Comparison of Fasting Bioavailability Among 100-mg Commercial, 100-mg Generic, and 50-mg Chewable Generic Sildenafil Tablets in Healthy Male Mexican Volunteers: A Single-Dose, 3-Period, Crossover Study

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ABSTRACT

Background: Sildenafil citrate (SIL) was the first oral drug registered in Mexico for the treatment of erectile dysfunction. However, succinct pharmacokinetic data are available in the Mexican population.

Objective: The goals of the present work were: (1) to design a specific method to quantify SIL plasma levels by using UPLC-MS/MS; (2) to compare oral SIL bioavailability in Mexican men with pharmacokinetic data in other populations; (3) to fulfill local regulatory requests; and (4) to describe the relative tolerability of a new 50-mg chewable tablet.

Methods: This was a randomized, single-dose, 3-period, 6-sequence crossover study in healthy male volunteers. In each period, subjects received single oral doses of 100 mg of sildenafil (1 commercial [reference*], 1 generic [test 1†], or 2 chewable generic tablets [test 2‡]), with a 4-day washout period between each dose. Serial blood samples were collected for up to 24 hours. SIL was measured in heparinized plasma by using a validated UPLC-MS/MS method. Pharmacokinetic parameters included C_{max}, T_{max}, AUC_{0-24}, and $AUC_{0-\infty}$. Bioequivalence was established if 90% CIs for mean test:reference ratios of log-transformed C_{max} and AUC fell within the range of 0.80 to 1.25. Tolerability was assessed on the basis of a clinical interview with the subject and monitoring of vital signs.

Results: Demographic data showed a homogeneous population. Validation of analytical method proved to be linear within the range of 1 to 1000 ng/mL, with selectivity, accuracy, and precision. 90% CIs for test 1:reference ratios were 86.52 to 113.56, 94.75 to 108.84, and 94.97 to 108.82 for the logarithm parameters C_{max}, AUC_{0-24}, and $AUC_{0-\infty}$, respectively. The 90% CIs for the test 2:reference ratios were 82.14 to 107.24, 98.26 to 112.56, and 99.19 to 113.34 for C_{max}, AUC_{0-24}, and $AUC_{0-\infty}$. Regarding relative tolerability, slight cephalea was the most common adverse effect.

Conclusions: The developed analytical method was validated in compliance with local requirements and was useful for sildenafil measurement. This single-dose study under fasting conditions suggests that both test products met the Mexican regulatory criteria for assuming bioequivalence in these healthy, male Mexican volunteers. The clinical data suggest that the chewable tablets were well tolerated by volunteers. Trial registration code number: DIC/09/407/02/020, Research Direction of Hospital General de México, Mexico City, Mexico. (*Clin Ther.* 2012;34:689–698)

Key words: CAS no. 171599-83-0, sildenafil chewable tablet tolerability, sildenafil citrate bioavailability, sildenafil pharmacokinetics, UPLC-MS/MS sildenafil quantification.

INTRODUCTION

Sildenafil citrate (SIL) (CAS no. 171599-83-0) was the first oral drug registered in Mexico (Pfizer, S.A. de

*Trademark: Viagra® (Pfizer, S.A. de C.V., Mexico City, Mexico).
†Trademark: Vimax 100® (Siegfried Rhein, S.A. de C.V., Mexico City, Mexico).
‡Trademark: Vimax 50® (Siegfried Rhein, S.A. de C.V., Mexico City, Mexico).

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