And then, the pharmacokinetic profile of omeprazole was examined in selected 15 volunteers (G1-G5, each three subjects). A correlation between the rate of metabolism of omeprazole and genotype was observed. There were significant ($p<0.05$ to 0.01) differences in the disposition kinetics of omeprazole between the subjects with patterns G1, G2, and G3 and the subjects with patterns G4 and G5. The results indicate that the 5-hydroxylation pathway of omeprazole is clearly impaired in subjects with m1/m2 and m1/m1.

[PE2-12] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

The Effect of Bile juice on the Bioavailability and Pharmacokinetics of Acebutolol and Diacetolol After Oral Administration of Acebutolol

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Acebutolol (ABT) is almost absorbed after oral administration, but its bioavailability is reduced because of considerable first-pass metabolism through the gastrointestinal and liver. The purpose of this study was to report the effect of bile juice on the bioavailability and pharmacokinetics of ABT and its metabolite, diacetolol (DAT) after oral administration of acebutolol in control rabbits and rabbits with bypass of bile duct. Plasma concentrations and the area under the plasma concentration-time curves (AUC) of ABT and DAT were increased compared to control rabbits, but that of DAT was significantly influenced ($p<0.05$). Absolute bioavailability(A.B.) of ABT in rabbits with bypass of bile duct(71.8%) was higher than control rabbits and also relative bioavailability(R.B.) of ABT was increased to 122%. Peak concentration time(Tmax) of ABT and DAT in rabbits with bypass of bile duct was significantly prolonged compared to control rabbits($p<0.01$). Mean Resident Time (MRT) of ABT and DAT in rabbits with bypass of bile duct were significantly increased ($p<0.05$) compared to control rabbits. Half-life of ABT and DAT in rabbits with bypass of bile duct were prolonged compared to control rabbits but that of DAT was significantly influenced ($p<0.05$). The results suggest that the dosage of acebutolol should be adjusted in disorder of bile juice flow.

[PE2-13] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Prediction of population pharmacokinetic parameters of aceclofenac using Monte Carlo simulations

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The aceclofenac data analysis suggested that pharmacokinetic parameters were an important predictor of efficacy outcome. The purpose of this study is to estimate the relationship between individual pharmacokinetic and population pharmacokinetic parameters using Monte Carlo method. Plasma data from 21 healthy male subjects who participated in pharmacokinetic studies of aceclofenac were included in this analysis. After each subject received a single 100 mg oral dose of aceclofenac, 2-compartment model was fitted to the aceclofenac data using WinNonlin. In addition, one thousand Monte Carlo simulations were conducted assuming that the normal distribution of the pharmacokinetic parameters, such as A, B, α, β, Ka, K21 and Tlag, obtained from the individual subjects. The results demonstrate that Monte Carlo simulations as adjuncts to the current methods could be used for prediction of population pharmacokinetic parameters of aceclofenac.

[PE2-14] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Brain Distribution of Dehydroevodiamine in Rats