

administration of AG-60. PRF was not detected after 24hr, but TRF concentration in platelets was maintained by 48hr.

[PE2-11] [10/19/2000 (Thr) 15:00 – 16:00 / [Hall B]]

Pharmacokinetics of Gentamycin After intravenous Administration in Acute and Chronic Alloxan-Induced Diabetes Mellitus Rabbits

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Many diabetic patients develop serious complications during the course of the disease, including cardiovascular disorders, nephropathy, neuropathy, and retinopathy. Because some physiological changes occurring in diabetes mellitus patients could alter the pharmacokinetics of the drugs to treat the disease.

Pharmacokinetics of gentamycin was investigated after intravenous administration of the drug (2mg/kg) to control rabbits and acute or chronic alloxan-induced diabetes mellitus rabbits(AIDRs).

After intravenous administration, the serum concentrations of gentamycin were significantly higher in AIDRs compared with these in control rabbits. This resulted in significant increase in AUC in acute ($26.04 \pm 3.01 \mu\text{g}/\text{ml}\cdot\text{hr}$) and chronic ($31.91 \pm 3.76 \mu\text{g}/\text{ml}\cdot\text{hr}$) AIDRs than that in control rabbits. This could be due to decrease of gentamycin by kidney excretion in the both AIDRs, since gentamycin is essentially excreted in kidney. Impaired kidney function in AIDRs were based on blood chemistry and tissue microscopy. Biological half-life ($t_{1/2}$) in AIDRs were significantly prolonged compared with that in control rabbits. Total body clearance (CL_T) in AIDRs were significantly decreased compared with that in control rabbits. Cumulative urinary excretion of gentamycin were decreased in AIDRs compared with that in control rabbits.

[PE2-12] [10/19/2000 (Thr) 15:00 – 16:00 / [Hall B]]

PHARMACOKINETIC DISPOSITION AND TISSUE DISTRIBUTION OF BISPHENOL A IN RATS AFTER INTRAVENOUS ADMINISTRATION

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This study examined the dose-linearity pharmacokinetics of bisphenol A, an EPA classified endocrine disruptor, in rats following i.v. administration. Upon i.v. injection of 0.2, 0.5, 1 or 2 mg/kg, serum levels of bisphenol A declined bi-exponentially, with mean initial distribution and elimination half-lives ranging from 4–8.2 min and 38.6– 62.2 min, respectively. There were no significant alterations in the systemic clearance rate (mean range, 90.1–123.6 ml/min/kg) and the steady-state volume of distribution (mean range, 4.6–6.0 l/kg) as a function of the administered dose. In addition, the area under the serum concentration-time curve linearly rose as the dose was increased. In a second study, bisphenol A was given by simultaneous i.v. bolus injection plus infusion to steady-state and levels were measured in serum and various organs. When expressed in concentration terms (e.g., amount accumulated per gram organ weight), bisphenol A was found predominantly in the lung, followed by kidneys, thyroid, stomach, heart, spleen, testes, liver and brain. Ratios of the organ to serum bisphenol A concentrations exceeded unity for all the organs examined (ratio range, 2.0–5.8) except for brain (ratio 0.75). Given the high systemic clearance and short elimination half-life, bisphenol A is unlikely to accumulate significantly in the rat.