Thesis Title Pharmacokinetics of Verapamil in Thais.

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ABSTRACT

The eighty milligrams verapamil tablets selected for this study were an imported product, product A and a local made product, product B. They were evaluated for the disintegration test, the dissolution test, the content of active ingredient and the uniformity of dosage units according to the specifications of the USP XXII and BP 1988. Both products were not significantly different and conformed to the USP XXII and BP 1988 requirements.

The bioavailability studies were performed in 10 healthy male volunteers. The mean age was 28.0 ± 1.5 years and the mean weight was 63.6 ± 3.2 kg. After single oral dose of 80 mg verapamil tablet, the plasma drug levels were determined by HPLC method with fluoresence detector. Pharmacokinetic parameters were determined from the PCNONLIN nonlinear estimation program V01-B. The best fit was the two compartment with lagtime model. For product A,

the mean maximum concentration (Cmax), time at maximum concentration (Tmax), area under the plasma concentration-time curve (AUC) and lagtime (Tlag) were 117.05 ± 7.87 ng/ml, 1.00 ± 0.00 hr, 474.25 ± 45.13 hr.ng/ml and 0.37 ± 0.02 hr, respectively. The mean Cmax, Tmax, AUC and Tlag for product B were 112.11 ± 10.23 ng/ml, 0.90 ± 0.04 hr, 521.17 ± 45.02 hr.ng/ml and 0.38 ± 0.03 hr, respectively. The relative bioavailability studies revealed that both products were bioequivalent. The average half life of verapamil product A and B were 1.54 ± 0.62 and 1.90 ± 0.70 hours, respectively.

Both products increased PR interval and decreased heart rate significantly. The decrease in blood pressure however was not significant. Plasma concentration of verapamil appeared to correlate with the effect on heart rate and the PR interval.