

Yang JaeHeon⁰, Kim YoungIl*, Chung KyuHo, Kim DaeSub

College of Pharmacy, Woosuk University, *Pharmaceutical engineering department, Konyang University

Microencapsulations of piroxicam using the mixture of Eudragit RS with RL or Eudragit L or E or S according to Eudragit RS were carried out. The Eudragit microspheres of piroxicam were prepared by solvent method. Piroxicam and Eudragit polymer were dissolved in methylene chloride and dispersed in 0.5% polyvinyl alcohol solution and solvent evaporated. The average diameters of various Eudragit microspheres were from 40 to 43 μm . A good and smooth surface of microspheres observed by SEM were shown in all type of microspheres. The incorporation ratios of piroxicam into the all type of microspheres were higher than 93 %. The dissolution of piroxicam from Eudragit microspheres is not related with the pH of dissolution medium but related with the combination of Eudragit types used for preparation. Increase of Eudragit RS portion to Eudragit RL decreased the release of piroxicam. In vivo evaluation of piroxicam from Eudragit microspheres of different polymer types showed that the bioavailability of piroxicam from microspheres were increased about 1.5 times than that of the suspension. The carrageenan induced swelling was reduced rapidly until 24 h and gradually reduced until 72 h from the Eudragit microspheres of piroxicam. while, increased until 24 h and continued until 72 h from the control group.

The similar patterns were observed when the serum enzyme activity was determined following carrageenan induced paw edema. All type of enzyme LDH and CPK was significantly reduced from the Eudragit RS/RL microspheres compare with suspension.

[PE1-6] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Solid Lipid Nanoparticles(SLN) as Controlled Release Subcutaneous Injections of Local Anesthetics

Park YongKeun⁰, Lee JongHwa, Kim DongWoo, Yoon JaeNam, Jun IlSoon, Lee EunMi, Lee Gyewon*, Jee UngKil

College of Pharmacy, Chungnam National University; *Dep. of Pharmaceutical Engineering Konyang University

Local anesthetics are used to reduce pain, but they are so frequently injected to patients. So we prepared lidocaine solid lipid nanoparticles for long acting subcutaneous injection to decrease the number of times of injection. Solid lipid nanoparticles were prepared by spray drying method. First, drug, lipid, plasticizer and surfactant were dissolved in methylene chloride, and we operated spray dryer using this solution at setting value. To evaluate the products we tested the dissolution rate in dialysis sacks, determined the particle size and zeta potential, and performed animal test in mice. It was enough to control the drug dissolution and the particle size was about 30 μm - 100 μm enough to inject into subcutaneous tissue. And spray drying method improved the entrapment efficiency. Almost 100% degrees of the lidocaine was entrapped into nanoparticles, surfactant and plasticizer improved about 20~30% degrees of the burst effect.

[PE1-7] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Ketoprofen-Polyethylene Glycol Conjugate: Pharmacokinetics, anti-inflammatory and analgesic activity

Jang MiHee⁰, Kim SooYeon, Jeong ChoonSik, Oh SeaungYoul

College of Pharmacy, Sookmyung Womens University, Seoul, Korea; College of Pharmacy, Duksung Womens University, Seoul, Korea

Ketoprofen (KP), a potent analgesic and non-steroidal anti-inflammatory drug, has some disadvantages such as gastro-intestinal irritation, short half-life (1.5-4 hour) in plasma and low solubility in aqueous solution. In order to minimize these disadvantages, we have recently prepared a KP prodrug, KP-polyethylene glycol conjugate (KPEG750, PEG Mw=750), and investigated its pharmacokinetic behavior, anti-inflammatory and analgesic effect. The change of plasma concentration of free KP with time was studied using rat after intravenous or intramuscular administration of KP and KPEG750 containing equivalent amount of free KP. Analgesic effect of KP and KPEG750 after intramuscular administration was estimated by Tail-flick method using rat. Anti-inflammatory effect after intramuscular administration was measured by carrageenan-induced paw edema in rats given KP and KPEG750 containing equivalent amount of free KP. Pharmacokinetic data showed that KPEG750 was hydrolysed rapidly in

plasma. The results of Tail-flick experiment and paw edema test showed that KPEG750 exhibited analgesic and anti-inflammatory effect for extended period of time, when compared to those of ketoprofen. These results indicate that KPEG750 can be a promising NSAID prodrug with minimal side effect and extended pharmacological effect.

[PE1-8] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Enhanced Paclitaxel Bioavailability after Oral Administration of Paclitaxel Coadministered with Quercetin in Rats.

Choi Jun Shik^o, Kim Je Ho, Lee Jin Hwan

College of Pharmacy, Chosun University

The purpose of this study was to investigate the effect of quercetin on the bioavailability of paclitaxel orally coadministered in rats. Paclitaxel is reported to be metabolized by cytochrome p-450(CYP3A) in both the liver and epithelial cells of small intestine and also absorption of paclitaxel is inhibited by p-glycoprotein efflux pump in the intestinal mucosa. This resulted in poor oral bioavailability of paclitaxel. Area under the plasma concentration-time curve (AUC) of paclitaxel in combination with quercetin were significantly ($p < 0.01$) higher than those of control. AUCs of paclitaxel were increased dose-dependently in the dose range of quercetin. The half-life of paclitaxel with quercetin was prolonged significantly compared to that of control. Peak concentration of paclitaxel (C_{max}) with quercetin was significantly increased ($p < 0.01$) compared to control. Based on these results, it might be considered that bioavailability of paclitaxel coadministered with quercetin was significantly enhanced due to both inhibition of metabolism (CYP3A) and inhibition of p-glycoprotein efflux pump in the intestinal mucosa.

[PE1-9] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Iontophoretic delivery of vitamine-C-2-phosphate

Kim SuYoun^o, Oh SeaungYoul

College of Pharmacy, Sookmyung Women's University

In order to develop an optimum formulation for iontophoretic delivery of vitamine-C-2 phosphate, we have prepared 3 different formulations using hydrophilic polymers, such as poloxamer, carbopol and HPMC and iontophoretic flux through skin from these hydrogel formulations was carried out. The effect of current density, drug concentration and current profile on flux was investigated. In-vitro flux study was performed at 36.5°C, using side-by-side diffusion cell. Full-thickness hairless mouse skin was used for this work. Skin was placed on diffusion cell and hydrogel formulation containing vitamine-C-2 phosphate (donor compartment) was applied on top of skin. The diffusion cell (receptor compartment) was filled with PBS buffer solution (pH 7.4). Cathode and anode were placed in the donor and receptor compartment, respectively. Rod-shaped Ag/AgCl electrode and plate-shaped SnCl₂ electrode were used for experiment. Vitamine-C-2-phosphate was analysed by HPLC. Without current (passive), no flux was observed. Application of current increased the flux markedly, and this increase was proportional to the increased in current density. Flux also increased as the concentration of drug increased. Flux from aqueous solution showed higher rate than that from hydrogel formulations. Pulsed application of the current showed lower flux, when the donor compartment was aqueous solution. Further study on various factors affecting the flux is underway and the results will be presented.

[PE1-10] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

THE RELATIONSHIP OF INTESTINAL ABSORPTION CLEARANCE AND PARTITION COEFFICIENT OF NINE BETA-BLOCKERS IN RATS