model without lag time rather than the other PK models. And also, weight, age and creatinine were not correlated with the pharmacokinetic parameters obtained from 1-compartment model without lag time.

[PE2-6] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Effects of cysteine on the pharmacokinetics of intravenous phenytoin in rats with protein-calorie malnutrition

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The effects of cysteine on the pharmacokinetics of phenytoin and one of its metabolites, 5-(p-hydroxyphenyl)-5-phenylhydantoin (pHPPH) were investigated after intravenous administration of phenytoin, 25 mg/kg, to control rats (4-week fed on 23% casein diet) and rats with PCM (4-week fed on 5% casein diet) and PCMC (PCM with oral cysteine supplementation, 250 mg/kg, twice daily starting from the fourth week). In rats with PCM and PCMC, the phenytoin hydroxylation (to form pHPPH) activities were significantly smaller (164, 103 and 95.3 pmol/min/mg protein for the control rats, and rats with PCM and PCMC, respectively) than that in control rats. In rats with PCMC, the intrinsic clearance of phenytoin, CLint, was significantly slower than those in control rats and rats with PCM (0.175, 0.131 and 0.044 ml/min). The above data suggested that the formation of pHPPH could be reduced in rats with PCM and PCMC. This was supported by significantly smaller 24-h urinary excretion of pHPPH (54.7, 35.6 and 32.5% of intravenous dose of phenytoin) in rats with PCM and PCMC than that in control rats. In rats with PCM, the maximum velocity (0.344, 0.203 and 0.196 mg/min), apparent volume of distribution in central compartment (44.4, 65.4 and 72.2 ml/kg) of phenytoin, and total area under the plasma concentration-time curve from time zero to time infinity (609, 714 and 1210 ug min/ml), renal clearance (20.5, 13.4 and 4.67 ml/min/kg) and 24-h urinary excretion (54.7, 35.6 and 32.5% of intravenous dose of phenytoin) of pHPPH were not returned to control levels by cysteine supplementation (rats with PCMC). This could be mainly due to the fact that the phenytoin hydroxylation activity in rats with PCMC was not returned to control level.

[PE2-7] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Bioavailability of new matrix metalloproteinase inhibitor SS11 series in rats

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We studied pharmacokinetics for the new sulfonamide derivatives, SS11 series, recently developed as a matrix metalloproteinase inhibitor(MMP) by Samsung Ad. Ins. Technol.. An high-performance liquid chromatography(HPLC) system with UV detection was employed for the determination of SS11 compounds in the rat plasma. Most of the compounds were well separated from the plasma with the retention times of <10 min and the recoveries of >75%. The limits of quantitation were 10-30 ng/ml. Of the new 24 sulfonamide derivatives investigated in the current study, only SS11-197, 229, 248, 299, 397 and 246 showed oral bioavailability. The plasma concentration-time data could be adequately described by an one or two-compartment open model. From the i.v. kinetic study at a dose of 10 mg/kg, the CLt of the bioavailable derivatives were 10-100 ml/hr/kg. The bioavailability of SS11-197, 229, 248, 299, 397 and 246 were approximately 78, 21, 26, 41, 59 and 68%, respectively. Moreover, these compounds have shown a selective activity against MMP-2 and MMP-9 enzymes associating with tumor metastasis and angiogenesis. Therefore, we will discuss possibility as new anti-tumor lead compounds for the new sulfonamide derivative SS11s.