use of 3-dimensional polymeric scaffolds implanted at a tissue defect site is usually involved. These scaffolds provided a framework for cells to attach, proliferate, and form extracellular matrix(ECM). The scaffolds may also serve as carriers for cells and /or growth factors. In the ideal case, scaffold absorb at a predefined rate so that the 3-dimensional space occupied by the initial scaffold is replaced by regenerated host tissue. In this study, for polymeric material for tissue engineering scaffold, PLGA and chitosan was selected. PLGA were most often utilized for tissue engineering with biocompatible and bioabsorbable, and among the few synthetic polymers with U.S. Food and Drug administration approval for human clinical use. But polylactides have been limited in further biomedical application due to lack of cell affinity owing to their hydrophobicity and no available functional groups to attach specific cell-recognizable ligand and their acidic metabolite. Chitosan has its structure similarity to glycosaminoglycan and neutralizing capacity for PLGA acidic metabolite. The objective of this study was to develop new biodegradable tissue engineering scaffolds chitosan/PLGA fibrous composite matrix functions as high biocompatible and bioactive scaffold for cartilage regeneration. Gene expression showed that seeded chondrocytes retained their biochemical phenotype-specific characteristics (GAG, aggrecan, collagen type II) for cartilage formation throughout the entire culture period. Increased content of chitosan shows high level of phenotype specific markers. Biodegradable PLGA/ chitosan fibrous composite matrix demonstrated good cellular compatibility and cartilage regenerative potential.

[PE1-35] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Effect of Rhus verniciflua strokes acetone extracts and its components on the proliferation, collagen synthesis, and hepatic fibrosis related proteins mRNA levels in rat hepatic stellate cells

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Hepatic stellate cells (HSC) and the derived myofibroblasts are known to play a central role in liver fibrogenesis. Rhus verniciflua Strokes (RVS) has traditionally been used in Korea herbal medicine for a stomachic tonic. In this study, we observed the effect of RVS acetone extract (Ra) and its five major components on the proliferation, the collagen synthesis, and hepatic fibrosis related proteins mRNA levels in HSC-T6 cells which is a fully activated rat hepatic stellate cell line. Ra inhibited the proliferation and decreased the content of collagen in the HSC-T6 cells. The mRNA levels of TGFb1, Timp-1 and procollagen 1a1 were reduced by Ra treatment. We determined five components of Ra which are butein, fustin, sulfuretin, ficetin and 3,4-dihydroxyphenol. The anti-fibrotic activity of each component of Ra did not excellence compared with that of total Ra judging by collagen excretion and mRNA levels of hepatic fibrosis related proteins. Collectively, Ra inhibited hepatic stellate cell proliferation and collagen synthesis that might have a protective role against liver fibrosis.

[PE2-1] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Risperidone pharmacokinetics in relation to CYP2D6 and MDR1 in healthy male Korean subjects

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The purposes of this study were to evaluate the relationship between the genetic polymorphisms in CYP2D6*10 allele, MDR1 (exon 21 and 26) gene and risperidone pharmacokinetics in healthy male Korean subjects. A single dose of 2 mg risperidone tablet was given orally to 23 healthy male Korean volunteers. Blood samples were taken during the 12 hours after the dose. Serum concentrations of risperidone and 9-hydroxyrisperidone were measured using HPLC with UV detector. 23 subjects were genotyped for CYP2D6*10 allele, MDR1 G2677T and C3435T by polymerase chain reaction-restriction fragment length polymorphism(PCR-RFLP). Of the 23 individuals analyzed, 6 were homozygous for CYP2D6*1, 10 for *10, while the remaining 7 subjects were heterozygous for these alleles. MDR1 G2677T genotyping revealed that homozygous wild-type (G/G) heterozygous (G/T) and

homozygous mutant-type (T/T) was 10, 12 and 1, respectively. MDR1 C3435T genotyping revealed that homozygous wild-type (C/C), heterozygous (C/T) and homozygous mutant-type (T/T) was 9, 11 and 3, respectively. A correlation between the risperidone pharmacokinetics and genotype was observed. There were significant differences ($p<0.05$) in the disposition kinetics of risperidone and 9-hydroxyrisperidone between homozygous for *1 and homozygous for *10. A significant relationship was observed between MDR1 genetic polymorphisms in exon 21 (G2677T), 26 (C3435T) and risperidone pharmacokinetics ($p<0.05$). The ratio between risperidone and 9-hydroxyrisperidone was related to the CYP2D6*10 allele and the MDR1 (exon 21 and 26) gene significantly ($p<0.05$) affected risperidone disposition kinetics.

[PE2-2] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Determination of lisinopril in human plasma by liquid chromatography tendem mass spectrometry and its application to human bioavailibility study

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This study was to develop a quantification method of lisinopril using liquid chromatography tendem mass spectrometry in human plasma. Quntitation of lisinopril by MRM(multiple reaction monitoring) in the electrospray positive mode was validated according to FDA guideline. Extraction of lisinopril and enalapril as internal standard from plasma was perfomed by means solide phase extraction. The calibration curve of lisinopril showed a good linearity in the concentration range 2~ 200ng/ml. The coefficients of variations for the inter-day and intra-day precision was less than 15%, and the inter-day and intra-day accuracy was 97.6~101.0%. The recovery of lisinopril in the SPE was approximately 80%. This analytical method was applied to bioavailibility study. Following oral administration of lisinopril tablets (10mg dose) in 9 healthy volunteers, bioavailibility parameters were calculated by BAcal 2002 for windows(ver 1.1.1). Bioavailibility parameters(mean±S.D) were as follows : AUC_{last} =581.4 ± 236 ng hr/mL, C_{max} =36.2±15.7 ng/mL, T_{max}= 6.7±1.0 hr, $T_{1/2}$ =9.9±2.6 hr, K_e= 0.069±6.9 hr^{-1} .

[PE2-3] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

High throughput approaches to predicting drug absorption potential using the immobilized artificial membrane phosphatidylcholine column and molar volume

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The purpose of this study was to evaluate the predictability of the fraction of drug absorbed in humans using the immobilized artificial membrane phosphatidylcholine column (IAMPC) under optimized conditions in comparison with a conventional IAMPC method. Twenty commercial drugs, both acidic and basic in nature, were used in the study, Drugs were dissolved in acetonitrile:water (50:50, v/v) at a concentration of 100 mg/ml, and were injected on HPLC/UVD at a mobile phase (acetonitrile:DPBS = 10:90,v/v) with a flow rate of 0.5 ml/min equilibrated at 37℃. The IAM capacity factor (K'_{IAM}) and the membrane permeability corrected for molecular size (K'_{IAM}/MW^n) were determined at different pHs (2.6, 5.5 and 7.0). A better correlation was found when the human fraction absorption Fa (%) was plotted as a function of K'_{IAM}/MW instead of K'_{IAM} (0.550 vs. 0.446). The predictability was further improved when plotted against the corrected molecular size ($K'_{IAM}/MW^{2.53}$) (r=0.873). The prediction of Fa was higher at the pH 5.5 than at pH 2.6 and pH 7.0. The pH dependence of membrane interaction for groups of acidic and basic drugs was in accordance with the pH partition theory. This optimized IAMPC method appears to provide a good prediction of the fraction of oral drug absorbed in humans.

[PE2-4] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]