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The compound of 2"-O-benzoylcinnamaldehyde(CB-ph) is a derivative of 2"-hydroxycinnamaldehyde whcih is a methanol extract of cinnamomum cassia blume. It"s a new anti-cancer agent which has been showed to inhibit the growth of various tumor cells in vitro and in vivo. In order to investigate the effective drug concentration and bio-distribution of CB-ph, the plasma protein binding was studied. In this study, the degree of the binding of Cb-ph to various serum proteins, the binding parameters, the binding site of CB-ph in human serum albumin, and the effect of some extensive protein-binding drugs on the protein binding of CB-ph in human serum albumin were investigated respectively by ultrafilteration and fluorescence spectrometry. From the results, it was found that CB-ph was a highly protein binding drug to human serum albumin, albumin was the major binding protein of CB-ph, and CB-ph bound especially to site I on human serum albumin according to an one-class model. The binding costant (Ka) was 55,377M^{-1} and the number of binding site of CB-ph to HSA was 0.6629 by Scachard plots, respectively. The protein bound fraction of CB-ph in HSA increased with an increase of HSA concentration. However, the binding of CB-ph was independent of incubation temperature. If CB-ph and site-I binding drugs, such as warfarin, were administered together, it was necessary to control the drug dosage regimen because of remarkable increasing of the protein unbound fraction of drug resulted from the protein binding displacement.

[PE2-13] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Pharmacokinetics of eupatilin, an active componets of Stillen?, a new antigastritic agent, in rats

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The pharmacokinetics of eupatilin (an active components of Stillen®, a new antigastritic agent) were investigated using UV-HPLC method. The quantitation limit of eupatilin was 10 ng/ml in plasma. After intravenous administration of eupatiln, 30 mg/kg to rats, the plasma concentrations of unchanged eupatilin declined rapidly with the mean terminal half-life of 0.101 hr. Total body clearance was 121 ml/min/kg, and fractions of dose excreted in urine and feces for 24 hr were only 2.5% and 0.919%, respectively. But hydrolysis of glucuronide conjugated form of eupatilin with β-glucuronidase, the mean terminal half life of eupatilin including glucuronide conjugated form was prolonged with 22hr and the fractions of dose excreted in urine for 24 hr was increased with the value of 15.9%. After oral administration of eupatilin, 30 mg/kg to the rats, the absolute bioavailability was only 3.87% even though including glucuronide conjugated form of eupatilin. GI residual % of dose as an intact drug at 24 hr after oral administration of eupatilin, 30 mg/kg to rats was 68.5%, and that of as including conjugated form was 90.8%. The large parts of eupatilin after oral administration were remained in gastrointestinal tract, an active site of drug.

[PE2-14] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Toxicokinetics of CJ-11555: Gender Difference and Minimum Accumulation

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Purpose: This study evaluated gender differences and extents of accumulation on chronic dose of CJ-11555 using rats. Method: 0, 10, 50 and 200 mg/kg/day of CJ-11555 (0.5% CMC) were orally administered to rats for 28 days and observed toxicokinetic parameters. Plasma concentrations were analyzed by LC-MS/MS Result: Exposure to CJ-11555 increased with the increase in dose level for both sexes. Mean concentrations at 10 and 50 mg/kg/day were generally similar on Days 1 and 28, but were generally higher on Day 28 than on Day 1 at 200 mg/kg/day. C_{max} and AUC_{0-24} values were generally slightly higher in females on both collection days. There were no marked (>2 fold) differences in C_{max} and AUC_{0-24} values on Day 28 compared to Day 1 (except for females administered 10 mg/kg/day). Following the administrations of 10, 50, and 100mg/kg/day, on Day 1, C_{max} and

AUC_{0-24} 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 AUC_{0-24} 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 retension 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 Cmax value were 1028.17 ±568.165 (ng/ml.hr) and 41.2487 ±10.8180 (ng/ml), respectively. And Mean Tmax and T1/2 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 Enalace™ Tablet to Renitec™ 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, Renitec™(MSD Korea Ltd.) and Enalace™(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 2×2 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 AUCt, Cmax and Tmax were calculated and ANOVA test was utilized for the statistical analysis of the parameters using logarithmically transformed AUCt, and Cmax, untransformed Tmax.