

This study was carried out to investigate the protective effect of honokiol and magnolol on tert.-butyl hydroperoxide (tBH) or D-galactosamine (GalN)-induced injury in primary cultures of rat hepatocytes. The cellular leakage of LDH and AST by 1 hour treatment of 1.5 mM tBH were significantly inhibited by treatment of honokiol (40 and 20 μ M) or magnolol (40 μ M). Hepatocyte death induced by tBH was significantly inhibited by treatment of honokiol (40 and 20 μ M) or magnolol (40 μ M). Treatment with honokiol or magnolol significantly inhibited lipid peroxidation in cells and in medium, generation of intracellular reactive oxygen species (ROS), and intracellular glutathione (GSH) depletion induced by tBH in primary cultured hepatocytes. In GalN-induced hepatocyte injury, the cellular leakage of LDH and AST by 24 hour treatment of 30 mM GalN were significantly inhibited by treatment of honokiol (20, 5, 1 and 0.2 μ M) or magnolol (20, 5, 1 and 0.2 μ M). Hepatocyte death was also significantly inhibited by treatment of honokiol or magnolol. Treatment with honokiol (20, 5 and 1 μ M) or magnolol (20 and 5 μ M) significantly inhibited the intracellular GSH depletion induced by GalN in primary cultured hepatocytes. These hepatoprotective effects of honokiol and magnolol on oxidative stress induced by tBH were probably via their antioxidant activity such as their ability of reducing intracellular ROS generation, preserving intracellular antioxidant defense system as shown by GSH preservation and inhibiting lipid peroxidation. Honokiol and magnolol also had protective effect on GalN-induced hepatotoxicity which model we used in this study as other than oxidative stress via inhibiting intracellular GSH depletion.

[PE1-3] [04/19/2002 (Fri) 10:00 – 13:00 / Hall E]

Nasal Stability of PEGylated Salmon Calcitonins

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The aim of this study was to evaluate the stabilization effect by PEGylation of salmon calcitonin (sCT) in nasal enzyme systems. It was investigated and compared to native sCT that the enzymatic degradation of positional isomers of mono-PEGylated sCT (mono-PEG-sCT) in rabbit nasal membrane homogenate and cultured human nasal epithelial cell (RPMI 2650) components. The three different positional isomers of mono-conjugated sCT with SP-mPEG (M.W. 2000), e.g., N-terminus-, Lys11-, Lys18- were directly separated by using reverse-phase HPLC and characterized by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Each sample was mixed with pre-incubated nasal membrane homogenate and RPMI 2650 cell components at 37°C, after various time intervals, the incubation was stopped by adding of ice-cold methanol solution. The residual amount and degradation products of each sample were quantified by HPLC and characterized by MALDI-TOF MS. The survival of mono-PEG-sCTs in nasal enzyme systems were increased so notable that the elimination rate constants of mono-PEG-sCTs were greater than that of native sCT by more 100 times. This finding suggests that the nasal application of mono-PEG-sCT would exhibit superior bioavailability and enhanced subsequent therapeutic effect.

[PE1-4] [04/19/2002 (Fri) 10:00 – 13:00 / Hall E]

Increased expression of nephroblastoma overexpressed gene in activated hepatic stellate cells

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The activation of the hepatic stellate cell (HSC) is a key step in liver fibrogenesis. The aim of this study is to obtain a deeper understanding of the molecular mechanisms of HSC activation. Utilizing large scale sequencing of a 3'-directed cDNA library, we investigated expression profiles of quiescent and activated rat HSCs. During the activation process, nephroblastoma overexpressed gene (NOV) was identified as one of the significant upregulated factors. Upregulation of NOV in cultured HSCs was confirmed by northern blot. NOV expression in models of experimental fibrosis and fibrotic human livers were investigated at the mRNA level using reverse transcription-polymerase chain reaction. In cultured HSC, a striking induction of NOV expression was observed after dexamethasone treatment and occurred in a time-dependent manner.