Bioequivalence study of 400-mg indinavir capsule in healthy Thai volunteers

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The objective of this study was to compare the rate and extent of absorption of a generic indinavir formulation (GPO, Thailand) with those of an original formulation (Merck & Co., Inc.) administered as a single dose of 2x400-mg capsules. A randomized, two-period, two-treatment, two-sequence, crossover study with a 2-week washout period was performed in 24 healthy Thai male and female volunteers. The two products met all pharmaceutical requirements and the difference of the content of active ingredient was less than 5%. The medication was administered to subjects after an overnight fast of at least 8 hours. A 5-mL blood sample was collected predose (0 hour), and at 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, and 10 hours postdose. Indinavir plasma concentrations were analyzed by validated HPLC method. One subject received the second formulation 2 weeks delayed from schedule, his washout period was thus prolonged to 4 weeks. When the data from 23 subjects with a 2-week washout period were analyzed, the rate of absorption determined by peak plasma concentrations (C_{max}) of the GPO indinavir capsule compared with the original formulation was (mean \pm SD) 9,487.88 \pm 1,428.77 ng/mL versus 10,027.45 \pm 2,401.28 ng/mL whereas time to peak plasma concentration (T_{max}) was 0.88 \pm 0.26 hr versus 0.83 \pm 0.30 hr, respectively. The extent of absorption which was evaluated by the area under the plasma concentration - time curve from time zero to time of last measurable concentration (AUC_{n-t}) and from time zero extrapolated to infinity (AUC_{n- ∞}) were 23,022.82 ± 6,491.13 ng/mLXhr and 23,473.51 \pm 6,555.77 ng/mLXhr, respectively, for the GPO indinavir capsule versus 22,615.85 \pm 5,970.53 ng/mL×hr and 23,077.98 \pm 6,110.53 ng/mL×hr, respectively, for the original formulation. There were no statistically significant differences between the two formulations regarding those pharmacokinetic parameters (p>0.05). The 90% confidence intervals of the ratio of log transformed data of C_{max} , AUC_{0-t} and AUC_{0- ∞} were 86.34 – 106.53%, 93.97 – 108.51% and 93.89 – 108.48%, respectively. When the data from all 24 subjects were analyzed, the results in terms of pharmacokinetic parameters and 90% confidence intervals of the relevant parameters were comparable to those obtained from the data of 23 subjects. This could be concluded that the generic indinavir formulation was bioequivalent to the original formulation in terms of the rate and extent of absorption when they were administered in the same dose.



Figure 1 Mean \pm SD of plasma concentration-time profile after single oral dose of Indinavir 400 mg capsule (2 capsules) of the test product (GPO) and the reference product [n = 24]