CHAPTER V

CONCLUSIONS

The bioequivalence study of two brands of glipizide tablets was accomplished. Results are summarized as follows:

1. *In Vitro* Studies

1.1 Both brands of 5 mg glipizide tablets met the criteria of the United States Pharmacopeia 27 specifications according to identification, uniformity of dosage units, assay and dissolution test, indicating pharmaceutical equivalence.

1.2 Dissolution profiles of a generic product and an innovator's product performed in buffer pH 6.8 were similar. The difference factor (f_1) and similarity factor (f_2) based on model independent method were in the acceptance range, ensuring their equivalence.

2. Bioanalytical Method for Determining Glipizide in Plasma

The high-performance liquid chromatographic method for determination of glipizide in plasma has been developed and validated. Phenyl cartridges were used to extract glipizide from plasma. The elute was evaporated to dryness and redissolved in mobile phase. They were injected in to HPLC via a μ-Bondapak® C_{18} reversed-phase column and detected at 225 nm. This method showed reasonable specificity, accuracy and precision which could be successfully applied in bioequivalent study.

2. *In Vivo* Bioequivalence Studies

2.1 Comparative bioavailability of the two brands was conducted in 12 healthy Thai male volunteers using randomized replicated crossover design with 1 week washout period between treatments. All subjects participated in this study did not experience any drug related side-effects or dropouts, although the study was conducted in subjects with fasting condition.

After an orally single dose administration, serial blood samples were collected for 12 hours and plasma concentrations of glipizide were determined by high performance liquid chromatography. Relevant pharmacokinetic parameters of the two brands were calculated from plasma glipizide concentration-time profiles and compared using analysis of variance.

Results showed that there were no statistically significant differences ($p>0.05$) in area under the plasma drug concentration-time curve (AUC) and peak plasma drug concentration (C_{max}) based on log-transformed data, including other pharmacokinetic parameters with respect to formulation effect of both products.

The 90% confidence intervals for the ratios of mean log-transformed data of a generic product relative to an innovator's product of AUC_{0-12}, $AUC_{0-\infty}$ and C_{max} were within 80-125%. Difference of t_{max} means was 20.45%. This indicated that the two brands tested were bioequivalent regarding to the rate and extent of absorption and could be used interchangeably for each other in clinical practice.

2.2 Pharmacokinetic parameters of glipizide in healthy Thai male volunteers found in this experiment agreed and closed to those previously reported.

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