Bioequivalence Study Of The Two 850-mg Metformin Tablet Formulations In Healthy Thai Male Volunteers

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ABSTRACT

Objective: To compare the rate and extent of absorption of a generic 850-mg metformin hydrochloride tablet with that of the reference formulation when given as equal doses.

Methods: The two formulations; Test product (Metformin hydrochloride manufactured by GPO, Bangkok, Thailand) and the reference, Glucophage® were administered as a randomized, single dose, two-treatment, two-period, two-sequence crossover design to 26 healthy Thai male volunteers. After drug administration, serial blood samples were collected over a period of 30 hours. The washout period between each treatment was 1 weeks. Plasma metformin concentrations were measured by a high performance liquid chromatography (HPLC) with UV detection after protein precipitation. The pharmacokinetic parameters were analyzed by noncompartmental analysis and the analysis of variance (ANOVA) was carried out using logarithmically transformed data of the AUC, C_{max} and untransformed T_{max}. Bioequivalence was obtained according to 90% confidence interval of the difference between formulations within 0.8-1.25 for the AUC and C_{max}. RESULTS: The median T_{max} of the test (2 h) and the reference (2.25 h) were similar and the mean [90%CI] for the T_{max} difference of 0.05 [(-0.33)-0.14] h was within the bioequivalence range of $\pm$ 0.49 h. The ANOVA also showed no statistically significant differences between the AUC and C_{max} values between the test and the reference preparations. The mean (90% CI) for the ratios $\frac{\text{Test}}{\text{Reference}}$ were 1.09 (1.04-1.16), 1.10 (1.04-1.16), and 1.12 (1.04-1.20), respectively for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max}. Since these values were within the bioequivalence range, our study demonstrated the bioequivalence of the two preparations.

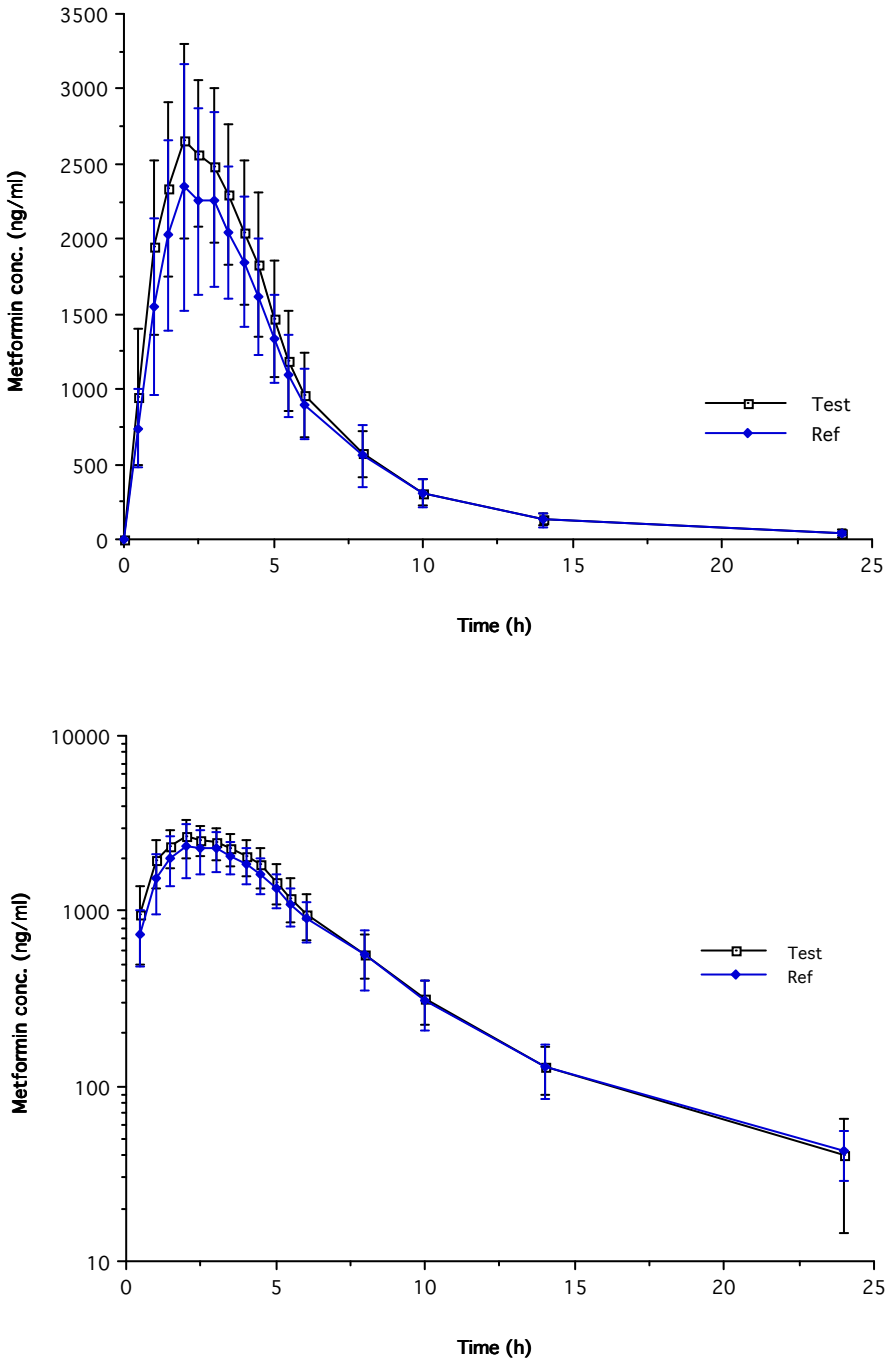

Figure 1 Mean ± SD of plasma concentration-time profiles after single oral dose of 850 mg metformin hydrochloride of the Test product and the Reference [Linear-Linear plot (upper) and Log-Linear plot (lower)].