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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

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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?

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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.

After 4-week treatment with control(23% protein diet) and PCM(5% protein diet)diets, the expression of P-gp in the liver was determined by Western blot.Also hepatic ATP level was measured.The canalicular transport of H^3-daunomycin and H^3-taurocholate measured. The pharmacokinetics of daunomycin,H^3-TBuMA, substrates of P-gp and C^{14}-TEA after intravenous infusion was also measured.
The expression of P-gp in the liver was suppressed(30-40% by Western blot analysis) and the hepatic ATP level was decrease in PCM rats. The kinetic analysis of the transport of H^3-daunomycin into cLPM vesicles revealed that the function of P-gp was decreased. Moreover, the biliary excretion was significantly decreased after intravenous infusion of daunomycin, this imples that hepatic ATP depletion may deteriorates hepatic activity of the P-gp,one of the hepatic ABC transporters.

[PE1-25] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Hydrolysis of coprecipitate from Coptidis Rhizoma and Scutellaria Radix by β-Glucuronidase

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Precipitation was formed during the preparation of decoction from the mixture of Coptidis Rhzoma and Scutellariae Radix. Berberin and baicalin were identified in coprecipitated products and these compoments were the active ingredients of two herbal medicine. The coprecipitated products were very slightly soluble in water and sparingly soluble in ethanol. The content of berberin and baicalin in the coprecipitated products were 26.8% and 23.1% but the content of active ingredients in supernatants were 0.3% and 0.7% respectively. For the purpose of hydrolyze the coprecipitate, some kinds of the intestine bacterias and these enzymes were tested and compared the rate of hydrolysis under various conditions. β-Glucuronidase from Escherichia coli hydrolyzed the coprecipitated product to berberin glucuronide and baicalein. The berberin glucuronide was absorbed rapidly in the small intestine of rats and maintained more higher serum level than the coprecipitated products.

[PE1-26] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Transport mechanism of berberine across Caco-2 cell monolayers

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Berberine, a quarternary isoquinoline alkaloid, is frequently utilized in the diarrheal treatment. In previous study, in vitro absorption of berberine across rat colonic segments was non-saturable and equal in both