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

concentration-time curve from time zero to time infinity (AUC) of OH-CZX was significantly greater (733 versus 1900 □g • min/mL), AUCOH-CZX/AUCCZX ratio was considerably greater (24.5 versus 105%), Cmax of OH-CZX was significantly higher (6.20 versus 20.6 □g/mL), Vmax (0.923 versus 1.83 nmol/min/mg protein), and CLint (0.0240 versus 0.0337 mL/min/mg protein) were significantly faster than those in control rats. It could also be expected that increased formation of OH-CZX in rats with dehydration could decrease in rats with glucose supplementation. This was also proven in the following results. In rats with glucose supplementation, AUC of OH-CZX was significantly smaller (1900 versus 1050 □g • min/mL), AUCOH-CZX/AUCCZX ratio was significantly smaller (105 versus 34.3%), Cmax was significantly smaller (20.6 versus 8.08 □g/mL), total amount excreted in 24-h urine as unchanged OH-CZX was significantly smaller (62.3 versus 42,7%), Vmax (1.83 versus 1.04 nmol/min/mg protein), CLint (0.0337 versus 0.0204 mL/min/mg protein) were significantly slower than those in rat with dehydration.

[PE2-11] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

BIOEQUIVALENCE EVALUATION OF RISPERIDONE 2 MG TABLETS IN HEALTHY MALE KOREAN VOLUNTEERS

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The purposes of this study were to evaluate bioequivalence (BE) using ln-transformed pharmacokinetic parameters obtained from two risperidone products and to develop the analytical methods for the quantitative determination of risperidone in human serum. In addition, the in vitro dissolution profiles of the two risperidone products in various dissolution media: pH 1.2, 4.0, 6.8 and water (KP Ⅶ Apparatus Ⅱ method) were assessed. BE was evaluated in 24 healthy male Korean volunteers in randomized crossover study. Single oral dose of 2 mg of each product was administered after overnight fasting. Blood samples were collected at predetermined time intervals and the concentrations of risperidone in serum were determined using HPLC method with UV detection. The dissolution profiles of two risperidone tablets were very similar at all dissolution media. Besides, the pharmacokinetic parameters such as AUCt, Cmax and Tmax were calculated and ANOVA test was utilized for the statistical analysis of the parameters using logarithmically transformed AUCt, Cmax and untransformed Tmax. The results showed that the differences in AUCt, Cmax and Tmax between two tablets based on the Risperdal® were -0.22%, 4.91% and -0.68%, respectively. And also, the 90% confidence intervals were within the acceptance range of log(0.8) to log(1.25) (e.g., 0.95~1.15 and 0.99~1.18 for AUCt and Cmax, respectively). Consequently, all parameters met the criteria of KFDA guideline for bioequivalence, indicating that Riperidone tablet is bioequivalent to Risperdal® tablet.

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

Effect of Intravenous Infusion Time on the Pharmacokinetics and Pharmacodynamics of the Same Total Dose of Torasemide in Rabbits

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The pharmacokinetics and pharmacodynamics of torasemide were evaluated after an intravenous