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The techniques that can potentially enhance the dissolution rate and extent of absorption of poorly soluble drugs is the formation of solid dispersion with polymeric materials. To increase the dissolution rate of furosemide, vitamin E TPGS (d-alpha tocopheryl polyethylene glycol 1000 succinate) was used as a drug carrier. The 1:2(w/w) solid dispersion was prepared by solvent method. The dissolution test, X-ray diffraction, Infrared spectra, thermal analysis of furosemide test systems were carried out. The dissolution rate of furosemide-vitamin E TPGS solid dispersion was enhaced markedly than that from the physical mixture or intact furosemide. The X-ray diffraction, IR, DTA, and TGA studies showed the physiochemical modification of the furosemide from the solid dispersion. The crystalline peaks of furosemide alone or furosemide contained within a physical mixture were disappeared in the solid dispersion indicating the amorphous form. An interaction, in the solid dispersion such as an association between the functional groups of furosemide and vitamin E TPGS might have occurred at the molecular level, changing the physicochemical property and increased the dissolution of furosemide. The results showed that the extent of dissolution was significantly enhanced, following formation of the solid dispersion, and the solid dispersion techniques with vitamin E TPGS provide a promising way to increase the dissolution rate of poorly soluble drug.

[PE1-14] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Circadian Changes in Pharmacokinetics of Acebutolol Orally Administered to Rabbits

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Effect of circadian rhythm on the pharmacokinetics of acebutolol and its metabolite, deacetylacebutolol was studied in rabbits after a single oral administration of acebutolol, 20mg/kg, in the morning (09:00 A.M.) and in the evening (21:00 P.M.). The plasma data were subjected to simultaneous computer nonlinear least squares regression analysis using a two-compartment pharmacokinetic model.

The elimination rate constant(β) of acebutolol were 0.072 ±0.016 hr^{-1} in the morning and 0.066 ± 0.013 hr^{-1} in the evening. The total body clearance(CLt) and area under the plasma concentration-time curve(AUC) of acebutolol were 3.02 ±0.52 L/hr/kg and 6.79 ±1.21 μg/ml·hr in the morning and 2.41 ±0.43 L/hr/kg and 9.16 ±1.69 μg/ml·hr in the evening. The plasma concentrations of acebutolol in the evening were increased during 4-12hr compared to those of acebutolol in the morning. The CLt of acebutolol in the evening were decreased significantly ($p < 0.05$) compared to that of acebutolol in the morning and the AUC of acebutolol in the evening were increased significantly ($p < 0.05$) compared to that of acebutolol in the morning.

However, the pharmacokinetic parameters of its metabolite were not significantly different between in the morning and in the evening.

[PE1-15] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Pharmacokinetic Changes of Intravenous Diltiazem in Alloxan-Induced Diabetes Mellitus Rabbits

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Because physiological changes occurring in diabetes mellitus patients could alter the pharmacokinetics of the drugs used to treat hypertention resulting from diabetic complications,the pharmacokinetics of diltiazem were investigated after intrvenous administration of the drug (4 mg/kg) to control rabbits and rabbits with acute and chronic diabetes induced by alloxan. Impaired kidney and