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Evaluating Bioequivalence of Two Formulations of Clarithromycin Immediate Release Film Coated Tablets in Healthy Sri Lankan Subjects under Fasting Conditions

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The WHO mandates therapeutic interchangeability of multi-source oral medicines with the respective innovator be proven either by bioequivalence (BE) or biowaiver studies. Clarithromycin is classified as BCS 11 and accordingly needs BE studies. The present study evaluates the BE of generic clarithromycin (immediate release) 500 mg [two tablets of 250 mg], (State Pharmaceutical Manufacturing Cooperation) with Klaricid® 500 mg tablet, (Innovator, Abbott Laboratories, India) in a randomized, two-treatment, two-period, two-sequence, open-label, single-dose, crossover trial under fasting conditions with one-week washout period. Twelve healthy subjects were recruited and sixteen blood samples obtained over 24 hours after drug administration at 0,0.2, 0.4, 0.6, 1.2, 1.4, 2, 2.5, 3, 4, 6, 8, 10, 12, 14 and 24. Reverse-Phase High-Performance Liquid Chromatography (RP-HPLC) UV spectrophotometric validated method with a mixture of acetonitrile: KH_2PO_4 (0.67 mM): methanol as the mobile phase at the ratio of 3:1:1 (v/v) was used. Detection of clarithromycin and internal standard Roxithromycin were done at 205nm. Pharmacokinetic parameters $C_{max,}$ T_{max}, area under the plasma concentration-time curve zero-infinity ($AUC_{0-\infty}$), AUC_{0-t}, lambda(z) (first-order elimination rate constant) and $t_{1/2}$ were evaluated statistically using PKMP version 1.03.28. The 90% confidence intervals (test/reference) of $C_{max,}$ $AUC_{0-\infty,}$ $AUC_{(0-t)}$ (logarithmically transformed) were 99.49-100.72%, 92.05, 87-110.69% and 99.51-102.19% respectively within the recommended confidence interval (i.e. between 80-120%). The extent of absorption ($AUC_{0-\infty}$ and AUC_{0-t}) and the rate of absorption (C_{max} and T_{max}) were not significantly different. The results conclude the two formulations to be therapeutically interchangeable in clinical practice.

Keywords: *bioequivalence, clarithromycin immediate release, healthy subjects, pharmacokinetic parameters*