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Bioequivalence of Metformin Hydrochloride USP XR 500 mg (Generic, Gamma Interpharm Pvt Ltd,) and the Comparator Glucophage XR 500 mg Oral Tablets (Merck Sante S A S, France), in Sri Lankan Healthy Subjects Under Fasting Conditions

RD Piyathilaka[1], P Jayasekara[2], J Munasinghe[2], US Kulasekara[2], DGP Kawyangana[2], PM Athauda-arachchi[2], D Govindapala[2], HS Jayasinghearachchi[1], and R Fernandopulle[2#]

[1]Institute for Combinatorial Advance Research and Education, General Sir John Kotelawala Defence University, Rathmalana, Sri Lanka

[2]Faculty of Medicine, General Sir John Kotelawala Defence University, Rathmalana, Sri Lanka

[#]rohinifernandopulle@gmail.com

Abstract

The World Health Organization (WHO) requires bioequivalence studies to evaluate if medication from various sources are therapeutically equivalent to the innovator product. In this study, the bioequivalence of generic metformin hydrochloride XR 500 mg (Gamma Interpharm Ltd) was compared to the innovator, glucophage XR 500 mg (Merck Sante S A S, France). This study was a randomized, two- treatment, two-period, two-sequence, open-label, single-dose, with crossover design, under fasting conditions, with a one-week washout, in twenty (20) healthy Sri Lankans. Seventeen blood samples were collected at time points (0, 1, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 7 , 8, 10, 12, 16, 24 h) post-oral-dose of 500 mg x2. Metformin plasma levels were assessed with validated Reverse-Phase High-Performance Liquid Chromatography UV spectrophotometry. The mobile phase was acetonitrile and phosphate buffer 20 mM (KH_2PO_4) in a 50:50 (v/v) ratio. Metformin and internal standard, ranitidine, were detected at 230 nm. Pharmacokinetic parameters Cmax (maximum plasma concentration), Tmax (time to reach Cmax), the area under the plasma concentration-time curve (AUC 0-infinity), and area under the plasma concentration-time curve from 0 to last measurable concentration (AUC 0-t) were analyzed statistically using PKMP (version 1.05, 2017, APL, USA). The 90% confidence intervals for Cmax, Tmax, AUC0-infinitive, and AUC 0-t (test/reference) were 97.97% - 103.89%, 99.45% - 105.37%, 94.42 - 108.38%, and 97.16% - 108.65% respectively. These were within the acceptable range (80-120%), indicating that the extent and rate of absorption of the two formulations did not differ significantly. Therefore, they can be considered therapeutically interchangeable (i.e. bioequivalent) in clinical practice.

Keywords: *Bioequivalence, Metformin Hydrochloride USP, Sri Lankan healthy subjects*