of intravenous azosemide in circulating blood for diuretic effects in NARs. The plasma protein binding of azosemide in control rats and NARs were 97.9 and 84.6%, respectively. The binding values of azosemide to rat α- and β-globulins were 82.6 and 68.9%, respectively, at α- and β-globulin concentrations equivalent to those in plasma of NARs. The percentage of intravenous dose of azosemide excreted in 8-h urine as unchanged diuretic was significantly greater in NARs (37.7 versus 21.0%) and this resulted in a significantly greater 8-h urine output in NARs (385 versus 221 mL/kg). In NARs, the AUC of azosemide was significantly smaller (505 versus 2790 mg min/mL). This could be due to significantly faster CLr (7.36 versus 0.772 mL/min/kg, because of significant increase in intrinsic renal active secretion) and CLnr (12.4 versus 3.05 mL/min/kg, because of approximately 3.5 folds increase in CYP1A2 in rats) than those in control rats. The renal sensitivities to azosemide were significantly greater in NARs than those in control rats in terms of 8-h urine output and 8-h urinary excretions of sodium, potassium,and chloride. This study supports the importance of binding of intravenous azosemide to α- and β-globulins in circulating blood for its diuretic effects.

[PE2-8] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

HPLC Analysis, Stability, Blood Partition, and Protein Binding of an Antifibrotic Agent, Oltipraz

Bae SooKyung○[1], Bu SeongChull[1], Kim EunJung[1], Kim SoHee[2], Kim SangGeon[1], and Lee MyungGull[1]

[1]College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University,[2]College of Dentistry and Research Institute of Stomatology, Kangnung National University

A high-performance liquid chromatographic method was developed for the determination of Oltipraz in rat plasma and urine. The sample preparation was simple, 2 volumes of acetonitrile were added to deproteinize the biological sample. A 50-μl aliquot of the supernatant was injected onto a C_{18} reversed-phase column. The mobile phase, acetonitrile : 0.5 mM ammoniun acetate (55 : 45, v/v for rat plasma and 45 : 55, v/v for rat urine), was run at a flow-rate of 1.5 mL/min. The column effluent was monitored using an ultraviolet detector set at 305 nm. The retention times for Oltipraz in rat plasma and urine were approximately 5.8 and 8.6 min, respectively. The detection limits of Oltipraz in rat plasma and urine were 20 and 50 ng/mL, respectively. Oltipraz was relatively stable in various pH (1-12) solutions for up to 48-h incubation, however, it was unstable in pH 13 solution and rat plasma and urine. Oltipraz reached an equilibrium fast (within 30 s mixing manually) between plasma and blood cells of rabbit blood and the plasma-to-blood cells concentration ratios were independent of initial blood concentrations of Oltipraz, 1 and 5 μ
g/mL, the ratios ranged from 0.908 to 1.004. The binding of Oltipraz to 4% human serum albumin (HSA) was independent of Oltipraz concentrations ranging from 1 to 100 μg/mL using an equilibrium dialysis technique: the mean value was 95.0%. However, the binding of Oltipraz was dependent on HSA concentrations and the buffer pHs.

[PE2-9] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Pharmacokinetics and Pharmacodynamics of Intravenous Bumetanide in Mutant Nagase Analbuminemic Rats: Importance of Globulin Binding for the Pharmacodynamic Effects

Kim EunJung○, and Lee MyungGull

College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University

The importance of plasma protein binding of intravenous furosemide in circulating blood for its urinary excretion and hence its diuretic effects in mutant Nagase analbuminemic rats was reported. Based on the furosemide report, the diuretic effects of another loop diuretic, bumetanide, could be expected in analbuminemic rats if plasma protein binding of bumetanide is considerable in the rats. This was proved by this study. After intravenous administration of bumetanide, 10 mg/kg, to analbuminemic rats, the