[PGE_1-EE] and [PGE_1] were well consistent with the simulated k values. In addition, the skin penetration study also supported the newly postulated hydrolysis pathway as explained above. .

[PE1-18] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Enhanced Dissolution of Tenoxicam by Solid Dispersion Technique

Park OkSun°, Chun InKOO

College of Pharmacy, Dongduk Women's University, Seoul 136-714, Korea

The effects of solid dispersions with cyclodextrins (CDs) on the dissolution rate of tenoxicam, which is known to be a very slightly soluble drug, were investigated. The solubility of tenoxicam was determined in the presence of various CDs [α-, β- and γ- CD, 2-hydroxypropyl- β- CD (HPCD), sulfobutyl ether- β- CD (SBCD), dimethyl- β-CD (DMCD) and trimethyl- β- CD (TMCD)] by shaking in water bath at 30℃. Solid dispersions were prepared with β- CD using solvent evaporation and freeze-drying process. The ratios of drug to carrier were 1:1 and 1:2 molar ratio. Tenoxicam was dissolved in ammonium hydroxide solution, mixed with CD solutions and dried. Dissolution tests were performed in gastric and intestinal juice. Solid dispersions were also formulated to tablets and then dissolution rates were compared with that of a commercial product. The solubility of tenoxicam increased in the rank order of SBCD > γ- CD > β- CD > HPCD > DMCD > α- CD > TMCD. Dissolution rate of the solid dispersions was higher than that of drug alone. As the ratio of carrier was higher, dissolution rate increased more. The dissolution rate of tenoxicam from the tablets prepared by freeze-drying at 1:2 molar ratio was fast, more than 80% was released within 15 min in gastric juice. All solid dispersion tablets prepared with β-CD at 1:2 molar ratio showed more rapid dissolution than commercial product. The formation of solid dispersion is an effective method for increasing the dissolution rate of poorly water soluble tenoxicam. β- CD was thought be a candidate carrier for solid dispersion.

[PE1-19] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Saturable Elimination of Tacrine from the Rat Cerebrospinal Fluid

Kim Jee-Hye° Choi Ok-Hui Chang-Koo Shim, Suk-Jae Chung

서울대학교 약학대학 약제학연구실

Tacrine is clinically used in the treatment of Alzheimer's disease. In this study, we have examined in vivo kinetics of elimination of tacrine from the cerebrospinal fluid to understand better the kinetics of tacrine in the brain. Sprague-Dawley rats were undergone a surgery involving catherterization of lateral ventricle (LV, drug administration) and cisterna magna (CM, CSF collection). Tacrine was administered via LV cannulae at the doses of 5, 25 or 125 ㎍ (in 5 ㎕). CSF (5 ml/sample) was collected at pre-determined times via the CM cannulae. Tacrine level in the CSF sample was assessed by an HPLC assay for tacrine. Clearance and volume of distribution of tacrine was estimated from the temporal profiles by the standard moment analysis. In some cases, phenol red was included in the injection mixture (dose, xx mg/rat) as a CSF volume marker. In all experimental condition, temporal profiles of tacrine concentration in the CSF were declined in a multi-exponential manner. Tacrine clearance from the CSF was 1970 ± 257 ㎕/min for 5 ㎍ dose. Since the reported bulk flow clearance ranges from 2-5 ml/min for rats, tacrine is apparently eliminated from the CSF via mechanism in addition to the bulk flow. Interestingly, apparent clearance for tacrine in CSF was decreased with dose, indicating that the elimination pathway, probably through the choroid plexus, the blood-CSF barrier, is saturable. Since Tacrine is not likely to be metabolized in the brain and, thus, saturable elimination from the CSF may represent a saturable efflux process for tacrine via choroids plexus.