CHAPTER V

CONCLUSION

1. All five commercial brands of 150 mg ranitidine tablets met the requirement for weight variation, percent labelled amount and disintegration times.

2. Dissolution profiles were determined for each product in simulated gastric fluid pH 1.2 and simulated intestinal fluid pH 7.5, using the USP Dissolution Apparatus Type I maintained at 100 rpm. Major differences were observed for both rate and extent of dissolved drug among brands only in acidic medium.

3. There were no significantly correlative between disintegration times and dissolution rates, indicating the independent of dissolution from disintegration of tablets.

4. The absolute and relative bioavailabilities of five brands of ranitidine tablets were studied in 12 healthy volunteers. Both single dose of 50 mg ranitidine injection and two 150 mg ranitidine tablets were given to the subjects in a crossover design. Plasma ranitidine levels were determined using high-performance liquid chromatography.

5. Plasma concentration-time data after intravenous dosing were best described biexponential models. Individual plasma data was analyzed according to statistical moment theory. The average mean residence time was 2.08 $\pm$ 0.34 hours and the mean biological half-life was 1.44 $\pm$ 0.24 hours.

6. Plasma concentration-time profile after oral administration showed the double peaks in some cases. All five brands of ranitidine tablets are bioequivalent with respect to both the rate and extent of absorption. The absolute bioavailabitily were 50.36 $\pm$ 14.53, 45.93 $\pm$ 12.48, 42.65 $\pm$ 12.27, 42.27 $\pm$ 12.44 and 67.24 $\pm$ 13.24% for brands A, B, C, D and E respectively. The relative bioavailability of four local manufactured brands with respect to innovator's (Brand A) were 97.36 $\pm$ 36.55, 91.09 $\pm$ 34.04, 94.33 $\pm$ 46.45 and 144.00 $\pm$ 47.70 % for brands B, C, D and E, respectively.

7. The pharmacokinetic parameters of ranitidine calculated from Thai normal volunteers following intravenous and oral administration of 50 mg and two 150 mg tablets, respectively, agree well with the previous studies. The mean absorption time ranged from 2.56 $\pm$ 0.52 to 2.94 $\pm$ 0.59 hours and the corresponding first order absorption rate constant ranged from 0.35 $\pm$ 0.07 to 0.41 $\pm$ 0.07 hr^{-1}. The mean residence time after oral administration was greater than that after intravenous administration, which were ranged from 4.64 $\pm$ 0.36 to 5.02 $\pm$ 0.59 hours.

8. The correlations between in vitro studies such as disintegration times, dissolution rate constants and in vivo bioavoilability were studied. The result illustrated that the correlation was attained in only one case which was the dissolution rate constant of drug in acidic medium VS. t_{max} . Therefore, the rate and amount of absorbed drug related to neither disintegration nor dissolution of tablet or in vitro data could not interpret bioavailability of ranitidine.