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SRISUPHAK DECHPONGSAPILAS : COMPARATIVE BIOAVAILABILITY STUDY OF FLUCONAZOLE CAPSULES IN HEALTHY THAI VOLUNTEERS. THESIS ADVISORS : CHUTHAMANEE SUTHISISANG, Ph.D., SURAJIT SUNTORNTHAM, M.D., BOARD CERTIFIED IN INTERNAL MEDICINE. 114 p. ISBN 974-662-994-8

Fluconazole is potentially an effective drug in the therapy of candidiasis. It is also approved for the treatment and prophylaxis of cryptococcal meningitis especially in AIDS patients who have high risk for opportunistic infections. The Research and Development Institute, Government Pharmaceutical Organization (GPO) has manufactured fluconazole capsules (100 mg) to support increasing use of fluconazole. This study was performed to compare bioavailability of fluconazole from the GPO product with that from the original product (Diflucan®) in healthy Thai volunteers. Seventeen Thai male volunteers were enrolled in this study. Their mean ± SD of age and body mass index were 21.47 ± 1.18 years and 22.66 ± 3.04 kg/m^2, respectively. A 100 mg single oral dose of each preparation was given to the subjects in a randomized crossover design with 2 weeks washout period. All subjects had to fast overnight or at least 10 hr before drug administration. Five milliliters of blood samples were collected before and at 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 6.0, 8.0, 10.0, 24.0, 48.0 and 72.0 hr after drug administration. Plasma fluconazole concentrations were determined by high performance liquid chromatography. Mean ± SD of pharmacokinetic parameters of fluconazole original and local (GPO) capsule, respectively, were as follow: The maximal plasma concentrations (C_{max}) were 1.4782 ± 0.1430 and 1.4660 ± 0.2518 μg/mL, time to reach maximal plasma concentration (T_{max}) were 2 hr for all subjects of both formulations, the elimination half-life ($t_{1/2}$) were 19.9005 ± 5.0208 and 23.1944 ± 7.8699 hr, the terminal elimination rate constants (k) were 0.0366 ± 0.0077 and 0.0327 ± 0.0094 hr^{-1}, areas under the plasma concentration versus time curves from 0 to 48 hr (AUC_{0-48}) were 22.7668 ± 1.3415 and 24.1360 ± 2.1478 μg·hr/mL, areas under the curve extrapolate to infinity ($AUC_{0-\infty}$) were 27.3902 ± 2.9851 and 31.1413 ± 5.9180 μg·hr/mL. The 90% confidence interval (CI) for log transformed data of the ratio means of C_{max}, AUC_{0-48} and $AUC_{0-\infty}$ between those 2 formulations were 92.3905-105.8509, 101.5915-110.2476 and 104.3094-121.6785, respectively. These values were within the acceptable bioequivalence range of 80-125% for log transformed data. It can be concluded that the GPO product was bioequivalent to the original product of the same strength. Thus, it can be prescribed interchangeably with the original product in order to reduce the cost of treatment of fungal infections in AIDS patients.