of capsaicin treated mice(i.p., 0.625 ~ 2.5 mg/kg). Also, downregulation of bcl-2 expression was observed in capsaicin treated cells, but there was no difference in the expression of bax and p53. Taken together these results, capsaicin may prevent pulmonary metastasis of B16-F10 melanoma cells through apoptosis by decreasing the bcl-2 expression and increasing of caspase-3 activity and suppression of VEGF and iNOS.

[PA4-28] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effect of skin and seed of Grape and on Dimethylnitrosamine-Induced Liver Damage in Rats

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Polyphenolic compounds have been reported to exhibit a wide range of pharmacological properties. In this study, we investigated the hepatoprotective effect of skin and seed of grape which contain abundant polyphenol compounds on dimethylnitrosamine(DMN)-induced liver damage in rats. Ingestion of skin and seed of grape (10% diet, daily for 4 weeks) into the DMN-treated rats remarkably prevented the elevation of serum alanine transaminase, aspartate transaminase and alkaline phosphatase, and bilirubin levels. They also increased serum protein level and reduced the hepatic level of malondialdehyde in DMN-treated rats. Furthermore, DMN-induced elevation of hydroxyproline content was reduced by the ingestion of grape seed and skin which result was consistent with a histochemical analysis of liver tissue stained with Sirius red. In conclusion, these results demonstrated that the in vivo hepatoprotective effect of grape against DMN-induced liver injury, and suggest that grape may be useful in the prevention of liver damage

[PA4-29] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Single and 28-day Repeated Dose Toxicity Studies of Botulinum Toxin Type A in Mice and Rats

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