

THESIS TITLE The Study of Pharmacokinetic Profile and
Bioavailability of Carbamazepine Tablets in
Healthy Thai Volunteers

NAME Chokchai Wongsinsup

DEGREE Master of Science (Pharmacy)

THESIS SUPERVISORY COMMITTEE

Oraphan P. Matangkasombut, Ph.D.

Krisana Kraisintu, Ph.D.

DATE OF GRADUATION 4 March B.E. 2536 (1993)

ABSTRACT

Carbamazepine (CBZ) is not only widely used antiepileptic drug, but also the drug of first choice for the treatment of trigeminal neuralgia. Dosage adjustment is essential because of its narrow therapeutic range and it can only be done properly by the experienced physician. The present investigation is the first attempt to establish the pharmacokinetic profile of CBZ in healthy Thai in order to provide important informations for an appropriate dosage adjustment. And to support the national policy in prescribing generic instead of the brand, the bioavailability of locally-made CBZ tablets is compared to the brand. Seventeen proven healthy volunteers, age 21-23 yrs, were given a single 2x200 mg oral dose of CBZ tablets in randomized crossover design with a wash-out period of 28 days. Venous blood samples were collected at appropriate times, the plasma were separated and concentrations of CBZ and its epoxide metabolite (CBZE) were determined by using HPLC. The pharmacokinetic parameters of CBZ

which were calculated by PCNONLIN nonlinear estimation program, using first-order one compartment model, in males and females are not difference. The estimated parameters of CBZ are C_{\max} (6.31 ± 1.02 mcg/ml), T_{\max} (7.46 ± 2.26 hr), $t_{1/2}$ (44.01 ± 10.07 hr), $AUC_{0 \rightarrow \infty}$ (444.64 ± 83.04 mg.hr/l), K_a (0.5299 ± 0.2179 hr⁻¹), K_e (0.0165 ± 0.0037 hr⁻¹) and V_d (1.00 ± 0.14 l/kg). And those of CBZE were C_{\max} (0.434 ± 0.113 mcg/ml), T_{\max} (31.17 ± 8.74 hr), $AUC_{0 \rightarrow \infty}$ (38.17 ± 8.74 mg.hr/l) and $t_{1/2}$ (37.39 ± 10.32 hr). The present results showed that C_{\max} and AUC are higher in Thai than that reported in Caucasian. This is correlated to the smaller size of Thai subjects. Moreover, the longer half-life of CBZ in Thai may also contribute to the higher AUC. Therefore, dosage reduction appears to be essential in order to avoid its toxic effect. And all of the bioavailability of the two CBZ tablets compared are not significant difference except the longer T_{\max} of the local made tablet (10.66 ± 5.16 vs. 7.46 ± 2.26 hr, respectively). This may support the prescribing the local made CBZ tablet instead of the brand.