plasma protein binding of bumetanide was 36.8% in the rats mainly due to considerable binding to α- and β-globulins (this value, 36.8%, was considerably greater than only 12% for furosemide), and hence the percentages of intravenous dose of bumetanide excreted in 6-h urine as unchanged drug was 16.0% in the rat (this value was considerably greater than only 7% for furosemide). After intravenous administration of bumetanide to analbuminemic rats, the AUC (1012 versus 2472 μg min/mL) was significantly smaller [due to significantly faster both CLr (1.49 versus 0.275 mL/min/kg) and CLnr (8.30 versus 3.71 mL/min/kg)], terminal half-life (9.94 versus 22.4 min) and MRT (4.25 versus 5.90 min) were significantly shorter (due to faster CL, 9.88 versus 4.05 mL/min/kg), and amount of 6-h urinary excretion of unchanged bumetanide (559 versus 261 mg, due to increase in intrinsic renal excretion) was significantly greater than that in control rats. The 6-h urine output and 6-h urinary excretions of sodium, chloride and potassium were comparable between two groups of rats.

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

Tissue distribution study in nude mice bearig solid lung tumor after administration of thermosensitive drug KBP93804A

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KBP 93804A is a thermosensitive anti-tumor drug conjugate for local delivery of the drug to solid tumors. The platinum distribution of KBP 93804A was compared with that of cisplatin in nude mice bearing solid lung tumor after single dose treatment. Various main organs such as liver, lung, heart, brain, tumor, kidney and whole blood were collected at 0.5, 1, 5, 12, 24, 48, 72 hours after intra-tumor administration. After digestion with HNO3 and then H202, Pt was measured with inductively coupled plasma-mass spectrometry(ICP-MS).
Platinum concentration at tumor after KBP93804A was significantly higher, whereas this concentration at kidney was much less than those of cisplatin. Based on these results, this novel platinum(II) thermosensitive compound (KBP93804A) represents a valuable lead in the development of a new anticancer chemotherapeutic agent capable of improving antitumor activity and low nephrotoxicity.

[PE2-11] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Metabolic Difference of Omeprazole Hydorxylation in Korean Subjects in relation to the Genetic Polymorphism of CYP2C19

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Pharmacogenetic entities extensively studied and showing an interethnic difference in the drug-metabolizing enzyme activity include N-acetyltransferase (NAT2) and cytochrome P450 (CYP) 2C (CYP2C9 and 19) and CYP2D6. But, there were few investigations about CYP2C19 genotype in a Korean population. The aim of this study was to evaluate whether inter-individual differences in the pharmacokinetic disposition of omeprazole are attributed to the genetic polymorphism of CYP2C19, which occurred by CYP2C19m1 and CYP2C19m2 in a native Korean population. Sixty-seven healthy Korean volunteers were genotyped with respect to CYP2C19m1 and CYP2C19m2 alleles with polymerase chain reaction-based diagnostic tests. Of the 67 individuals analyzed, 13 were homozygous for the wild-type (wt) allele in both exon 5 and exon 4 (wt/wt, 19.4%, pattern G1), 27 were heterozygous for the CYP2C19m1 (wt/ml, 40.3%, G2), 7 were heterozygous for the CYP2C19m2 (wt/m2, 10.4%, G3), 15 were heterozygous for the two defects (m1/m2, 22.4%, G4), and 5 were homozygous for the CYP2C19m1 (m1/m1, 7.5%, G5). The allele frequencies of the m1 and m2 mutation were 0.39 and 0.16, respectively.