

cytotoxicity of all the flavonoids tested was not affected by P-glycoprotein mediated MDR.

[PE1-19] [04/21/2000 (Fri) 10:30 – 11:30 / [1st Fl, Bldg 3]]

Antifibrotic Effects of the *Rhodiola sachalinensis* in Fibrotic Rats induced by carbon tetrachloride

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This study was carried out to investigate the protective effects of hot water extract from *Rhodiola sachalinensis* (RS) on carbon tetrachloride-induced liver fibrosis in rats. Liver injury was induced by oral administration of carbon tetrachloride (1 ml kg⁻¹) twice a week during 4 weeks of RS treatment. The RS (50, 100 and 200 mg kg⁻¹) treatment in carbon tetrachloride (CCl₄) rats reduced the serum AST, ALT and ALP levels significantly (p<0.01 for 50, 100 and 200 mg kg⁻¹). RS treatment reduced levels of liver hydroxyproline content (p<0.05 for 50 mg kg⁻¹ and p<0.01 for 100 and 200 mg kg⁻¹) and liver malondialdehyde content (p<0.05 for 50 mg kg⁻¹ and p<0.01 for 100 and 200 mg kg⁻¹). The morphological characteristic of fibrotic liver which appeared in CCl₄ group were improved in RS treated CCl₄ groups. Immunohistochemical examination showed that RS markedly reduced numbers of alpha-smooth muscle actin positive hepatic stellate cells in the CCl₄ rats. These results indicate that RS has an antifibrotic effect on fibrotic rats induced by CCl₄.

[PE1-20] [04/21/2000 (Fri) 10:30 – 11:30 / [1st Fl, Bldg 3]]

Effect of *Salvia miltiorrhiza* on biliary liver fibrosis in rats and on cultured rat hepatic stellate cells

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This study was carried out to investigate the antifibrotic effect of traditional Chinese medicinal herb, *Salvia miltiorrhiza*, on liver fibrosis induced by biliary obstruction and the antiproliferative effect on cultured rat hepatic stellate cells (HSC). Secondary biliary fibrosis was induced in male Sprague-Dawley rats by bile duct ligation/scission (BDL). Water soluble extract of *Salvia miltiorrhiza* roots (SM) was administered orally (100 mg/kg), daily after surgery. The animals were killed after 4 weeks. In BDL rats, levels of AST, ALT, alkaline phosphatase, total-bilirubin, total-cholesterol in serum and hydroxyproline, malondialdehyde content in liver were significantly increased. The SM treatment reduced the serum AST, ALT, alkaline phosphatase, and total-cholesterol levels significantly (p<0.01). Liver hydroxyproline content and malondialdehyde content in SM treated BDL rats was also reduced to 45% and 60%, respectively, that of BDL control rats (p<0.01). The morphological characteristic of fibrotic liver which appeared in BDL control group were improved in SM treated BDL groups. Immunohistochemical examination showed that SM markedly reduced numbers of alpha smooth muscle actin (α-SMA) positive HSCs in the BDL rats. SM markedly suppressed bromo-deoxy-uridin incorporation in HSCs stimulated by platelet-derived growth factor-B subunit homodimer in a concentration-dependent manner. These results indicate that traditional Chinese medicinal herb, water soluble extract of *Salvia miltiorrhiza*, significantly reduces BDL-induced progressive portal fibrosis in rats and the antifibrotic effect may be due to the inhibition of HSC proliferation.

[PE1-21] [04/21/2000 (Fri) 10:30 – 11:30 / [1st Fl, Bldg 3]]

Long-term stability and pharmacodynamic effects of PGE1 in urethral injection for erectile dysfunction

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Prostaglandin E1(PGE1), a potent peripheral vasodilator, is used in erectile dysfunction treatment, but very unstable in aqueous conditions due to degradation mechanism by dehydration. It is well known that PGE1 readily undergoes dehydration in both acidic and basic aqueous solutions to produce prostaglandin A1(PGA1) which further isomerizes to prostaglandin B1(PGB1) in alkaline conditions. In this study, long-term stability of PGE1 over 12 months was evaluated and the major degradation products of PGA1 and PGB1 was identified with standards. The amounts of degradation product, PGA1, was increased, but no trace amount of PGB1 was found at 4°C, the shelf storage condition of 4°C. Semilog plots of residual PGE1 were tried for the stability assessment of urethral injections and temperature dependences of degradation were analysed by Arrhenius plot. Pharmacodynamic effects, including intracavernous pressure(ICP), penile length and duration of erectile response of urethral injection were studied also with cats. The effects were similar to those of intracavernosal injection as control.

[PE1-22] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Characterization of Salmon Calcitonin in Microsphere by Capillary Electrophoresis with Off-Line Mass Spectrometry

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The potential of capillary electrophoresis (CE) with off-line matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS) has been demonstrated for stability and chemical changes of peptides in microspheres during in vitro release test. In this study, PLGA microsphere containing salmon calcitonin (sCT) was prepared using a solvent extraction/evaporation method. CE profiles of sCTs extracted from microspheres during in vitro release test showed the presence of an additional peak in addition to the native sCT. As the time goes on, the additional peak was increased, whereas native sCT was reduced. Using the photodiode array detection of CE, the similarity index of two peaks was 0.921, indicating the additional peak is the derivative of sCT. The fractions of two peaks were then collected for the determination of MALDI-TOF MS. MALDI-TOF mass spectrum of first peak fraction was corresponded to the mass of the native sCT (3436.46 m/z), while the second peak fraction showed two peaks (3494.15 and 3552.16 m/z). These two peaks are consistent with the mass of the complex between sCT and polymer fragments. These results indicate that some interaction between peptide and polymer within the microsphere occurs during the in vitro release test. The combination of CE and MALDI-TOF MS could be applied as a powerful tool for the characterization of peptide in the microsphere with the advantages of speed, high resolution, and small sample consumption.

[PE1-23] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Comparison of Salmon Calcitonin Release Properties Between Hydrophilic and Hydrophobic PLGA Microspheres

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