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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