over 700 to 1100 nm was used to develop a calibration model. The milk samples from milking cow were measured without homogenization. The transmittance spectra were collected by using glass test tubes. The calibration model was developed and predicted by using partial least squares (PLS) algorithm. In order to reduce the scattering effect from fat globules in NIR milk spectra, multiple scattering correction was carried out and the scattering effect was successfully reduced. Accurate determination of milk composition was performed, showing the potential use of this method for real time on-line monitoring in a milking process.

Oral Presentations - Field E

[E1. Pharmaceutics] [E2. Pharmacokinetics] [E3. Physical Pharmacy]

[OE-1] [04/20/2001 (Fri) 13:30 - 13:45 / Room 4]

Processing Pharmaceuticals using Supercritical Fluids

Youn-Woo Lee°

Supercritical Fluid Research Lab., Korea Institute of Science and Technology 39-1 Haweolkok-dong, Sungbuk-ku, Seoul 136-791 Korea

The application of dense gases for the processing of pharmaceuticals has attracted considerable interest in recent years. Supercritical anti-solvent (SAS) recrystallization process is considered a promising technology for the production of micron or submicron particles for pharmaceuticals. In this process, carbon dioxide is used as antisolvent for the solute, which is initially solubilized in a conventional solvent. Upon CO2 addition, the dissolving power of the initial solution is reduced, and solute precipitation is triggered. Drugs are rapidly precipitated from organic solvents and resulting in the production of micro or submicro-particles with narrow particle size distribution.
We have developed a continous flow type apparatus for the process of Solution Enhanced Dispersion by Supercritical fluids (SEDS) and demonstrated that supercritical techniques are suitable for producing polymeric micro-particles such as poly(lactide-co-glycolide) (PLGA), poly(L-lactic acid) (PLLA) and polyglycolide (PGA) and submicro-particles of model proteins such as lysozyme and albumin. It is found that supercritical fluid process gives fine-tuning of particle size and particle size distribution by simple manipulations of the process parameters. We are able to produce large amount of pharmaceutical micro-particles continuously without any residual solvents. The proposed method will be applied as the basis of a new process for the preparation of drug delivery system.

[OE-2] [04/20/2001 (Fri) 13:45 - 14:00 / Room 4]

Adsorption of cyclosporin A during permeability study using Caco-2 cell monolayers

Lee DH°, Han YH, Cui Y, Rhee YS, Park ES, Chi SC

성균관대학교 약제학연구실

The concentration of cyclosporin A (CsA) in diffusion cells was known to decrease significantly during transport across Caco-2 cell monolayers due to the adsorption of the drug onto the material of the diffusion cells. To find out the extent of adsorption of CsA, the adsorbed amounts of CsA on glassware and diffusion cells were determined. When 0.5μM-10μM CsA solutions were filled in 100ml

volumetric flasks made of glass, the percent adsorbed of CsA adsorbed on glassware were about 30-40% of the total CsA. In the Snapwell™and side-by-side diffusion chamber, about 50% and 40% of CsA were adsorbed respectively. In order to solve the adsorption problem of the drug for accurate monitoring of the drug transport, the amount of transported CsA across Caco-2 cell monolayers was determined with the modified Augustijns et al (1993) method and the permeability of CsA across Caco-2 cell monolayers in the Snapwell™ was also investigated. At 0.5μM CsA, average permeability coefficient (Papp) value obtained in the apical (AP) to basolateral (BL) direction was 20-fold lower than the reverse (BL to AP) process. The results indicated that the modified method of Augustijns et al. (1993) was effective in evaluating the transport of CsA across Caco-2 cell monolayers.
Key Words: cyclosporin A; Caco-2 cell; adsorption; permeability.

[OE-3] [04/20/2001 (Fri) 14:00 - 14:15 / Room 4]

Membrane- and substrate selective damage in the hepatobiliary transport of drug by carbontetrachloride

Hong SS°, Chung SJ, Shim CK

College of Pharmacy, Seoul National University

The purpose of the present study was to investigate the effect of the CCl4-EHF on unit processes for the hepatobiliary transport of Organic Cations(OCs). TEMA and TBuMA were selected as model OCs, because they are not protein bound in either plasma or liver cytosol and are not metabolized. The study was performed using an isolated hepatocyte preparation as well as in vivo experimental systems.
AUCs up to 3 hr were increased slightly by the CCl4-EHF, although no significance was observed for the increase. Cumulative biliary excretion were decreased by the CCl4-EHF to 13.2 % (60 % decrease) for TBuMA, but not for TEMA. As a consequence, a 66 % decrease in the CLb of TBuMA, but not for TEMA, was observed by the CCl4-EHF. An apparent decrease in the uptake rate by the CCl4-EHF was observed for both compounds. And the Vmax, efflux, but not the Km, efflux or CLlinear, efflux, of TEMA was decreased significantly (81.9 % decrease) by the CCl4-EHF. On the other hand, the CCl4-EHF had no significant effect on any of the kinetic constants for the efflux of TBuMA from hepatocytes. Also the transport of both OCs across the bile canalicular membrane was not influenced by the CCl4-EHF, which is contrary to the case for the sinusoidal membrane (i.e., uptake and efflux). In conclusion, the membrane- and substrate selective damage should be kept in mind in utilizing the CCl4-EHF as a model for the liver diseases.

[OE-4] [04/20/2001 (Fri) 14:15 - 14:30 / Room 4]

POPULATION PHARMACOKINETICS OF LOXOPROFEN

Yun JH°, Cho HY, Kim SJ, Ahn MR*, Choi SO*, Chung HJ*, Yang JS*, Lee YB

College of Pharmacy and Research Institute of Drug Development, Chonnam National University, Kwangju 500-757, Korea; *Department of Pharmacology, National Institute of Toxicology Research, KFDA, Seoul 122-704, Korea

The purposes of this study were to evaluate the population pharmacokinetics of loxoprofen according to several pharmacokinetic (PK) models and to investigate the influence of characteristics of subjects such as body weight, age and creatinine on the pharmacokinetics of loxoprofen. Plasma data from 98 healthy male subjects who participated in several different studies were used for this analysis under the assumption that all data were distributed as a log-normal pattern. After overnight fast, each subject received a single 60 ㎎ oral dose of loxoprofen; blood samples were collected for 8 hours.