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

Cho HeaYoung°, Kang HyunAh, Lee YongBok

College of Pharmacy and Institute of BE and Bridging Study, CNU

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

Kim YuChul°, Lee MyungGull, Kim SoHee

College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University; Department of Pharmacology, College of Dentistry and Research Institute of Oral Science, Kangnung National University

The pharmacokinetics and pharmacodynamics of torasemide were evaluated after an intravenous

administration of the same total dose of torasemide at a dose of 1 mg/kg to rabbits with different infusion times, 1 min (treatment I), 30 min (treatment II), and 2 h (treatment III). The loss of water and electrolytes in urine induced by torasemide was immediately replaced with infusion of equal volume of lactated Ringer···s solution. All of the pharmacokinetic parameters of torasemide were independent of infusion times. For example, the mean values of terminal half-life (13.3, 13.7, and 15.8 min for treatments I쩃III, respectively), total area under the plasma concentration쩃time curve from time zero to time infinity (108, 74.4, and 101 꺷g min/ml), total body clearance (9.30, 13.4, and 10.0 ml/min/kg), and apparent volume of distribution at steady state (117, 181, and 148 ml/kg) were not significantly different among three treatments. However, 8-h urine output (235, 534, and 808 ml) and 8-h urinary excretion of sodium (24.2, 80.1, and 89.2 mmol) and chloride (27.1, 89.2, and 94.0 mmol) were significantly greater in treatments II and III than those in treatment I although the total amount of 8-h urinary excretion of unchanged torasemide (1210, 1210, and 1310 꺷g) were not significantly different among three treatments. This could be due to the higher diuretic efficiencies in treatments II and III.

[PE2-13] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Determination of a histone deacetylase inhibitor SD-2007 by LC/MS and application to a pharmacokinetic study in rats

Shin Beom Soo°, Yoon Chi Ho, Park Min Young, Jun Yoon Sik, Yoo Sun Dong

College of Pharmacy, Sungkyunkwan University

SD-2007 ia an apicidin analogue, possessing a potent histone deacetylase inhibiting activity. A rapid and senstive LC/MS method was developed for the determination of SD-2007 and its major active metabolite, apicidin, in rat serum. SD-2007 and apicidin was extracted by liquid-liquid extraction using methyl t-butyl ether. SD-2007 and apicidin were monitored in a SIM mode at m/z of 679 and 622, respectively. The chromatographic run time was 7 min and the limit of quantitation was 1 ng/ml for both SD-2007 and apicidin. This method was applied to a pharmacokintic study after i.v. (8 and 12 mg/kg doses) and oral (40 mg/kg dose) administration of SD-2007 in rats. The t1/2 and Vss ranged from 34.9-35.4 min and 3.1-3.4 L/kg, respectively, for SD-2007, and these values were similar to those found for apicidin. The absolute oral bioavailability of SD-2007 was low (2.0 ± 1.7%). However, AUC and Cmax values of the active metabolite, apicidin, were >27-fold greater than those of the parent compound.

[PE2-14] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Effects of the rate and composition of fluid replacement on the pharmacokinetics and pharmacodynamics of intravenous torasemide

Kim YuChul°, Lee MyungGull, Kim SoHee

College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University; Department of Pharmacology, College of Dentistry and Research Institute of Oral Science, Kangnung National University

The effects of differences in the rate and composition of intravenous fluid replacement for urine loss on the pharmacokinetics and pharmacodynamics of torasemide were evaluated using rabbits as the animal model. Each rabbit received 2-h constant intravenous infusion of 1 mg kg 쩃1 of torasemide with 0% replacement (treatment I, n = 6), 50% replacement (treatment II, n = 9), and 100% replacement with lactated Ringer's solution (treatment III, n = 8) as well as with 100% replacement with 5% dextrose in water (D-5-W, treatment IV, n = 6). Total body (4.53,