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 bioavailability study
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This study was to develop a quantification method of lisinopril using liquid chromatography tendem mass spectrometry in human plasma. Quantitation 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 performed 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 bioavailability study. Following oral administration of lisinopril tablets (10mg dose) in 9 healthy volunteers, bioavailability parameters were calculated by BACal 2002 for windows(1.1.1). Bioavailability parameters(mean±S.D) were as follows : AUClast =581.4 ± 236 ng hr/mL, Cmax =36.2±15.7 ng/mL, Tmax = 6.7±1.0 hr, T½ =9.9±2.6 hr, Ke = 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°C. The IAM capacity factor (K IAM) and the membrane permeability corrected for molecular size (K IAM/MW) 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/MW0.53) (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 ]
Drug Interaction between Nifedipine and Paclitaxel in Rats
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The purpose of this study was to investigate the effect of nifedipine (10 mg/kg) on the pharmacokinetic parameters and the bioavailability of paclitaxel (50 mg/kg) orally coadministered and pretreated in rats. The plasma concentration of paclitaxel in combination with nifedipine was significantly (p<0.05 at 10 mg/kg coadmin., p<0.01 at pretreat.) increased compared to that of control, from 2 hr to 24 hr. Area under the plasma concentration-time curve (AUC) of paclitaxel with nifedipine was significantly (p<0.05 at 10 mg/kg coadmin., p<0.01 at pretreat.) higher than that of control. Peak concentration (Cmax) of paclitaxel with nifedipine were significantly (p<0.05 at 10 mg/kg coadmin. and pretreat.) increased compared to that of control. Elimination rate constant (Kel) of paclitaxel with nifedipine were significantly (p<0.05 at pretreat.) reduced compared to those of control. Half-life (t½) and mean residence time (MRT) of paclitaxel with nifedipine was significantly (p<0.05 at pretreat.) prolonged compared to that of control. Absolute bioavailability (AB%) of paclitaxel with nifedipine was significantly (p<0.05 at 10 mg/kg coadmin., p<0.01 at pretreat.) increased compared to that of control. Based on these results, it might be considered that nifedipine may inhibit cytochrome P450 and P-glycoprotein, which are respectively engaged in paclitaxel absorption and metabolism in liver and gastrointestinal mucosa.

[PE2-5] [ 2003-10-11  09:00 - 12:30 / Grand Ballroom Pre-function ]

Bioavailability of Procarcinamide HCl in human plasma using a simple HPLC
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We aimed at determining bioavailability of procarcinamide HCl, an antiarrhythmic drug, and developing a simple analysis in human blood using HPLC. A rapid and sensitive HPLC method was developed and validated using reverse-phase C18 column with retention time and limit of quantification of procarcinamide HCl being 2.58 min and 50ng/ml, respectively. Quantification was performed at 275 nm with caffeine as internal standard. The method involved a simple extraction. In order to study blood level profile in time, eight volunteers were enrolled and orally took 250 mg procarcinamide HCl once. The blood samples were collected from 0 to 10 h after the drug administration. Mean AUC and Cmax value were 4.42±0.94 (ug/ml.hr) and 1.30±0.32 (ug/ml), respectively. And Mean Tmax and T1/2 value were 0.94±0.26 (hr) and 2.86±0.49 (hr). From the results we determine the bioavailability of procarcinamide HCl using a newly developed and useful HPLC method.

[PE2-6] [ 2003-10-11  09:00 - 12:30 / Grand Ballroom Pre-function ]

Pharmacokinetic Study of Levosulpiride Tablets in Human Volunteers
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The purpose of this trial was to determine pharmacokinetic parameters and to characterize bioavailability of levosulpiride after oral administration in Korean healthy male volunteers. Thirty subjects were received a single oral dose of a tablet (Isomeric®) containing 25 mg of levosulpiride. The plasma concentrations of levosulpiride were measured by a validated FLD-HPLC method and compared with those reported in the literature. Levosulpiride was absorbed slowly, revealing peak concentrations between 4 and 6 hr after oral administration. Based on the first-order kinetics, the rate constant for the absorption phase was obtained by method of residuals. Pharmacokinetic parameters for Isomeric® tablet were revealed as follows: AUCint 737.1±176.9 ng×hr/ml, Cmax 56.4±20.1 ng/ml, Tmax 4.2±1.6 hr, K0,1 1.00±1.99 hr−1, K10 0.08±0.02 hr−1, and t1/2 8.8±1.9 hr. In the aspect of bioequivalence, there was no significant difference between Isomeric® tablet and the other product, Levopride® tablet, which is available in the Korean market. In comparison with the published data in the literature, even though there was a linear relationship between dose and extent of bioavailability, there were not only intersubject