CHAPTER V

CONCLUSION

In order to study structure-activity relationships of 1-substituted-4-oxygenated-β-carbolines, the antimalarial activity and chemical constituents of *P. javanica* were reinvestigated. The result demonstrated that the hexane extract of *P. javanica* stembark showed high level of an *in vitro* antimalarial activity against *P. faciparum* K1. Further fractionation provided Fraction V that still showed high level of the *in vitro* antimalarial activity against *P. faciparum* K1. Further isolation of Fraction V provided six fractions. According to ^{1}H- and ^{13} C-NMR spectra, it could be concluded that the major compound in Fraction V-3 was β-sitosterol. Unfortunately antimalarial activity of β-sitosterol can not be determined because of its low solubility in DMSO. However, Fraction V-2 and V-4 still showed high level *in vitro* antimalarial activity against *P. faciparum* K1. On the other hand, the chloroform extract of *P. javanica* stembark showed the high level of an *in vitro* antimalarial activity against *P. falciparum* K1. Further isolation using acid-base extraction method provided low percentage yield of alkaloidal portion, however, that still showed high level of the *in vitro* antimalarial activity against *P. falciparum* K1. Further analysis by GC-MS technique indicated the peak of major compound in GC chromatogram. According to EI and CI mass spectra, it could be concluded that the major compound was 1-vinyl-4-methoxy-β-carboline. After purification by preparetive TLC, the CI mass spectrum showed the molecular ion peak at *m/z* at 226 that represented the molecular weight of 1-ethyl-4-methoxy-β-carboline. These results encouraged us to study structure-activity relationships of 1-substituent-4-oxygenated-β-carbolines. Therefore the synthesis methods for 1-substituent-4-oxygenated-β-carbolines were developed by using compound **3** as the model compound. Compound **3** was synthesized by modification of Cook's method and combined with modification of Suzuki's method. The four-step method for synthesis **3** using tryptamine as starting material was applied to 1-methoxy-1-methyl-β-carboline. Also, the synthesized compounds were evaluated for *in vitro* antimalarial activities against chloroquine sensitive *P. falciparum* FCR-3 strain and cytotoxicities against mouse mammary tumor FM3A. N-2 methylated compound 10 and 15 showed high level of *in*

vitro anti-malarial activities and selective cytotoxicities. Further optimization of 1-substituent-4-oxygenated-β-carbolines could lead to high potential candidates for antimalarial agents.