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.

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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