lower (the AUC0-12 hr was significantly smaller) and 24-hr urinary excretion of M3 (including its 'conjugates') were significantly greater than those in rats with PCM, suggested that the formation of M3 increased significantly by cysteine supplementation by restoring the enzyme system(s) that metabolize adriamycin to M3. The altered pharmacokinetic parameters of adriamycin mentioned above in rats with PCM returned to greater than those of control rats after cysteine supplementation (rats with PCMC). Above data suggested that other hepatic cytochrome P450 isozyme(s) which catalyze(s) the formation of M3 from adriamycin could be induced by cysteine supplementation.

[PE2-7] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Tissue Distribution and Urinary Excretion of Nifedipine Orally Given to Rats: Administration Time Dependency

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Administration time dependency of tissue distribution and urinary excretion of nifedipine (NFP) were investigated in rats orally given to rats at three different administration times (08:00, 16:00, 00:00). At 30min after dosing, the highest plasma concentration was observed when given at 08:00 followed by 16:00 and 00:00. Drug concentrations were relatively higher in stomach and intestine but lower in liver. The drug concentration orally given at 08:00 was higher in most tissues except liver and pancreas when compared with 00:00 and 16:00. At 2hr after dosing, tissue distribution of NFP was irregularly changed and reversed when compared with 30min. Generally, the drug concentration orally given at 00:00 was significantly higher in most tissues (heart, kidney, spleen, pancreas and plasma) except liver and stomach when compared with 08:00 and 16:00. Drug concentration in stomach was invariably the highest at 30 min and 2h after dosing when given at 08:00. It was noted that decreasing power of drug concentration from 30 min to 2h in tissues was relatively higher when given at 08:00 compared with 00:00 and 16:00. The amount of NFP excreted as unchanged drug was so low and gave less than 0.03-0.013% of the dose. The cumulative urinary excretion of NFP orally given at 08:00 was significantly higher when compared with 16:00 and 00:00. It was evident that there was an administration time dependency of tissue distribution and urinary excretion of NFP. However, tissue distribution was quite variable by the collection time of organs. Both timing of administration and NFP dosage formulations must be simultaneously considered in clinical studies to efficiently control the blood pressures.

[PE2-8] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Pharmacodynamics of cyclosporin A in lymph on rats

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Cyclosporin A (CSA) is a potent immunosuppressive drug in transplantation medicines and for the treatment of autoimmune disease. The mechanism of CSA is that CSA inhibits selectively the interleukin-2 (IL-2) driven proliferation of activated T lymphocytes (CD4 T-cells) at the transcription levels. The target of CSA is activated T lymphocytes which are distributed highly to the lymphoid organ such as lymph node, spleen and so on. So, we attempted to investigate the pharmacodynamic characteristics of CSA in lymph on rats after CIPOL Inj.® (Chong Kun Dang Pharm., Seoul, Korea) was administered (10 mg/kg). The lymphocyte suspensions (106 cells/ml) were prepared from the isolated lymph node and spleen and whole blood, the CD4 T-cell counts were measured by the flowcytometer (Becton Dickinson Immunocytometry System, Mountain View, CA, U.S.A.) with the fluorescein isothiocyanate (FITC)-conjugated mouse anti-rat CD4 monoclona