CHAPTER IV

CONCLUSION

1. *In vitro* studies, all six commercial brands of 600-mg praziquantel tablets met the B.P. 1980 and 1973 specifications for film-coated tablets except brand D failed to meet the disintegration time requirement.

2. Dissolution profiles were determined for each product in two different media ; simulated gastric fluid without enzyme [I] and simulated intestinal fluid without enzyme [II]. Studies were performed using the U.S.P. Dissolution Apparatus Type II 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. Rank orders of dissolution rates in terms of mean percent drug dissolved in [I] at 60 min were : Brand B $>$ Brand A $>$ Brand F , Brand E $>$ Brand C $>$ Brand D (at $p < 0.05$). While those in [II] were : Brand C $>$ Brand B $>$ Brand A, Brand E $>$ Brand F $>$ Brand D (at $p < 0.05$).

3. There were good correlations between disintegration times and dissolution rates, indicating the disintegration time of tablets might be a rate-limiting step of praziquantel dissolution.

4. The comparative bioavailabitity of four brands of praziquantel tablets, with differences in *in vitro* dissolution characteristics, was studied in normal subjects. Single dose of 40 mg/kg of praziquantel was administered to eight subjects in a crossover design. Serum praziquantel level were determined by a high-pressure liquid chromatographic

method. Individual serum profile was analyzed according to one compartment model using PCNONLIN computer program. Statistically significant differences($p < 0.05$) were observed regarding to specific parameters among drug product formulations. More than 20 percent differences in $C_{p\ max}$, t_{max}, and $[AUC]_0^\infty$ values between brand D and brand A (reference standard), indicating the two products were bioinequivalent. The relative bioavailabilities of praziquantel (with respect to brand A) were 91.25%, 80.95%, and 69.86% for brand B,C, and D, respectively.

5. In this study, the pharmacokinetics of praziquantel tablets after oral administration of 40 mg/kg of the drug in Thai healthy volunteers showed that absorption was rapid, the mean individual peak serum concontrations ranged from 1.007 to 1.625 µg/ml and the corresponding time required to reach the peak ranged from 1.72 to 2.81 hours. The biological half-life of praziquantel was 1.15 hours (0.94-1.25 hours). These results are in good agreement with those previously published data.

6. Comparision of the *in vitro* and *in vivo* data for the four different brands of praziquantel tablet were made. Results indicated that the rate and amount of praziquantel absorption may be related to dissolution rates (in simulated gastric fluid without enzyme).

7. Different brands of praziquantel tablets gave presumably different disintegration times, dissolution rates and bioavailabilities due to different tablet formulations and/or manufactured processes.

8. From the bioavailabitity point of view, one can evaluate and select the economical products to provide equivalently therapeutic effects.