

## CHAPTER V

### CONCLUSION

1. All four brands of 250 mg ciprofloxacin film-coated tablet tested for weight variation and content of active ingredient met the requirements of the British Pharmacopoeia 1988 and the United States Pharmacopoeial Convention specifications.

2. All brands disintegrated in distilled water within the limits for film-coated tablet. The disintegration time of brand D was significantly longer than that of brand A. The rank order in terms of mean disintegration time was brands  $D > A = B > C$ .

3. Dissolution profile was determined for each brand in carbon dioxide free water using the United States Pharmacopoeia apparatus type II. All four brands dissolved over 80 % of the labeled amount in 30 minutes as specified in the met United States Pharmacopoeial convention. No significant differences of the dissolution rate constants among these brands' were observed. The rank order of the dissolution rate constants were brands  $B > C > A > D$ .

4. Bioavailability of ciprofloxacin tablets were studied in twelve healthy male volunteers using the complete crossover design. One brand is the innovator's product which was assigned as reference product. The sensitive HPLC analysis method, with fluorescence detector, was used to quantitate the amount of drug in plasma sample. From

individual plasma-time profile, pharmacokinetic parameters were obtained using the CSTRIP computer program.

5. The peak plasma concentration and the time to peak plasma concentration were directly observed from the plasma concentration-time profile of each subject. The mean peak plasma concentration of four brands of ciprofloxacin ranged from 1.86-2.13 mcg/ml with the mean time to peak plasma concentration were from 0.96-1.20 hours. The area under the plasma concentration-time curves ranged between 6.59-7.42 mcg.hr/ml. All of these pharmacokinetic parameters were not statistically significant differences, referring that all brands were complete bioequivalence.

The relative bioavailability of brands B, C and D with respect to brand A, an innovator's product were 95.92, 105.82 and 108.01 %, respectively.

6. Analysis of the data by the CSTRIP computer program revealed that two compartment open model with first order absorption and elimination and without lag time was well described the concentration-time profile after oral administration ciprofloxacin tablet.

The absorption rate constants obtained ranged from 2.20 - 3.04  $\text{hr}^{-1}$ . There were no statistically significant difference among this parameter of all four brands.

The biological half-lives of ciprofloxacin ranged from 3.55 - 3.81 hr. No statistically differences were observed among the half-lives of the drug from all brands.

Some pharmacokinetic parameters  $C_{max}$ , AUC and  $K_e$  in this study were greater than those reported by other investigators. Reasons were from the differences of subject participated in the study (i.e. the differences in the race, age, weight and normal habits), assay method and/or the study condition. However  $t_{max}$  and  $t_{1/2}$  were in good agreement.

7. The correlation between the in vitro such as disintegration time and dissolution rate constants and in vivo parameters studied was not significant. Therefore, the bioavailability of ciprofloxacin tablet could not be predicted by using the in vitro testing both disintegration and dissolution.

In general slow disintegration time of solid dosage form would result to slow dissolution. But in this study brand D with show disintegration could yield about the same relevant pharmacokinetic parameters values as other brands did. This was probable due to absorption of the drug into systemic circulation was slower than disintegration and/or dissolution.

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