prolonged ($p< 0.05$) compared to that of control. Based on these results, it might be due to both inhibition of the enzyme cytochrome P450 and P-glycoprotein, which engaged in paclitaxel absorption and metabolism in liver and gastrointestinal mucosa.

[PE2-7] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

PK/PD Modeling for Glucose-lowering Effect of Metformin in Korean Volunteers

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Metfotrmin is a biguanide antihyperglycemic agent often used for the treatment of non-insulin dependent diabetics(NIDDM). Metformin lowers both fasting and postprandial plasma glucose concentrations by improving insulin sensitivity at hepatic and peripheral tissues.
The pharmacokinetics and pharmacodynamics of metformin were studied in Korean healthy volunteers at fasting state over 10 hours. Plasma concentrations of metformin were determined by HPLC with UV detection. In order to evaluate the amount of glucose-lowering effect of metformin, the plasma concentrations of glucose were measured for a period of 10 hours followed by the administration of metformin(oral 500mg) and placebo respectively. After single administration of drugs, blood samples were collected for a period of 12 hours. All volunteers were consumed with 13g of white sugar 10 minutes after drug intake to maintain standard initial plasma glucose concentration.
The time courses of the plasma concentration of metformin and the glucose-lowering effect were analyzed through PK/PD modeling using ADAPT II program. The time versus plsma concentration curve of metformin was fitted to an oral two compartment model. The estimated Cmax, Tmax, CL/F(apparent clearance), V/F(apparent volume of distribution), and half-life of metformin were 1.33±0.06㎍/ml, 2.46±0.18hr, 71.2±4.4L/hr, 276.99±21.7L, and 2.66±0.05hr respectively. The maximal decrease in plasma glucose concentration was 54.39 % and detected at 6hr after administration of the drug.
The concentration of metformin and glucose-lowering activity was linked via an effect compartment model. Thus, indirect link model could describe the PK/PD characteristics of metformin and its glucose-lowering effect.

[PE2-8] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Bioequivalence Assessment of Domperidone Maleate Tablets in Healthy Human Volunteers

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The bioequivalence of two 12.72 mg domperidone maleate tablets (Sinil "Perinal®" tablets vs. Janssen Korea "Motirium-M®" tablets) was assessed in healthy volunteers after oral administration of two tablets in a randomized crossover study. Blood samples were collected at specified time intervals, and plasma was analyzed for domperidone base using a validated HPLC method. The pharmacokinetic parameters of T_{max}, $Cmax_{max}$, $AUC_{o\rightarrow 1ast}$, and $T_{1/2}$ were determined from plasma concentration-time profile of two formulations, and then statistically

compared to evaluate bioequivalence between two formulations, according to Korea Food and Drug Administration Guideline. The analysis of variance did not show any significant differences between the two formulations and 90% confidence limits fell within the acceptable range (80-120%) for bioequivalence. Based on these data it was concluded that two domperidone maleate tablets showed comparable pharmacokinetic profiles, which means that the Sinil Perinal®" tablet is bioequivalent to the Janssen Korea "Motirium-M®" tablet.

[PE2-9] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

The Study on the drug pharmacokinetics according to the progression of liver disease

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We underwent this study to know correlation between the amount of portosystemic shunt/hepatic fibrosis and bioavailability parameters such as AUC, Cmax, Tmax and t1/2 of high extraction ratio drug, propranolol, in CCl4-induced liver cirrhosis model of rats.
This study describes the bioavailability study of propranolol(5 mg/kg), Shunt Index using thallium-201 per rectum scintigraphy to measure the amount of portosystemic shunt indirectly and intrahepatic hydroxyproline content performed in the CCl4-induced liver cirrhosis model of rats. In addition an analysis of interrelationship between the results of bioavailability parameters and the amount of portosystemic shunt/intrahepatic hydroxyproline content are included.
There was a significant linear correlation between Shunt Index and AUC and between Shunt Index and Cmax (e.g., r=0.604 $p<0.001$, r=0.377 $p<0.05$, respectively). Also there was a significant linear correlation between intrahepatic hydroxyproline content and AUC between intrahepatic hydroxyproline content and Cmax (e.g., r=0.581 $p<0.001$, r=0.343 $p<0.05$, respectively). And linear regression between AUC and Shunt Index and between AUC and intrahepatic hydroxyproline content was significant(e.g., r square=0.364 $p<0.001$, 0.338 $p<0.001$, respectively). These results suggest that Shunt Index may be an important marker for predicting AUC of high extraction ratio drug in patients with chronic liver disease.

[PE2-10] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Effects of Glucose Supplementation on the Pharmacokinetics of Intravenous Chlorzoxazone in Rats with Water Deprivation for 72 Hours

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In rats with water deprivation for 72 h (rats with dehydration), hepatic cytochrome P450 2E1 (CYP2E1) was 3-fold induced with an increase in mRNA, and glucose supplementation instead of food during 72-h water deprivation inhibited the CYP2E1 induction. Chlorzoxazone (CZX) is metabolized to 6-hydroxychlorzoxazone (OH-CZX) mainly by CYP2E1 in rats. Hence, the effects of glucose supplementation on the pharmacokinetics of CZX and OH-CZX were investigated after an intravenous administration of CZX at a dose of 25 mg/kg to control rats, rats with dehydration, and rats with glucose supplementation. Based on the results of CYP2E1, the formation of OH-CZX increased in rats with water deprivation compared with in control rats. This was proven by the following results. In rats with dehydration, the total area under the plasma