CHAPTER V

CONCLUSION

The effects of smoking, sex and age on theophylline pharmacokinetics were studied in 40 healthy Thai volunteers divided into 4 groups: nonsmoking males, nonsmoking females, smoking males and children. The results obtained were concluded as follows:

1. The pharmacokinetics of theophylline after oral administration was well described by one-compartment open model with first-order absorption and first-order elimination.

2. The absorption of theophylline from syrup dosage form was very rapid. Oral dose of 2.4 mg/kg body weight of theophylline gave the mean peak plasma concentration approximately 4.5 to 5.5 mcg/ml with the average time to reach peak plasma concentration ranged from 1.0 to 1.4 hours.

3. The apparent volume of distribution in nonsmoking females (0.380 L/kg) was smaller than nonsmoking males (0.484 L/kg), with the larger in both AUC and C_{max} ($p < 0.05$). The total body clearance was also smaller in nonsmoking females (0.030 L/kg/hr) than in nonsmoking males (0.038 L/kg/hr), whereas no difference in elimination rate constant was observed. Both smaller V and

Cl in nonsmoking females indicated that the nonsmoking females should receive lower theophylline dose than the nonsmoking males. Since the relative total body clearance of the nonsmoking females was 0.8 times of that of nonsmoking males, the theophylline maintenance dose for females is suggested to be 0.8 times of the dose required for the males.

4. Cigarette smoking had a tendency to increase theophylline metabolism as shown by significantly increased elimination rate constant ($p < 0.05$) and decreased elimination half-life in smokers as compared to those in nonsmokers. Mean K and $t_{1/2}$ were 0.1020 hr^{-1} and 6.80 hr in the smoking males, and 0.0787 hr^{-1} and 8.81 hr in the nonsmoking males, respectively. The total body clearance in smokers (0.047 L/kg/hr) was also higher than in nonsmokers (0.038 L/kg/hr), but not statistically significant difference at 0.05 significant level. However, the higher Cl observed in smokers will be useful for estimating the appropriate theophylline dose for this group of patients. The relative total body clearance of the smokers was 1.2 times of that of nonsmokers. Consequently, the relative maintenance dose for Thai smoking patients may be 1.2 times of that for Thai nonsmoking patients, but are not as twice of that needed for nonsmokers, as suggested by the other investigators which conducted in the other countries.

5. The results obtained from both significantly increasing theophylline elimination rate constant (0.1327

hr^{-1}) and total body clearance (0.056 L/kg/hr) with decreasing elimination half-life (5.22 hr) in children group, clearly suggest that children be able to eliminate theophylline faster and require higher doses than adults, in order to obtain similar therapeutic serum levels. The relative maintenance dose of theophylline for children patients should be 1.5 times of that for nonsmoking adults.