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 ($t_{1/2}$) 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 Procainamide HCl in human plasma using a simple HPLC

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We aimed at determining bioavailability of procainamide 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 retension time and limit of quantification of procainamide 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 procainamide 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 procainamide 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: AUC_{inf} 737.1±176.9 ng×hr/ml, C_{max} 56.4±20.1 ng/ml, T_{max} 4.2±1.6 hr, K_a 1.00±1.09 hr^{-1}, K_{el} 0.08±0.02 hr^{-1}, and $t_{1/2}$ 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

variations between groups, but also race differences between Korean and western people.

[PE2-7] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Pharmacokinetics of CJ-11555:Improvement of Bioavailability

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Purpose: The objective of the study was to elucidate the pharmacokinetics of CJ-11555, anti-cirrhotic agent, in different physical properties and vehicles. Methods: 8-week-old male intact rats were administered CJ-11555 either intravenously (20 mg/0.6 mL/kg, NMP:PEG400, 1:1) or orally (50 mg/2 mL/kg, various vehicles). Different particle sizes of CJ-11668 and various vehicles were applied to characterize CJ-11555 in vivo. Following the administration in rats, the plasma concentrations were determined by HPLC. Result: Micronized particle showed a significant increase in AUC by 160% as compared with non-micronized CJ-11555. However, no statistical different pharmacokinetic profiles among micronized CJ-11555s were found with the exception of Tmax. Suspensions in PEG and olive oil also play role in increasing AUC by 13% and 149%, respectively, as compared with suspension in saline. Conclusion: CJ-11555 has a low bioavailability due to its physical properties, however this study showed that smaller particle and liphophilic vehicle were beneficial to improve its bioavailability. In addition, this study suggest that dissolution rate would be the major concern to optimize the formulation of CJ-11555 in the future.

[PE2-8] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Drug Interaction between Diltiazem and Quercetin in Rabbits

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The purpose of this study was to investigate the effect of quercetin(2.0, 10, 20 mg/kg; combined or pretreated) on the pharmacokinetic parameters and the bioavailability of diltiazem(15mg/kg) orally to rabbits. The plasma concentration of diltiazem pretreated with quercetin(pretreated group) were increased significantly ($p<0.01$) compared to that of control, but those of diltiazem combined with quercetin(combined group) were not affected. Area under the plasma concentration-time curve (AUC) of diltiazem pretreated with quercetin was significantly ($p<0.01$) higher than that of control. Peak concentration (Cmax) of diltiazem pretreated with quercetin were significantly increased ($p<0.01$) compared to that of control. Time to peak concentration (Tmax) of diltiazem pretreated with quercetin decreased significantly ($p<0.05$) than that of control. Half-life ($t_{1/2}$) of diltiazem pretreated with quercetin was significantly prolonged ($p<0.05$) compared to that of control. Based on these results, it might be concluded that quercetin may enhance bioavailability of diltiazem due to the inhibition of cytochrome P450 and P-glycoprotein, which are engaged in diltiazem absorption and metabolism in liver and gastrogintestinal mucosa, respectively.

[PE2-9] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

New Analytical Method of Methyltestosterone in Human Serum by Gas Chromatography/ Maa Spectrometry for Pharmacokinetics and Bioequivalence Studies in Human Volunteers

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A simple, specific and sensitive method for the determination of methyltestosterone (MT) in human serum has been developed by gas chromatography/mass spectrometry with the purpose of conducting pharmacokinetic and bioequivalence studies of MT. This method involves the use of liquid-liquid extraction with diethyl ether and