

quite fast, but faster in plasma and even faster in blood. It was found that the fraction of systemic clearance of triflusal (Fmi) was 0.9573. These results showed that triflusal was metabolized by 95.73% in rats and the residue would be hydrolyzed via the other route. Therefore, it would be necessary for the investigation of metabolite kinetics of triflusal to HTB to incorporate the degradation process of triflusal in blood into the pharmacokinetic model.

[PE2-5] [ 10/19/2000 (Thr) 15:00 – 16:00 / [Hall B] ]

### **Effects of rehydration on the pharmacokinetics of chlorzoxazone in water deprived rats**

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In rats with water deprivation (DH, 72-hr water deprivation), hepatic cytochrome P450 2E1 levels was induced markedly and cytochrome P450 2E1 mRNA increased significantly compared with those in control rats, however, the values were completely returned to control levels by water supplementation (from 48 hr after water deprivation, rats with RH) (Kim, Kim et al., *J. Appl. Toxicol.*, in press). Chlorzoxazone (CZX), which is extensively metabolized to 6-hydroxychlorzoxazone (OHCZX) by cytochrome P450 2E1, was administered intravenously in 1-min to control rats and rats with DH and RH. In rats with DH, the plasma concentrations of OHCZX was significantly higher, and AUC increased significantly (15%) compared with that in control rats. The 24-hr urinary excretion of OHCZX and total body clearance of CZX also increased (28% and 55%, respectively) in rats with DH. Above data suggested that the metabolism in rats with DH increased by induction of CYP2E1 and this supported by previous study (Kim, Kim et al.). In rats with RH, however, most of altered pharmacokinetic parameters in rats with DH restored to the level in control rats: AUC (38% increase), total body clearance (28% decrease) and 24-hr urinary excretion of OHCZX (14% decrease) were returned to control level compared with those in rats with DH. Above data suggested that increased metabolism of CZX in rats with DH decreased by water supplementation and this might be due to altered expression of CYP2E1 and this was supported by previous molecular biological study (Kim, Kim et al.).

[PE2-6] [ 10/19/2000 (Thr) 15:00 – 16:00 / [Hall B] ]

### **EFFECTS OF CYSTEINE ON THE PHARMACOKINETICS OF INTRAVENOUS ADRIAMYCIN IN RATS WITH PROTEIN-CALORIE MALNUTRITION**

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In rats with protein-calorie malnutrition (PCM, 5% caseine diet for 4 weeks), hepatic cytochrome P450 levels suppressed markedly and cytochrome P450 mRNAs decreased significantly compared with those in control rats (23% caseine diet for 4 weeks), however, the values completely (or partially) returned to control levels by a week (from fourth week) of cysteine supplementation (rats with PCMC) (Cho, Kim et al., *Arch. Biochem. Biophys.* 1999, 372: 150-158). The formation of aglycone metabolites of adriamycin and adriamycinol, M3 and M4, respectively, seemed to be induced (Lee and Lee, *Res. Commun. Mol. Pathol. Pharmacol.* 1999, 105: 87-96) by pretreatment with dexamethasone (possibly by hepatic cytochrome P450 RL 33/cDEX, Komori and Oda, *J. Biochem.* 1994, 116: 114-120) in rats. Adriamycin, 16 mg/kg, was administered intravenously in 1-min to control rats and rats with PCM and PCMC. In rats with PCM, the plasma concentrations of adriamycin was higher (the area under the plasma concentration-time curve from time zero to 12 hr, AUC<sub>0-12 hr</sub>, tended to be higher) and 24-hr urinary excretion of M3 (including its 'conjugates') seemed to increase than those in control rats, suggested that the formation of M3 was inhibited in rats with PCM. In rats with PCMC, the plasma concentrations of adriamycin were