ABSTRACT

The bioequivalence of a pharmaceutically equivalent drug-product, clarithromycin 500 mg tablet (Clacina®) manufactured by The Government Pharmaceutical Organization, relative to the reference product (Klacid®) was studied in 24 healthy Thai male volunteers. Each subject received a single oral dose of 500 mg tablet of both products in a randomized two-way crossover design. Blood samples were collected at appropriate time intervals and they were quantified for clarithromycin contents by LC-MS. Individual plasma clarithromycin concentration-time profile was analyzed for relevant pharmacokinetic parameters; the peak plasma clarithromycin concentration, $C_{\text{max}}$, the time to peak plasma clarithromycin concentration, $t_{\text{max}}$, and the area under the plasma clarithromycin concentration-time curve, $\text{AUC}_{0-t}$ and $\text{AUC}_{0-\infty}$. Data analysis showed that the mean $C_{\text{max}}$, $\text{AUC}_{0-t}$, and $\text{AUC}_{0-\infty}$ values of the test and the reference products were 2176.51 ng/mL and 2351.78 ng/mL, 17199.44 ng·hr/mL and 17683.86 ng·hr/mL, and 17787.56 ng·hr/mL and 18195.46 ng·hr/mL, respectively. The average $t_{\text{max}}$ values of the test and the reference product were 2.15 hr and 2.06 hr, respectively. Analysis of variance for two-way crossover study revealed that there were no statistically significant differences (p>0.05), between the corresponding $C_{\text{max}}$, $\text{AUC}_{0-t}$ and $\text{AUC}_{0-\infty}$ values with respect to formulation effect of both products. Difference of $t_{\text{max}}$ means was 4.37%. The 90% confidence interval for the ratios of the $C_{\text{max}}$, $\text{AUC}_{0-t}$ and $\text{AUC}_{0-\infty}$ means of Clacina® relative to those of the reference product based on Ln-transformed data were found to be 81.56-101.04, 90.65-104.14, and 91.72-105.63 for the $C_{\text{max}}$, $\text{AUC}_{0-t}$ and $\text{AUC}_{0-\infty}$, respectively. All these ratios were within 80-125% and power of the test were greater than 80%, referring, the two products were bioequivalent in terms of both the rate and the extent of drug absorption into systemic circulation.
Figure 1  Mean plasma clarithromycin concentration-time profiles of 24 subjects following oral administration of 500 mg tablet of test and reference product

- □ = Test product
- △ = Reference product