BIOEQUIVALENCE STUDY OF PIOGLITAZONE TABLETS IN THAI HEALTHY VOLUNTEERS

KHIN MYO OO

A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR
THE DEGREE OF MASTER OF SCIENCE IN PHARMACY
(PHARMACEUTICS)
FALCULTY OF GRADUATE STUDIES
MAHIDOL UNIVERSITY
2007

BIOEQUIVALENCE STUDY OF PIOGLITAZONE TABLETS IN THAI HEALTHY VOLUNTEERS

KHIN MYO OO 4837398 PYPT/M
M.Sc. in Pharm. (PHARMACEUTICS)

THESIS ADVISORS: KORBTHAM SATHIRAKUL, Ph.D., GAYSORN CHANSIRI, Ph.D.

ABSTRACT

Pioglitazone hydrochloride is a thiazolidine antidiabetic agent used in the treatment of type 2 diabetes. Pioglitazone decreases insulin resistance in the periphery and liver, resulting in increased insulin-dependent glucose disposal and decreased hepatic output. This study was performed to compare the bioavailability of locally made pioglitazone with that of innovator's pioglitazone by using data obtained from plasma pioglitazone concentration for determining bioequivalence between these two products. Twenty-four Thai volunteers participated in this study that was of a crossover design, with a one week wash-out period. After an overnight fast, a single 30 mg pioglitazone tablet of either the reference product or the test product was orally administered to each subject. A venous blood sample of five milliliters was drawn prior to dosing and 0.25, 0.50, 0.75, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 24 and 48 hours after dosing. The plasma sample was analyzed for pioglitazone concentration by LC/MS/MS analysis method. A volunteer violated the protocol because of a mistake of sequencing between test and reference product. Therefore, corresponding data was removed accordingly and the pharmacokinetic parameters of pioglitazone from 23 healthy Thai subjects were calculated using the WinNonlin edition version 3.1.

The results showed Mean ± SEM values of maximum plasma concentration (C_{max}) of pioglitazone were 1650 ± 106 and 1620 ± 120 ng/ml for the reference and the test product, respectively. Mean ± SEM values of area under the plasma concentration time curve from time zero to last time ($AUC_{0\text{-}last}$) of pioglitazone were 17400 ± 1260 and 16500 ± 1220 hr.ng/ml for reference and test product, respectively. Mean ± SEM values of area under the concentration time curve from time zero to the infinity time from observed ($AUC_{0\text{-}inf(observed)}$) of pioglitazone were 18200 ± 1470 and 17000 ± 1260 hr.ng/ml for reference and the test product, respectively. Mean time to reach maximum concentration (T_{max}) was 2.00 and 1.50 hours in reference and test product, respectively. The difference mean of C_{max}, $AUC_{0\text{-}last}$ and $AUC_{0\text{-}inf(observed)}$ between the two products was not statistically significant. The 90% confidence interval for logarithm transformation data of the ratio of mean of (C_{max}), ($AUC_{0\text{-}last}$) and ($AUC_{0\text{-}inf(observed)}$) between those treatments were 96.3372 (91.2499-108.7501), 93.6375 (87.7570-112.2430) and 92.9277 (86.8619-113.1381), respectively.

It can be concluded that the test product was bioequivalent to the reference product based on the criteria that the percent ratio of test parameters was within the range of 80.00-125.00% with a 90% confidence interval.

KEY WORDS : PIOGLITAZONE / BIOEQUIVALENCE / PROTEIN PRECIPITATION / PHARMACOKINETICS

116 pp