CHAPTER V

CONCLUSIONS

1. All four commercial brands of 300 mg gemfibrozil capsules met the requirements of the United State Pharmacopoeia XXII (United State Pharmacopoeial Convention Inc., 1990) for weight variation, content of active ingredient, and disintegration time.

2. All four commercial brands of 300 mg gemfibrozil capsules disintegrated within the limit time of hard capsule. The disintegration time of brand B was statistically significant longer than that of brand A ($p < 0.05$). The rank order in term of mean disintegration times were brands B > A > C > D.

3. Dissolution profile for each brand was performed in phosphate buffer (pH 7.5 $\pm$ 0.1), using the USP Dissolution Apparatus Type II maintained at 50 $\pm$ 2 rpm. Major differences were observed for the rate and the extent of dissolved drug. The rank order in term of dissolution rate constants were brands C > D > B > A. The dissolution rate constant of brand C and D were statistically significant ($p < 0.05$) higher than those of brands A and B.

4. There were no statistical correlative ($p > 0.05$) between the disintegration time and the dissolution rate constant of all brands.

5. The bioavailability of all four commercial brands A, B, C and D were studied in twelve Thai healthy volunteers. A single dose of two 300 mg gemfibrozil capsules were administered to each subject in a cross over design. Plasma gemfibrozil concentrations were determined by high performance liquid chromatography and detected by UV detector at 225 nm. Individual plasma concentration-time profile was analyzed for relevant pharmacokinetic parameters. The data were well described by a biexponential equation.

The mean peak plasma drug concentration ranged from 19.68 to 31.72 mcg/ml. Statistical results indicated that peak plasma drug concentrations of brands B and C were significant different from that of brand A ($p < 0.05$) meanwhile that of brand D was not.

The average time to peak plasma drug concentrations ranged from 1.83 to 2.33 hours. There were no statistical difference among the four commercial brands ($p > 0.05$).

The area under the plasma drug concentration versus time curves ranged from 75.22 to 97.00 mcg.hr/ml. Statistical results indicated that area under the plasma drug concentration versus time curve of brands B and C were

significant different from that of brand A ($p < 0.05$). This results were the same as the C_{max} of brands B and C did.

The relative bioavailability of three locally manufactured brands with respect to innovator's product (Brand A) were 77.55, 83.74 and 97.90 percent for brands B, C and D, respectively.

Only brand D was complete bioequivalent to brand A with respect to both the rate and the amount of drug absorption into general circulation.

6. The pharmacokinetics of gemfibrozil following oral administration of two 300 mg capsules were well described by a mean of one compartment open model.

The average absorption rate constant obtained from the CSTRIP program ranged from 1.24 to 1.80 hr^{-1} and no statistically difference among these values ($p > 0.05$).

The average elimination rate constant also obtained from the CSTRIP program ranged from 0.42 to 0.51 hr^{-1} and no statistically difference among these values ($p > 0.05$).

The average biological half-life of gemfibrozil ranged from 1.40 to 1.67 hours and no statistically difference among these values ($p > 0.05$).

The results of pharmacokinetic parameters established in this study were in agreement with those previously published data.

7. There were no statistical correlation ($p > 0.05$) between the in vitro and in vivo data of four commercial brands of gemfibrozil capsules.