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A BIOWAIVER STUDY TO DETERMINE THE QUALITY AND THE IN VITRO EQUIVALENCE OF THE MOST WIDELY AVAILABLE METRONIDAZOLE PRODUCT IN COLOMBO, SRI LANKA

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Bioequivalence studies conducted in healthy volunteers are the usually accepted method to determine the therapeutic equivalence of two drug products. As these in vivo bioequivalence studies are time consuming and expensive to conduct, major regulatory authorities now accept biowaiver studies, using in vitro dissolution testing, for selected drugs belonging to Biopharmaceuticals Classification System(BCS) class 1 and III drugs as they correlate with in vivo equivalence results. We conducted a biowaiver study for a product of metronidazole, a BCS I antibiotic. A market survey was performed in 20 private pharmacies in Colombo and the National Hospital Sri Lanka(NHSL), to identify the most commonly used metronidazole products and to select products for the in vitro study. Quality testing was done according to the British Pharmacopeia 2012 and United State Pharmacopeia 2011 to determine pharmaceutical equivalence. In vitro equivalence was determined using the biowaiver testing procedure recommended by the World Health Organization. Dissolution profiles were generated at pH 1.2, 4.5 and 6.8 using validated spectrophotometric method at 278 nm. According to the market survey, only ten products were available, although there were 32 registered oral dosage forms. Metrogyl was used in NHSL and was also the most widely available metronidazole brand in the private sector. Therefore “metrogyl” was used as the test product. The innovator product and reference listed drug in the Orange Book of United States, “flagyl” was used as the reference product, which was also the second most commonly available metronidazole brand in the market. The two metronidazole products, complied with all the pharmacopoeial quality requirements making them pharmaceutically equivalent. Both products showed more than 85% dissolution in less than fifteen minutes making similarity factor(f2) calculation unnecessary as they can be categorized as very rapidly dissolving drugs. We conclude that ‘metrogyl’ was bioequivalent to the reference product using in vitro methodology and the two products could be interchangeable during clinical use, provided that metrogyl complies with the excipient requirements given in the metronidazole biowaiver monograph published by International Pharmaceutical Federation(FIP). This study shows that in vivo bioequivalence requirement can be waived using the in vitro method for selected pharmaceuticals for which biowaiver monographs are available by FIP.

Keywords: *Metronidazole, Biowaivers, Dissolution profiles, BCS.*