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

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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

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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.