CHAPTER V

CONCLUSION

1. In vitro studies, all five commercial brands of 400 mg cimetidine tablets met the United State Pharmacopoeia XXI 3 rd Supplement, British Pharmacopoeia 1973 and 1980 specifications for percent labeled amount, weight variation and disintegration,respectively.

2. Dissolution profiles were determined for each product in carbondioxide-free deionized water. Studies were performed using the U.S.P. Dissolution Apparatus Type I maintained at 100 rpm and a temperature of 37 ± 0.5 °C. Major differences were observed for the rates and extent of dissolution among brands. Brands A, B and C met the United State Pharmacopoeia XXI 3rd Supplement specifications for drug dissolution while brands D and E failed to meet the specifications. There were no significant differences in dissolution rate constants among brands A, B and C. Also, the mean dissolution rate constants of these 3 brands were significant greater than those of brands D and E ($p < 0.05$).

3. There was no significantly correlative between the disintegration and the corresponding dissolution for these five brands ($p > 0.05$).

4. Different brands of cimetidine tablets gave presumably different disintegration times and dissolution rates due to different tablet formulations and/or manufactured processes.

5. Since the dissolution rate may be an important factor affecting the bioavailability, brand B which had about the same in dissolution rate constant as brand A and also was the least retail price product, was chosen to compare the bioavailability with brand A. The bioavailability was studied in 9 normal subjects. Both single dose of 200 mg cimetidine injection and 400 mg cimetidine tablets were given to the subjects following a crossover experiment. Plasma cimetidine levels were determined by a high pressure liquid chromatographic method.

6. Following intravenous administration, the plasma concentration profile follows multicompartmental characteristics. Individual plasma profile was analyzed according to statistical moment theory. The result showed that the mean residence time was 1.88 ± 0.13 hours and the effective half life was 1.31 ± 0.09 hours. The time for which the cimetidine concentration remained above 0.5 μg/ml was at least 4 hours in most subjects.

7. Following oral administration of cimetidine, two plasma concentration peaks were frequently observed. This is probably due to discontinuous absorption in the intestine. The absolute bioavailability of cimetidine

tablets in Thai healthy volunteers were 76.13 ± 3.54 % for Brand A and 71.15 ± 4.62 % for Brand B, respectively. This incomplete absorption may be due to first pass effect and/or stability of cimetidine in gastrointestinal tract. The relative bioavailability of cimetidine Brand B with respect to Brand A was 94.23 %. The mean absorption time ranged from 1.45 ± 0.22 to 1.75 ± 0.20 hours and corresponding first order absorption rate constant ranged from 0.67 ± 0.11 to 0.90 ± 0.18 $hour^{-1}$. The mean residence time after oral administration was greater than that after intravenous administration and ranged from 3.34 ± 0.22 to 3.63 ± 0.16 hours. The time for which the plasma concentration remained above 0.5 μg/ml was about 6 hours.

8. There were no statistically significant difference between Brands B and A with respect to the values of area under the concentration-time curve, the first order absorption rate constant, the mean residence time and the time for which the plasma concentration remained above 0.5 μg/ml. These parameters are in good agreement with those previously published data.

9. Brands B and A were bioequivalent. Therefore one can select the economical product to provide equivalently therapeutic effects.