# CHAPTER V

## CONCLUSIONS

1. All nine commercial brands of 250 mg. naproxen tablet used in this study met the USP XXI and the B.P. specifications for percent labelled amount and weight variation.

2. Tablet hardness, the non-official specification was also investigated in this study. Results showed that brand I had a maximum hardness, more than 20 kp , and the rank orders of hardness were I > A > F > G > H > B > E > C > D. All of them differed statistically significant at $p < 0.05$ resulting from the difference in tablet formulations and/or manufacturing processes.

3. The disintegration time tests showed that all brands met the USP XXI requirement, within 30 minutes. The statistically differences among all various brands were observed at $p < 0.05$

4. Dissolution profiles were determined for each product in two types of dissolution media, simulated gastric fluid pH 1.2 and simulated intestinal fluid pH 7.5. Studies were performed using the USP dissolution apparatus type II maintained at 50 rpm. and a temperature of $37 \pm 0.5$ °C. Statistical results of dissolution rate constant, with respect to brand A, showed that significant differences of brands B, D, E, H, I and brands B, D, H, I were found in simulated gastric fluid and simulated intestinal fluid, respectively. The amount and rate of naproxen dissolved in simulated intestinal fluid were much greater than those in simulated gastric fluid because of the physico-chemical property of naproxen.

5. differences in disintegration times and dissolution rates of these nine commercial brands may be due to their formulations and manufacturing methods.

6. There were no statistically significant linear correlation between hardness and disintegration times, or dissolution rates in both dissolution media of all brands at $p > 0.05$

7. The bioavailability of brands A, B, C, D and E, with difference in dissolution characteristics, were studied in 8 Thai healthy subjects. Single dose of 250 mg. naproxen tablet was administered to subject following a crossover experiment. Plasma naproxen concentrations were determined by a high performance liquid chromatographic method. Individual plasma profile and pharmacokinetic parameters were analyzed according to noncompartmental method.

8. The pharmacokinetics of naproxen tablets after oral administration of 250 mg. tablet in Thai healthy volunteers showed that the mean peak plasma concentration reading directly from individual data ranged from 24.51 to 30.18 µg/ml. and statistical results exhibited no significant difference of this value among all brands studied ($p > 0.05$).

The mean time to peak plasma level also reading directly from each data ranged from 1.44 to 1.94 hours and no statistical difference of this parameter among five different brands were observed at $p > 0.05$

The absorption rate constant were 1.15, 0.77, 0.72, 0.72, and 0.90 $hour^{-1}$ for brands A, B, C, D and E, respectively. Statistical results were the same as those of time to peak plasma level.

The biological half-lives of naproxen ranged from 12.39 to 15.17 hours. They are in good agreement with those previously published reports.

9. Bioequivalence of all naproxen tablets studied here were evaluated. It could be concluded that brands B, C, D, and E were bioequivalent to the innovater's product (brand A) in terms of both the rate and the extent of drug absorption. Therefore, one can select the economic product of naproxen tablet in order to provide the equivalent therapeutic effects.

10. It should be note that eventhough all brands of naproxen tablets were bioequivalent based on statistical evaluations, it appears that brands D and A seem to be likely bioinequivalent according to Figure 15.

11. The correlation tests between in vitro and in vivo data for five different brands of naproxen tablets showed that there were no significantly correlative between disintegration time and in vivo parameters, $AUC_o^{\infty}$, Ka, $Cp_{max}$, $T_{max}$, at $p > 0.05$ (for the absorption rate constant using 99% confidence limits and/or when brand A was excluded). The dissolution rate constant and the in vivo data were not significantly correlative as well at $p > 0.05$.