

## CHAPTER VII

### CONCLUSIONS

The findings obtained from the present study can be summarized as follows:

#### 1. Short term *in vitro* sensitivity assay

1.1 The range of IC<sub>50</sub> values for five drugs obtained from the short term *in vitro* sensitivity assay were markedly wide, especially for pyrimethamine. The IC<sub>50</sub> values measured for DHFR inhibitors showed that WR99210 inhibited growth most potently when compared to pyrimethamine and chlorcycloguanil. The IC<sub>50</sub> values measured for DHPS inhibitors were extremely high, but dapsone was more potent than sulfadoxine.

1.2 A trend of increasing mean IC<sub>50</sub> values was observed with increasing number of *Pvdhfr* mutations from double to quadruple. WR99210 retained its activity even against parasites that carry the quadruple mutant alleles of *Pvdhfr*.

#### 2. Yeast expression system

2.1 All mutant alleles showed increase resistance to pyrimethamine and chlorcycloguanil by more than 50 folds when compared with wild-type.

2.2 All mutant alleles were relatively sensitive to WR99210, particularly the double mutant alleles.

2.3 Chlorcycloguanil was particularly ineffective against all mutant alleles.

#### 3. Geographical distribution of *Pvdhfr* and *Pvdhps*

3.1 Seven different alleles of *Pvdhfr* and eleven different alleles of *Pvdhps* were identified from 160 isolates of *P. vivax* originating from different geographical

endemic areas of Thailand. Ninety-seven isolates (60.6%) harbored at least quintuple mutant alleles of the combined *Pvdhfr-Pvdhps* gene.

3.2 Double and single mutations of *Pvdhfr* and *Pvdhps* were commonly found in isolates collected from Thai-Cambodian and Thai-Malaysian borders whereas quadruple and double mutations of *Pvdhfr* and *Pvdhps* were predominant in isolates obtained from Thai-Myanmar border.

