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The purposes of this study were to evaluate bioequivalence (BE) using ln-transformed pharmacokinetic parameters obtained from two fluconazole products and to develop the analytical methods for the quantitative determination of fluconazole in human serum. In addition, the in vitro dissolution profiles of the two fluconazole products at dissolution media: 0.1 M hydrochloride (KP Ⅶ Apparatus Ⅱ method) were assessed. BE was evaluated in 20 healthy male Korean volunteers in randomized crossover study. Single oral dose of 150 mg of each product was administered after overnight fasting. Blood samples were collected at predetermined time intervals and the concentrations of fluconazole in serum were determined using HPLC method with UV detection. The dissolution profiles of two fluconazole capsules were very similar. 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 capsules based on the Diflucan® were 4.96%, 5.65% and -13.76%, respectively. And also, the 90% confidence intervals were within the acceptance range of log(0.8) to log(1.25) (e.g., 1.01~1.08 and 1.00~1.12 for AUCt and Cmax, respectively). Consequently, all parameters met the criteria of KFDA guideline for bioequivalence, indicating that Flucona capsule is bioequivalent to Diflucan® capsule.

[PE2-17] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Improved Dissolution Characteristics of Silymarin and Their Bioavailability in Human Volunteers

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Silybin is the main component of *Cardus marianus* extracts (Silymarin) originated from Silybum marianum, called as milk thistle. It has a hepato-protective effect and is used clinically for the treatment of liver disease. But it is water-insoluble and is poorly absorbed from the gastrointestinal tract, resulting in very low oral bioavailability. Polymeric mixed-micelle precursor formulation containing surfactants, co-solvents, and block-co polymers with *Cardus marianus* extracts was made to enhance the dissolution rate of silybin and encapsulated with soft gelatin capsule. This precursor formulation forms micelle spontaneously when it contacts with gastro-intestinal fluid, and thereby can be absorbed rapidly. The oral bioavailability of the new formulation was estimated in twelve healthy male volunteers, and compared with that of a marketed product. After oral administrations of two capsules at a dose of 120 mg/kg as silybin, pharmacokinetic parameters including Cmax, Tmax, and AUC were obtained from the plasma concentration-time profiles of silybin : Cmax and $AUC_{0\sim8hrs}$ of the new formulation were 4.3 times and 2.4 times greater, respectively, than those of a marketed product.

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

Dose-Independent Pharmacokinetics of a New Neuroprotective Agent for Ischemia-Reperfusion Damage, KR-31543, after Intravenous and Oral Administration to Rats: