[PE1-20] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Identification of JG-381 metabolite in rats

Chung Dong-Jin° Shim Chang-Koo, Chung Suk-Jae

서울대학교 약학대학 약제학연구실

JG-381, an etomoxir derivative, is a hypoglycemic agent that has been developed as a new drug candidates for the treatment of the diabetes. In our previous study, we found that Caco-2 permeability of JG-318 appears adequate for the oral formulation for the drug and that the compound is extremely unstable in the presence of plasma protein. Because of the instability of the drug, the parent drug concentration was not detectable in all blood samples that are collected 3 min after the intravenous administration, indicating that the compound is rapidly converted to its metabolite in the presence of plasma protein. Because serum albumin is known to catalyze de-esterification, we hypothesize that the product of the conversion in the presence of plasma protein is de-esterified form(s) of JG-381. Two potential degradation products of JG-381, diol-acid and epoxide-acid, were chemically synthesize and the chemical properties compared with that found in in vitro. Chromatographic and spectrometric comparisons indicated that the epoxide-acid form is consistent with the degradation form found in in vitro. Subsequently, JG-381 was administered to rats to determine whether the metabolism occurred in in vivo. The epoxide metabolite was readily detectable in all plasma samples collected from rats that received iv administration of JG-381. Considering that hypoglycemic activity is well documented in rats for JG-381 and that the parent drug is rapidly de-esterified in the animal, the epoxide metabolite of JG-381 may be responsible, at least in part, for the anti-diabetic activity of the etomoxir derivative.

[PE1-21] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Pharmacokinetics of the Paclitaxel of New Micelle Formulation

Lee SeungYun°, Kim HyeJin, Kim KilSoo

College of Pharmacy, Ewha Womans University

Paclitaxel is a antitumor agent with poor water solubility and its pharmacokinetics are nonlinear. Cremophor EL, a surfactant used in the formulation of paclitaxel, may cause adverse effects. Alternative drug delivery systems are under development in recent years to reduce drug toxicity and improve efficacy. We studied pharmacokinetics of novel polymeric micellar paclitaxel with new solubilizers, Aceporol 330(BLK330) and GO460(BLK460), in rat. The formulations of Paclitaxel diluted with 5% glucose injection was administerd at 5mg/Kg by iv infusion in rat. Plasma were collected between 2 min and 4 h after administration. The of BLK330, BLK460 and Taxol were 1025.28㎍L-1min, 481.50㎍L-1min and 818.820㎍L-1min. When we added 7, 15 and 30mg of ascorbyl palmitate to BLK460, the were changed to 289.39㎍L-1min, 394.12㎍L-1min, 892.83㎍L-1min.
The surfactant of micellar paclitaxel can alter the blood distribution. We evaluated the linearity of BLK330. Mice received paclitaxel by iv injection at 2.5, 5 and 10mg/Kg by dilution of the formulations of paclitaxel with 5% glucose injection. Whole blood and plasma were collected up to 24 h after administration. Pharmacokinetics of paclitaxel were evaluated using whole blood and plasma. Paclitaxel was quantified by HPLC with UV detection at 227nm.

[PE1-22] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Thermosensitive liquid suppository containing diclofenac sodium : in vivo evaluation in rats

Kim Yong-Il°, Kim Hak-Mi, Quan Qi-Zhe, Yong Chul Soon, Rhee Jong-Dal, Kim Chong-Kook*, Choi Han-Gon