CHAPTER V

CONCLUSIONS

1. All brands of 25 mg. diclofenac sodium enteric-coated tablets met the general requirement of pharmacopoeia (B.P. 1988, USP XXII) for weight variation (range from 143.94 to 174.76 mg.) and content of active ingredient (range from 95.50 to 108.56%).

2. All brands except brand F of 25 mg. diclofenac sodium enteric-coated tablets met the USP XXII requirement for disintegration of enteric-coated tablets. The disintegration time of all brands except brand B were statistically longer than that of brand A ($p < 0.05$). The rank order in term of mean disintegration time was brands H > E > C > D > G > A > B.

3. Dissolution profile for each brand was performed in simulated intestinal fluid TS without enzyme (pH 7.5 $\pm$ 0.1). Major differences were observed for the rate and the extent of dissolution among these brands. The rank order of the dissolution rate constant was brands B > A > G > F > D > E > C > H. The dissolution rate constant of brand A was statically significant ($p < 0.05$) higher than those brand C, D, E and H.

4. The statistical correlation ($p < 0.05$) was

found between the disintegration time and the dissolution rate constant of each brand.

5. The bioavailability of brands A, B, D and H with difference in dissolution characteristics were studied in twelve Thai healthy volunteers. A single dose of two 25 mg. diclofenac sodium enteric-coated tablets was administered to each subject in a crossover design. Plasma diclofenac sodium concentrations were determined by high performance liquid chromatography with organic solvent extraction and detected by UV detector at 225 nm. Individual plasma concentration-time profile was analyzed using the conventional method and the CSTRIP computer program for compartmental analysis. The data were well described by a biexponential equation. The observed values of all pharmacokinetic parameters were used for comparisons.

The mean peak plasma concentration of each treatment ranged from 1.1871 to 1.9353 mcg./ml.

The average times to peak plasma level ranged from 1.63 to 2.50 hours for the four different brands.

The area under the plasma concentration-time curves of all brands ranged from 2.4126 to 2.8060 mcg.hr./ml.

There was no statistically significant difference of the relevant pharmacokinetic parameters among these brands ($p > 0.05$).

All brands were bioequivalent to brand A.

6. The pharmacokinetics of diclofenac sodium following oral administration of two 25 mg. enteric-coated tablets were well deseribed by a mean of one compartment open model.

The average absorption rate constant obtained for brands A, B, D and H were 1.1321, 1.8850, 0.9085 and 1.2066 $hr.^{-1}$, respectively. Statistical results indicated that the absorption rate constant of brands D and H were not significant difference from that of brand A. Only brand B had the absorption rate constant significantly higher than that of brand A ($p < 0.05$).

The average elimination rate constant obtained were 0.5865, 0.9714, 0.5565 and 0.5376 $hr.^{-1}$ for brands A, B, D and H, respectively. Only brand B had the elimination rate constant significantly higher than that of brand A ($p < 0.05$).

The mean biological half-life of diclofenac sodium ranged from 1.40 to 2.52 and no statistically significant difference ($p > 0.05$) among these values.

7. The correlation study between the in vitro and in vivo data of the four different brands of diclofenac sodium enteric-coated tablets revealed that the disintegration time showed statistically significant correlation with the C_{max} ($p < 0.05$) and the dissolution rate constant showed statistically significant correlation with t_{max} ($p < 0.05$). The dissolution rate constant might be used to predict the bioavailabity of diclofenac sodium enteric-coated tablet in term of the rate of drug absorption.