Ahn Sugn-Hoon[O] Jeon Seng-Ho Shim Chang-Koo, Chung Suk-Jae

서울대학교 약학대학 약제학연구실

Dehydroevodiamine (DHED) is an experimental new drug candidate that is intended for use in the treatment of Alzheimer's disease. The drug is thought to exert its pharmacological action via cholinesterase inhibition, similar to tacrine and donepezil. The objective of this study is to characterize kinetics of brain distribution for DHED in rats. The drug was intravenously infused (0.2, 0.5, 0.02 mg/min) for 15 min to Sprague-Dawley rats (body weight 280-350 g). At predetermined time, the animal was sacrificed by decapitation and the brain was immediately removed. In addition, trunk blood was collected. The tissue was then weighed and homogenized in 2 fold volume of saline (pH 7.4). The concentration of DHED in the brain homogenate was compared with that in the plasma by an HPLC assay for DHED. In the dose range studied (1 mg/kg-10 mg/kg), temporal profiles of brain DHED concentration was almost identical to those in plasma, indicating that the drug crosses the blood brain barrier by passive diffusion. As a result, brain to plasma concentration ratio (Kd brain) is approximately 1. To determine whether DHED was first transported to the cerebrospinal fluid (CSF) and subsequently to the systemic circulation, temporal profile of DHED concentration in the CSF is also monitored. In all samples collected, CSF concentration of DHED was negligible, indicating that the drug may not be primarily eliminated via the blood-CSF barrier. Therefore, these data indicate that distribution kinetics of DHED from the systemic circulation to the brain is primarily mediated by the passive diffusion in the plasma concentration between 2 and 800 ng/ml

[PE2-15] [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

Chun SungKuk

College of Pharmacy, Kyung Hee University

KBP93804A is a developing thermosensitive anti-tumor drug in solid tumors. The platinum distribution of KBP93804A 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.

[PE2-16] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

HPLC Analysis, Stability, Blood Partition, Protein Binding, and Dose-independent Pharmacokinetics of A New Reversible Proton Pump Inhibitor, KR-60436, after Intravenous and Oral Administration to Rats

Yu SuYeon[O1], Kim EunJung[1], Kim YoonGyun[1], Kim SunOk[2], Lee DongHa[2], Lim Hong[2], Kim SoHee[3], and Lee MyungGull[1]

College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul Nat'l Univ.[1], AgroPharma Research Institute, Dongbu Hannong Chemical Company[2], and College of Dentistry, Kangnung Nat'l Univ.[3]