CHAPTER V

CONCLUSION

Since the insecticide resistance in *Ae. aegypti*, vector of dengue and dengue hemorrhagic fever, still is a problem for mosquito vector control. In *Ae. aegypti* PMD-R strain which is resistant to DDT and permethrin has been demonstrated that a mutation in the voltage-gated sodium channel gene (*kdr*) was conferred a mainly mechanism and partially by enzymes-based resistance (Yanola e*t al.,* 2010). The aim of this study was to define enzymatic involvement in permethrin metabolism pathway in *Ae. aegypti* resistant strain. Based on the larval bioassay, the LC_{50} of both strains was reduced in the presence of PBO while the effect of BNPP was not observed. The total level of P450s was similar in both strains and had 4-fold activity higher than the susceptible Rockefeller strain. These results reflect the in vivo involvement of P450s in detoxification of permethrin in both strains, agreeing with the result in the in vitro assay. Although the permethrin metabolic product, PBCOOH, was small amount detected in both strains, but PMD-R produced more PBCOOH than PMD when PBOH and PBCHO were used as the substrates in the presence of NADPH (cofactor of P450s) particular NAD^+ (cofactor of ADHs and ALDHs). However, one should be aware that in vitro experiments with model substrates do not necessarily reflect the in vivo situations of insect metabolizing insecticide molecules. In conclusion, the permethrin resistance mechanism in the *Ae. aegypti* PMD-R strain is conferred mainly by the *kdr* gene and partially by oxidative enzymes involving P450s, ADHs and

ALDHs. Therefore, it is important that care is taken in the appropriate choice of insecticide, using those that are less affected by *kdr* and oxidase based resistant mechanisms where necessary.