

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

pharmacokinetic parameters and the bioavailability of paclitaxel(50mg/kg) orally in rats. The plasma concentration of paclitaxel pretreated with quercetin(pretreated group) were increased significantly ($p<0.01$) compared to that of control, but those of paclitaxel combined with quercetin(combined group) were not affected. Area under the plasma concentration-time curve (AUC) of paclitaxel pretreated with quercetin was significantly ($p<0.01$) higher than that of control. Peak concentration (C_{max}) of paclitaxel pretreated with quercetin were significantly increased ($p<0.01$) compared to that of control. Time to peak concentration (T_{max}) of paclitaxel pretreated with quercetin decreased significantly ($p<0.05$) than that of control. Half-life ($t_{1/2}$) of paclitaxel pretreated with quercetin was significantly prolonged ($p<0.05$) compared to that of control. Based on these results, it might be concluded that quercetin may enhance bioavailability of paclitaxel due to the inhibition of cytochrome P450 and P-glycoprotein, which are engaged in paclitaxel absorption and metabolism in liver and gastrointestinal mucosa, respectively.

[PE2-21] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Bioequivalence of Two Enalapril Maleate Tablets (Enalapril maleate 20 mg)

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Bioequivalence of two enalapril maleate tablets, formulation A and B, was evaluated according to the Korean Guidelines for Bioequivalence Test (KGBT 2001). Twenty healthy male volunteers (19–27 years old) were randomly divided into two groups and a randomized 2x2 cross-over study was performed. Following oral administration of enalapril maleate tablets (20 mg dose), blood sample was taken at pre-determined time intervals and the concentrations of enalapril in plasma were determined using LC-MS. A statistical difference of bioavailability parameters (AUClast, C_{max} , and T_{max}) between the two formulations was tested by ANOVA(EquivTest ver 2.0, Statistical Solutions Ltd.). The result showed that the differences in AUClast, C_{max} , and T_{max} between the two formulations were 3.36%, 0.44%, and -1.11%, respectively. Ninety percent confidence intervals of Log(AUClast) and Log(C_{max}) were 0.9829~1.2002 and 0.9491~1.1237, respectively.

[PE2-22] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Plasma Pharmacokinetics and Urinary Excretion of Isoflavones After Ingestion of Soy Products with Different Ratio of Aglycone/Glucoside in Korean women

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Lately, soybeans have received considerable public attention for their potential roles in the prevention of the chronic diseases. Epidemiologic study showed that Asian countries have significant health benefits because of the high contents of the isoflavones in their traditional diets(soybean-rich diet). This study was carried out to determine pharmacokinetic parameters of isoflavone in Korean woman. Pharmacokinetic study of three soy products(isogen, soymilk, and fermented soybean) with different ratio of aglycone/glucoside in 26 healthy female volunteers(20-30 years of age) was performed. After ingestion of three soy products, the plasma and urine concentrations of isoflavones were measured by HPLC. The pharmacokinetic parameters were estimated using the WinNonlin program. The plasma AUC of daidzein in soymilk($2101\pm352 \mu\text{g hr/L}$) ingested group was significantly lower than those of isogen($2628\pm573 \mu\text{g hr/L}$) and fermented soybean($2593\pm465 \mu\text{g hr/L}$) ingested group. The plasma C_{max} of daidzein in soymilk($231\pm44\text{ng/ml}$) ingested group was significantly higher than those of isogen($160\pm32\text{ng/ml}$) and fermented soybean($195\pm35\text{ng/ml}$) ingested group. The half-life of daidzein and genistein in soymilk ingested group(5.9h and 5.6h respectively) was significantly shorter than those of in isogen(9.6h and 8.5h respectively) and fermented soybean(9.5h and 8.2h respectively) ingested group. The urinary recovery of daidzein and genistein were 42% and 17% in isogen ingested group, 46% and 23% in fermented soybean ingested group, and 33% and 22% in soymilk ingested group. In conclusion, soy products containing high aglycone forms of isoflavone are more effective than soy products containing low isoflavone