CHAPTER IV

CONCLUSION

1. All 13 commercial brands of 40 mg. furosemide tablets met the requirement for weight variation, percent labelled amount, and disintegration times.

2. Dissolution profiles were determined for each product in phosphate buffer pH 5.8, using the U.S.P Dissolution Apparatus Type II maintained at 50 r.p.m. Great differences were observed for both rate and extent of dissolution among brands. Dissolution rate constant from each brand could be ranked in 4 groups; (a) brand L, (b) brand A, B, E, F, G, H, I, K and M (C) brand C, J and (d) brand D (at $p < 0.05$). Ranked in terms of mean percent drug dissolved at 30 min. were : (a) brand L, (b) brand A, B, E, F, G, H and I, (c) brand K and M, (d) brand C, J and (e) brand D (at $p < 0.05$).

3. There were poor relationship between disintegration times and dissolution rates, indicating the independent of dissolution from disintegration of tablets.

4. The comparative bioavailability of 4 brands of furosemide tablets, with differences in dissolution profiles, was studied in normal volunteers. Oral single dose of 40 mg tablet was administered to 8 subjects in a crossover design. Plasma furosemide level were determined by a high-performance liquid chromatography. Each plasma

data was analyzed following one compartment model using PCNONLIN program. No statistically significant differences were noted regarding to Ka, t_{max} and Cp_{max} obtained from such brand, indicating that there were no differences in rate and extent of furosemide absorption and the 4 brands are bioequivalent. The relative bioavailability (with respect to brand A) were 70.29%, 113.41%, and 94.93% for brand B, C and D respectively.

5. The pharmacokinetic parameters of furosemide estimated from Thai normal volunteers after oral administration of 40 mg of drug showed that absorption was rapid, the peak plasma level ranged from 0.609 to 1.124 μg/ml and the time to peak ranged from 1.625 to 1.997 hr. The terminal half-life was ranged from 1.00 to 1.76 hr.

6. The correlations between in vitro studies such as disintegration times, dissolution rate constant and percent drug dissolved at 30 min. and in vivo bioavailability were studied and revealed that the correlation coefficients were rather small which interpreted that bioavailability was independent determinant of in vitro studies or the sample size was too small or not varied enough to reveal significant correlation.

7. Clinical response to 4 different brands of furosemide tablets were evaluated in terms of diuresis and electrolyte excretion. No significant differences among brands could be observed, implying clinical equivalence of the four brands.

8. In vitro-in vivo clinical response correlations revealed that clinical response to furosemide did not depend on its in vitro properties.