Thesis Title	The Mitochondrial Cytochrome Oxidase Subunit III Gene and Protein Sequence Analysis in Chloroquine-Resistant *Plasmodium falciparum*
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Abstract

Chloroquine has been an important antimalarial drug for several decades. It is effective against all strains of *P. vivax*, *P. malariae* and *P. ovale* and was the drug of choice for *P. falciparum* infection. The spread of drug-resistant *P. falciparum* has made the prophylaxis and treatment of malaria increasingly difficult. The mechanism of chloroquine resistance has not yet been established. Chloroquine resistance phenotype shows a rapid efflux of the drug from the parasite's digestive vacuole 40-50 times more than the sensitive one. In this study, the mitochondrial cytochrome *c* oxidase subunit III gene (CO III) and protein sequence which is the part of electron transport system was analysed in chloroquine-resistant *P. falciparum* found in Thailand and compared with that of the sensitive one. By the method of PCR, this gene was amplified from eleven malarial isolates, ten chloroquine-resistant and one sensitive strain, and cloned into pUC 18 plasmid vector. The gene was then sequenced by dideoxy-chain termination method of Sanger. The nucleotide and amino acid sequence of this gene were analysed and the secondary structure of this protein was predicted.

Two point mutations were found at nucleotide position 771 and 1484 of the gene. The T771C base substitution changed amino acid codon 268 from isoleucine to valine whereas the A1484G base substitution changes amino acid codon 30 from phenylalanine to serine. Although the I268V were highly conserved among species, the replaced amino acid had the same chemical property and did not alter the predicted secondary structure. The F30S was in hypervariable region of the gene. The minor alteration was shown in predicted secondary stucture even though their chemical properties were different. Moreover, both mutations were not specific and consistent to the chloroquine-resistant strain examined. These mutations in CO III gene may or may not be involved in the mechanism of chloroquine resistance in *P. falciparum*.