plasma. The results of Tail-flick experiment and paw edema test showed that KPEG750 exhibited anlagesic 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.

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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 orall 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 (Cmax) 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]

Iontophreotic delivery of vitamine-C-2-phosphate

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In order to develope 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℃, 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

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On the basis of recognizing that physicochemical properties (lipophilic/hydrophilic), intestinal absorption clearance and pharmacokinetic characteristics of drug are the fundamental parameters controlling the rate and the extent of drug absorption, the biopharmaceutics classification system for the correlation between drug lipid-solubility and intestinal absorption clearance is proposed. The aim of this study was to assess whether the partition coefficient in n-octanol/buffer (pH 7.4) and intestinal absorption clearance of nine beta-blockers such as atenolol, sotalol, nadolol, acebutolol, pindolol, metoprolol, timolol, labetalol, propranolol can be correlated or not. In vivo intestinal absorption clearance was determined by using in situ single-pass perfusion at steady state. So as to do, a constant concentration of each drugs were applied to rat intestinal lumen side. At the steady state, we measured the concentration of each drugs to be remained of intestinal lumen side using HPLC with UV or fluorescence detection. From the results, we know that the higher partition coefficient of beta-blockers, the more permeable except sotalol, acebutolol and timolol.

[PE1-11] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Preparation and release characteristics of PVP-based solid dispersion capsules containing solubilizers

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Purpose. To prepare PVP-based solid dispersions containing lovastatin (LOS) and solubilizers (sodium lauryl sulfate, Tween80, oleic acid) to enhance dissolution of practically insoluble LOS. Methods. Solid dispersions containing LOS were prepared by dissolving two different organic solvent systems (acetone/ethanol or acetonitrile/ethanol). Results. The stickiness and flowability of solid dispersion powders were dependent on the composition and ratio of the solubilizers. LOS contents was decreased when acetone/ethanol was used instead of acetonitrile/ethanol. The solubilizers were useful to increase dissolution rate of LOS in gastric or intestinal fluid. Most of all, simultaneous use of the solubilizers in PVP-based solid dispersion capsule gave the best dissolution, reaching 76 and 60% in gastric and intestinal fluid, respectively. Conclusions. The various solubilizers could be applicable to solid dispersion system for enhanced dissolution and bioavailability of poorly water-soluble drugs. Supported by ministry of health & welfare (02-PJ1-PG11-VN02- SV01-0002).

[PE1-12] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Solubilization of poorly water-soluble drugs using solid dispersions

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Purpose. To prepare polymer based physical mixtures or solid dispersions containing solubilizing compositions using a spray-dryer. Methods. Lovastatin,simvastatin,aceclofenac and cisapride were selected as poorly water-soluble drugs. Dextrin, poly(vinylalcohol), poly(vinylpyrrolidone)and polyethylene glycol were chosen as solubilizing carriers for solid dispersions. The solid dispersions containing solubilizing compositions without drug were prepared without using organic solvents or tedious changes of formulation compositions. This system could be used to quickly screen the dissolution profiles of poorly water-soluble drugs by simply mixing with drugs thereafter. In case of solid dispersion containing drug, organic solvent systems could be used to solubilize model drugs. Results. The dissolution rates of the drugs were higher when mixed with drug and solid dispersions containing solubilizing compositions. However, solid dispersions of LOS, AFC, and CSP simultaneously containing drug and solubilizing compositions in organic solvent systems were more useful than physical mixtures of drug and solid dispersions without drug except SIMS. Conclusions. Based on solubilizing capability of polymer based physical mixtures in gelatin hard capsules, optimal solid dispersion system of poorly water-soluble drugs