4036980 PYCP/M : MAJOR : CLINICAL PHARMACY ; M.Sc. in Pharm. (CLINICAL PHARMACY)
KEY WORDS : CEFDINIR/ PHARMACOKINETIC
SUTTASINEE SUWANNAKUL : PHARMACOKINETIC STUDY OF CEFDINIR IN HEALTHY THAI VOLUNTEERS. THESIS ADVISORS: KORBTHAM SATHIRAKUL, Ph.D., ASDA VIBHAGOOL, M.D., M.A.C.P., WINAI WANANUKUL, M.D., CERTIFICATE OF CLINICAL PHARMACOLOGY AND TOXICOLOGY. 144 P. ISBN 974-663-624-3

Cefdinir is a new oral third generation cephalosporin recently launched in Thailand. Clinical trials in Thai patients confirmed its effectiveness in the treatment of community-acquired respiratory tract infections, urinary tract infections, skin and soft tissue infections as well as gastrointestinal tract infections. However, its pharmacokinetics in Thai people have never been studied. This study was performed to investigate the pharmacokinetics of cefdinir in 12 healthy Thai male volunteers with an average age of 22.3 ± 1.7 years. After an overnight fast, each subject received a single oral dose of 200 mg cefdinir. Five milliliters of venous blood samples were drawn prior to dosing and at 1, 2, 3, 4, 5, 6, 7, 8, 10 and 12 hr after dosing. Urine was also collected at intervals of 0 to 2, 2 to 4, 4 to 6, 6 to 8, 8 to 12 and 12 to 24 hr after dosing. Plasma and urine samples were analyzed for total cefdinir concentration by high performance liquid chromatography with UV detector (HPLC/UV).

The results showed that cefdinir was quite slowly absorbed with a mean absorption rate constant (K_{01}) of 0.51 hr^{-1}, a mean lag time (T_{lag}) of 0.78 hr and a mean time to reach maximum plasma concentration (T_{max}) of 4.42 hrs. The maximum plasma concentrations (C_{max}) of all subjects ranged from 0.73 to 2.62 μg/mL. Mean ± SEM of elimination rate constant (K_{10}) and elimination half-life ($T_{1/2}$) were 0.39 ± 0.02 hr^{-1} and 1.86 ± 0.11 hrs, respectively. Average values (± SEM) of other pharmacokinetic parameters were as follows: apparent volume of distribution (V_d/F) was 1.29 ± 0.10 L/kg, apparent total body clearance (CL/F) was 23.3 ± 1.9 L/hr and area under the plasma concentration-time curve from time zero to infinity ($AUC_{(0-\infty)}$) was 9.37 ± 0.90 μg.hr/mL. Urinary excretion within 24 hrs ($\%Ae_{(0-24)}$) was 24.9 ± 2.0% of administered dose and renal clearance was 5.56 ± 0.45 L/hr. In this study, plasma concentration-time profiles for multiple dosing of 100 mg three times daily and 200 mg twice daily were also simulated. The time intervals that simulated plasma levels exceeded the MIC_{90} of susceptible pathogens were evaluated. The results showed that both dosage regimens provided plasma levels that maintained above the MIC_{90} of *H. influenzae*, *M. catarrhalis*, *S. pyogenes*, *Salmonella spp.* and *Shigella spp* for 64-100% of the dosing interval. However, those plasma levels were below the MIC_{90} of *S. pneumoniae* and *K. pneumoniae* reported in Thailand. Against *S. aureus* and *E. coli*, only 200 mg twice daily regimen provided plasma levels that exceeded the MIC_{90} with time intervals of 31.7% and 40.8% of the dosing interval, respectively.

It is concluded that 100 mg administered three times daily and 200 mg administered twice daily are likely to provide plasma concentrations maintained above the MIC_{90} for the majority of the dosing interval against the pathogens mentioned above except *S. pneumoniae* and *K. pneumoniae*. This indicates possible clinical use of both dosage regimens in treatment of common community-acquired bacterial infections caused by susceptible Gram-positive and Gram-negative pathogens. However, for the treatment of infections caused by *S. aureus* and *E. coli*, 200 mg twice daily should be recommended.