BIOPHARMACEUTICS & DRUG DISPOSITION
Biopharm. Drug Dispos. **25**: 203–209 (2004)
Published online in Wiley InterScience (www.interscience.wiley.com). **DOI**: 10.1002/bdd.399

Bioequivalence Evaluation of Two Brands of Ketoconazole Tablets (Onofin-K® and Nizoral®) in a Healthy Female Mexican Population

G. Marcelín-Jiménez*, José Hernández, Alionka P. Ángeles, L. Contreras, M. Hinojosa, L. Rivera, L. Martínez-Rossier, O. Amancio and A. Fernández
Servicio de Investigación de Farmacología Clínica, Hospital General de México, México City, México

ABSTRACT: A randomized, crossover study was conducted in 24 healthy female volunteers to compare the bioavailability of two brands of ketoconazole (200 mg) tablets; Onofin-K® (Farmacéuticos Rayere S.A., México) as the test and NIZORAL® (Janssen-Cilag, México) as the reference products. The study was performed at the Clinical Pharmacology Research Center of the Hospital General de México in Mexico City. Two tablets (400 mg) were administered as a single dose with 250 ml of water after a 12 h overnight fast on two treatment days separated by a 1 week washout period. After dosing, serial blood samples were collected for a period of 12 h. Plasma harvested was analysed for ketoconazole by a modified and validated HPLC method with UV detection in the range 400–14000 ng/ml, using 200 µl of plasma in a full-run time of 2.5 min. The pharmacokinetic parameters AUC_{0-t}, $AUC_{0-\alpha}$, C_{max}, T_{max} and $t_{1/2}$ were determined from plasma concentrations of both formulations and the results discussed. AUC_{0-t}, $AUC_{0-\alpha}$ and C_{max} were tested for bioequivalence after log transformation of data, and no significant differences were found either in 90% classic confidence interval or in the Anderson and Hauck test ($p < 0.05$). Based on statistical analysis, it is concluded that Onofin-K® is bioequivalent to Nizoral®. Copyright © 2004 John Wiley & Sons, Ltd.

Key words: ketoconazole; bioequivalence; HPLC; pharmacokinetics

Introduction

Ketoconazole (*cis*-1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3,-dioxolan-4-yl]methoxy]phenyl]piperazine is an imidazole derivative with antimycotic properties. Its main effect when it reaches serum levels during systemic administration is the inhibition of sterole 14-α-demethylase in fungi. This enzyme is coupled with the CYP450 complex and such an inhibition allows the accumulation of ergosterol in the cytoplasmic membrane of fungi, modifying the phospholipid arrangement and disrupting the function of ATPases and other membrane electronic transporter systems, resulting in the blocking of fungi proliferation [1].

Ketoconazole has been used clinically in the treatment of blastomycosis, histoplasmosis, coccidiomycosis and some types of candidiasis with a high degree of success [2]. Recently, there has been renewed interest in the clinical use of ketoconazole in certain opportunistic infections in immunocompromised patients [3,4] due to its effect on preventing metastases of certain kinds of cancer [5,6], and for its effect on enhancing the bioavailability of other drugs [7,8].

*Correspondence to: Servicio de Investigación de Farmacología Clínica, Unidad Analítica (405-E), Hospital General de México, Dr. Balmis No. 148, Col. Doctores, México D.F., México.
E-mail: gabmarcelin@hotmail.com

Received 19 August 2003
Revised 5 January 2004
Accepted 20 January 2004