antibody (PharMingen, A Becton Dickinson Co., San Diego, CA, U.S.A.). We established the four modified indirect pharmacodynamic model (A~D) to estimate the parameters of CD4 T cell counts in lymph nodes and whole blood. We used the estimated concentration of CSA derived from the proposed pharmacokinetic model in lymph node and blood. The profiles of CD4 T cells were well fitted to these four pharmacodynamic models. So, in order to identify the pharmacodynamic model having physiological meaning from the above pharmacodynamic models, it was suggested that the pharmacological response in lymph was needed to be investigated *in vitro*.

[PE2-9] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Pharmacokinetics of Diltiazem and Deacetyldiltiazem after Oral Administration of Diltiazem in Mild and Medium Folate-Induced Renal Failure Rabbits

Jung EJ, Choi JS, and Burm JP°

College of Pharmacy, Chosun University, Chosun Nursing College

Diltiazem inhibits calcium channels and leads to vascular smooth muscle relaxation and negative inotroic and chronotropic effects in the heart. Diltiazem is almost completely absorbed after oral administration, but its bioavailability is reduced because of considerable first-pass hepatic metabolism. The main metabolite of diltiazem is deacetyldiltiazem. Diltiazem is able to dilate renal vasculature and can increase the glomerular filtration rate and renal sodium excretion.
The purpose of this study was to report the pharmacokinetic changes of diltiazem (DTZ) and the metabolite, deacetyldiltiazem (DAD) after oral administration of diltiazem to control rabbits and mild and medium folate-induced renal failure rabbits (FIRRs).
The AUC and Cmax of DTZ were significantly increased in mild and medium FIRRs. The metabolite ratio of the DAD to DTZ were significantly decreased in mild and medium FIRRs. The Volume of distribution (Vd) and total body clearance (CLt) of DTZ were significantly decreased in mild and medium FIRRs. The elimination rate constant (β) of DTZ was significantly decreased in FIRRs, but that of DAD was significantly increased. These findings suggest that the hepatic metabolism of diltiazem was inhibited and Vd, CLt and β of DTZ were significantly decreased in mild and medium folate-induced renal failure rabbits.

[PE2-10] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Distribution of AG-60, a Potential Anticancer Agent, in Tissues and Platelets of the Rat.

Yeom ZH°, Lee SU, Hwang JI, Chung YB and Han K

College of Pharmacy, Chungbuk National University, Cheongju, Chungbuk 361-763, Korea

The purpose of the present study was to investigate the distribution of AG-60 in rats. For this purpose, the distribution of AG-60 in tissues and platelets for 48hr was measured after its im administration. Pharmacokinetics of AG-60 was reported in a our previous presentation. AG-60 is a potential anticancer agent which is a 1:1 complex of acriflavine (ACR) and guanosine. ACR is a 1:2 mixture of proflavine(PRF) and tripaflavine (TRF). The distribution of TRF and PRF was relatively high in the kidney, lung and liver, low in the intestine and the muscle. The tissue concentration of TRF was higher compared with that of PRF. The tissue concentration of both TRF and PRF was not detected after 24hr. On the other hand, we measured distribution of AG-60 in plasma, blood cells and platelets. The concentration of PRF and TRF in plasma and blood cells were not detected after 6hr, and blood cells concentration was similar to plasma concentration. We also measured the concentration of PRF and TRF in platelets and found that 0.183x10E8 platelets existed in 1 mL blood. Amount of PRF and TRF per 1.0x10E8 platelets was calculated. PRF concentration levels were two times higher than TRF concentration level at 1hr after im