

AUC₀₋₂₄ increased 1:5.3:7.4 fold and 1:13:42 fold in males and 1:3.3:5.0 fold and 1:8.9:32 fold in females, respectively. On Day 28, C_{max} and AUC₀₋₂₄ increased 1:6.4:11 fold and 1:13:37 fold in males and 1:1.6:3.6 fold and 1:2.5:10 fold in females, respectively. Conclusion: CJ-11555 is dose-dependent in systemic exposure and show better absorption in female with minimum accumulation after multidosing.

[PE2-15] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Bioavailability of Clonazepam in human plasma using a simple HPLC

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We aimed at determining bioavailability of clonazepam, an anxiolytic 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 retention time and limit of quantification of clonazepam being 2.58 min and 5ng/ml, respectively. Quantification was performed at 235 nm with p-hydroxybenzoic acid ethyl ester 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 6 mg clonazepam once. The blood samples were collected from 0 to 120 h after the drug administration. Mean AUC and C_{max} value were 1028.17 ±568.165 (ng/ml.hr) and 41.2487 ±10.8180 (ng/ml), respectively. And Mean T_{max} and T_{1/2} value were 1.08375 ±0.42604 (hr) and 30.7823 ±3.26003 (hr). From the results we determine the bioavailability of clonazepam using a newly developed and useful HPLC method

[PE2-16] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Pharmacokinetic disposition of apicidin possessing histone deacetylase inhibiting activities

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The objective of this study was to characterize the absorption and pharmacokinetic disposition of a novel cyclic tetrapeptide, apicidin, in rats. Apicidin was administered to SD rats by i.v. bolus injection (1, 2 or 4 mg/kg) and oral gavages (10 mg/kg). Serum levels of apicidin were monitored by LC/MS over 8 hours following each administration. Upon i.v. injection, serum levels of apicidin were best fit by a multi-exponential equation. The t_{1/2}, Cl_s and V_{ss} ranged from 0.9-1.1 hr, 52.8-56.5 ml/min/kg, and 2.6-2.7 L/kg, respectively. No significant difference was found in these parameters as a function of the administered doses. The mean absolute oral bioavailability was 8.1±3.4%. The fraction of unchanged drug excreted in urine was low (<0.1%).

[PE2-17] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Bioequivalence of EnalaceTM Tablet to RenitecTM Tablet(Enalapril maleate 10 mg)

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ABSTRACT-The purpose of the present study was to evaluate the bioequivalence of two enalapril maleate tablets, RenitecTM(MSD Korea Ltd.) and EnalaceTM(Welfide Korea Ltd.), according to the guidelines of Korea Food and Drug Administration (KFDA). Twenty-four normal male volunteers, 22.33 ± 2.55 year in age and 66.54 ± 8.30 kg in body weight, were divided into two groups and a randomized 2x2 cross-over study was employed. After two tablets containing 10 mg of enalapril maleate per tablet were orally administered, blood was taken at predetermined time intervals and concentrations of enalapril in plasma were determined using LC-MS-MS. Pharmacokinetic parameters such as AUC_t, C_{max} and T_{max} were calculated and ANOVA test was utilized for the statistical analysis of the parameters using logarithmically transformed AUC_t, and C_{max}, untransformed T_{max}.

There were no sequence effects between two formulations in these parameters. The 90% confidence intervals for the log transformed data were acceptance range of log0.8 to log1.25(e.g., log1.02~log1.14 and log1.03~log1.19 for AUCt and Cmax, respectively). The major parameters, AUCt and Cmax, met the criteria of KFDA for bioequivalence indicating that Enalace™ tablet is bioequivalent to Renitec™ tablet.

[PE2-18] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Pharmacokinetics of DA-8159, a new PDE5 inhibitor, after single and 1-week repeated oral administrations in mice

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DA-8159 is a new PDEV (Phosphodiesterase V) inhibitor, synthesized by Dong-A Pharm., as an oral agent to treat male erectile dysfunction. To make a selection of the dosage of oral administration in carcinogenic studies, we studied preliminarily the pharmacokinetics of DA-8159 after single (at the 1st day) and 1-week (at the 7th day) oral administrations of the drug at doses of 15, 50 and 150 mg/kg/day, to male ICR mice. In 15mg/kg single and 1-week repeated oral administration groups, the concentrations of DA-8159 and DA-8164(the main metabolite of DA-8159) were below the limit of quantitation(LOQ:50ng/ml). The AUC of DA-8159 was not significantly different between single and 1-week oral administration at 50mg/kg/day. But the AUC of DA-8159 150mg/kg/day 1-week oral administration group was two times higher than that of single administration group. The metabolic ratios (AUC of DA-8164 divided by AUC of DA-8159) of 1-week oral administration at 50mg/kg/day and 150mg/kg/day were increased than those of single oral administration groups. And the metabolic ratios of DA-8159 in mice were very high(over 100%). The metabolic ratio from DA-8159 to DA-8164 of mice was more than those of rats(48.9%), dogs(10.0%) and humans(59.4%).

[PE2-19] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Determination of Prazosin in Human Plasma Using a Validated HPLC Method and Bioavailability of a Tablet Formulation

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A rapid and reproducible high performance liquid chromatographic assay of prazosin in human plasma was developed. After addition of internal standard (IS, terazosin hydrochloride) and alkalization of the plasma, the drug and IS were extracted into t-butylmethylether. The organic phase was back-extracted with 0.05% phosphoric acid and 50 µl of the acid solution was injected into a reverse-phase C18 column with a mobile phase consisting of water : acetonitrile : triethylamine = 75 : 25 : 0.1 (pH 5.0). The samples were detected utilizing a fluorescence detector. Prazosin and IS showed good resolutions and an excellent linear relationship was ($r^2 = 1$) was obtained between the peak area ratios and the corresponding concentrations in the ranges of 0.5-50 ng/ml. The applicability of the method was demonstrated by analysis of plasma after oral administration of a single 2-mg dose to 16 healthy subjects. From the plasma prazosin concentration vs. time curves, the mean $AUC_{0 \rightarrow 12}$ was 108.4 ± 74.2 ng · h/ml and Cmax of 23.1 ng/ml reached 2.1 h after administration. The mean biological half-life of prazosin was 2.5 ± 0.6 h. (This study was supported by a grant from Korea Food and Drug Administration; KFDA-03142-EQ1-519)

[PE2-20] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

The Effect of Quercetin on the Pharmacokinetics of Paclitaxel in Rats

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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