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Evaluating Bioequivalence of Two Formulations of Metformin Hydrochloride US 500 mg XR Oral Tablets under Fasting Conditions in Healthy Sri Lankan Subjects

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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. This study aimed to evaluate the bioequivalence of two generic Metformin hydrochloride (MET) USP XR 500 mg oral tablets (CIC Lifesciences Ltd., Sri Lanka) with the innovator Glucophage XR 500 mg (Merck Sante S A S, France) in a randomized, two-treatment, two-period, two-sequence, open-label, single-dose, crossover trial under fasting conditions with one-week washout period. Eighteen healthy subjects were recruited, and seventeen blood samples (4 mL each) were withdrawn from each subject at different time points (0,1, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 7, 8, 10, 12, 16, 24 h) after administration of single dose of 1000 mg (500 mg x 2). Reverse-Phase High-Performance Liquid Chromatography (RP-HPLC) UV spectrophotometric validated method with a mobile phase consisted of Acetonitrile: water (25:75) with 20 mM of KH_2PO_4. Detection of metformin and internal standard Ranitidine were done at 230 nm. Pharmacokinetic parameters C_{max}, T_{max}, area under the plasma concentration-time curve zero-infinity (AUC0-∞), AUC0-t, were evaluated statistically using PKMP version 1.03.28. The 90% confidence intervals for (test/reference) of C_{max}, T_{max} $AUC_{0-\infty}$, $AUC_{(0-t)}$ were 96.88%-100.64%, 101.3%-108.871%, 103.39%-109.75% and 103.39%-109.75% respectively that fall 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. Therefore, MET USP XR 500 mg oral tablet generic CIC can be therapeutically interchangeable with innovator drug in clinical practice.

Keywords: *bioequivalence, Metformin hydrochloride USP XR, Sri Lanka, single dose*