BIOEQUIVALENCE OF CLARITHROMYCIN 500 MG TABLETS

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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 interval 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, Cmax, the time to peak plasma clarithromycin concentration, t_{max}, and the area under the plasma clarithromycin concentration-time curve, AUC_{0-t} and AUC_{0- ∞}. Data analysis showed that the mean C_{max}, AUC_{O-t}, and AUC_{O-∞} 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_{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 difference (p>0.05), between the corresponding C_{max}, AUC_{O-t} and AUC_{O-∞} values with respect to formulation effect of both products. Difference of t_{max} means was 4.37%. The 90% confidence interval for the ratios of the C_{max}, AUC_{O-t} and AUC_{O-∞} 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_{max} , AUC_{0-t} and AUC_{0- ∞}, 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

$$--- = Test product$$
$$--- \Delta --- = Reference product$$