College of Pharmacy, Yeungnam University: *College of Pharmacy, Seoul National University

Solutions of poloxamers and sodium chloride were previously reported to undergo a phase transition to bioadhesive gels at body temperature. For the development of a thermosensitive diclofenac sodium-containing liquid suppository, here we studied the dissolution and pharmacokinetics of diclofenac sodium delivered by the liquid suppository systems composed of poloxamer P 188, P 407 and sodium chloride. Poloxamer P 188 delayed the dissolution rates of diclofenac sodium from liquid suppositories. However, sodium chloride showed no significant effect on the dissolution rates of diclofenac sodium from liquid suppositories. Dissolution mechanism analysis showed the release of diclofenac sodium was proportional to the time. The initial plasma concentrations of diclofenac sodium in the liquid suppository [diclofenac sodium/P 407/P 188/sodium chloride (2.5/15/17/0.8%)] were significantly higher compared with those in solid suppository. Furthermore, it gave significantly faster Tmax of diclofenac sodium than did solid suppository, indicating that the diclofenac sodium from liquid suppository could be absorbed faster than that from solid one in rats. It did not cause any morphological damage to the rectal tissues. These results suggested that thermosensitive liquid suppository with sodium chloride could be a more physically stable, effective and convenient rectal delivery system of diclofenac sodium.

[PE1-23] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Pharmacokinetics of new solubilizer in the intravenous micelle formulation of paclitaxel

Kim JiNa°, Lee SunA, Han KyuWon, Kim KilSoo

College of Pharmacy, Ewha Womans University

New solubilizer (Aceporol 330, Aceporol 460) were developed to reduce side-effect of CrEL and increase the effect of drug as surfactant used in the intravenous micelle formulation of anticancer drug paclitaxel. We studied easy, rapid quantitative determination of Aceporol 330, Aceporol 460 in rat plasma samples, which was achieved by complexation of the compound with the Coomassie brilliant blue G-250 dye in protein-free extracts. The binding of the dye to Aceporol 330, Aceporol 460 caused a shift in the absorption maximum from 400nm to 700nm. The assay permited estimation of Aceporol 330, 460 concentrations in the range 0.3-10.0μL/mL. Pharmacokinetics of new solubilizer was studied by this method. Rats were treated with Aceporol 330, 460, each at dose levels of 18.8, 14.6 and 11.3mL/m2. Rat samples were collected up to 5h after start of infusion. AUC(0-300) of Aceporol 330, 460 were 6834.08μL.min/mL, 482.26μL.min/mL(at 18.8mL/m2), 4569.11μL.min/mL, 675.86μL.min/mL(at 14.6mL/m2) and 2924.50μL.min/mL, 335.95μL.min/mL(at 11.3mL/m2). Also, we investigated pharmacokinetics of anticancer drug paclitaxel and BLK 330, BLK 460 containing Aceporol 330, 460. When we compared pharmacokinetics of new solubilizers and BLK 330, BLK 460, results revealed that new solubilizers had not effect on tmax of paclitaxel but they affected at Cmax of paclitaxel.

[PE1-24] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Does hepatic ATP level significantly affect on the functional activity of the P-glycoprotein, ATP binding cassette transporter, in Protein Calorie Malnutrition?

Lee Youngmi° Chung Sukjae Shim Changkoo

Department of Pharmaceutics, College of Pharmacy, Seoul National University

Protein Calorie Malnutrition(PCM), another form of oxidative stress, may alter the hepatic ATP activity and synthesis. Also, to know the expression and functional activity of P-glycoprotein(P-gp), one of the ATP binding cassette(ABC) transporters, is important, because several disease states can lead to malnutrition and may change the pharmacokinetics of P-gp substrates including anticancer agents, AIDS drugs.In this study, examined the effect of PCM in rats on the expression and functional activity of P-gp and on the biliary excretion of daunomycin, P-gp substrates and TEA.