

caprate (medium chain fatty acid salts), sodium lauryl sulfate (synthetic surfactant) and sodium taurodeoxycholate (bile acid salts) were investigated for their possibility of absorption enhancers. The apparent permeability constants of rhEGF across conjunctiva epithelia were 10–20 times higher compared with across nasal membranes. On the other hand, the apparent permeability of rhEGF across cornea was negligible. Enhancing effects on the rhEGF permeability across the nasal and conjunctiva were as the following order: alpha-cyclodextrin = dimethyl-beta-cyclodextrin > sodium-taurodeoxycholate > hydroxypropyl-alpha cyclodextrin > dimethyl-alpha-cyclodextrin > beta-cyclodextrin > hydroxypropyl-beta-cyclodextrin > sodium lauryl sulfate > sodium caprate. The penetrated amount of rhEGF across nasal by 4 hr was less than 1.0%, whereas being increased up to 5% by the addition of alpha-cyclodextrin (α -CD) or dimethyl-beta-cyclodextrin (DM- β -CD). The present results suggest that cyclodextrins, especially DM- β -CD and α -CD may serve as potent absorption enhancers for the nasal delivery of rhEGF.

[PE2-19] [10/19/2001 (Fri) 09:00 – 12:00 / Hall D]

Predicting Pharmacokinetic Parameters of Bisphenol A in Humans from Animals Using Allometric Scaling

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Allometric scaling was used to extrapolate the pharmacokinetic parameters of bisphenol A from animals to humans. Bisphenol A was injected intravenously to mice (2 mg/kg), rats (1 mg/kg), rabbits (1 mg/kg) and dogs (1 mg/kg), and serial blood samples were collected. Serum concentrations of bisphenol A were determined by HPLC with fluorescence detection at excitation and emission wavelengths of 278 and 315 nm. The steady-state volumes of distribution of bisphenol A were 0.1, 1.3, 7.1 and 20.0 L in mice, rats, rabbits and dogs, respectively, and the systemic clearances were 0.3, 1.9, 12.6 and 27.1 L/hr, respectively. A regression of the logarithm of the pharmacokinetic parameter and the body weight produced a linear relationship for these parameters. Using the allometric equation, the values of Cls, Vss, and t_{1/2} predicted for a 70 kg human were 127.1 L/hr (Cl_s = 5.264 W^{0.749}), 125.3 L (V_{ss} = 2.994 W^{0.879}), and 43.6 min (t_{1/2} = 40.723 W^{0.016}), respectively. Based on these values, bisphenol A is expected to be eliminated rapidly from humans, with its elimination occurring via the hepatic as well as other routes.

[PE2-20] [10/19/2001 (Fri) 09:00 – 12:00 / Hall D]

Maternal-Fetal Disposition of Bisphenol A in Pregnant Rats

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This study examined the maternal-fetal disposition of bisphenol A and its distribution into the placenta and amniotic fluid after i.v. injection (2 mg/kg) to pregnant SD rats. Bisphenol A was distributed extensively to the placenta and fetus, but the distribution of bisphenol A into the amniotic fluid was low. The decay curve of bisphenol A in the placenta, fetus and amniotic fluid paralleled that of the maternal serum during the terminal elimination phase. A 5-compartment open model consisting of the maternal central, maternal peripheral, placental, fetal and amniotic fluid compartments was used to describe the disposition of bisphenol A in pregnant rats, with the elimination occurring from the maternal central and fetal compartments. Based on this model, bisphenol A was transferred from the placenta primarily to the fetus (65.4%), with the remaining fraction transported to the maternal central (33.2%) and amniotic fluid (1.4%) compartments. Bisphenol A was eliminated from the amniotic fluid by the fetal (63.9%) and placental (36.1%) routes. On the other hand, bisphenol A was eliminated from the fetus primarily by the placental route back to mother (100%), with the amniotic route playing an insignificant role in the fetal elimination. The pharmacokinetic model used in this study provides insights into the routes of elimination of bisphenol A in the maternal-fetal rat upon maternal administration.