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JUREE CHAROENTEERABOON: INACTIVATION OF ARTEMISININ BY NORMAL AND VARIANT ERYTHROCYTES. THESIS ADVISORS: PRAPON WILAIRAT, Ph.D., YONGYUTH YUTHAVONG, D.Phil. 99 p. ISBN 974-662-512-8

Malaria continues to be a major public health problem in many parts of the tropical world, including Thailand. The resistance of *P. falciparum* to antimalarial drugs, such as chloroquine, quinine, mefloquine and Fansidar, has spread rapidly. Artemisinin, an endoperoxide-containing compound, and its derivatives are effective against multidrug-resistant strains of *P. falciparum*. Thalassemia also has a high incidence in malaria endemic areas. *In vitro* studies have demonstrated resistance to artemisinin by *P. falciparum*-infected α-thalassemic erythrocytes compared with normal controls. This resistance is host specific and not due to parasites. Artemisinin was inactivated by both types of α-thalassemic erythrocytes, Hb H and Hb H/Hb CS, to a greater extent than normal cells, accounting for artemisinin resistance in *P. falciparum*-infected α-thalassemic erythrocytes. Both cytosol and membrane components from α-thalassemic erythrocytes inactivated artemisinin. Unlike α-thalassemic red cells, intact β-thalassemic erythrocytes did not behave differently from normal erythrocytes, but lysate and membrane fractions could inactivate artemisinin. The presence of 50% (v/v) human serum or greater could prevent artemisinin inactivation by normal red cells, but human serum could only retard slightly the rate of artemisinin inactivation by both types of α-thalassemic erythrocytes. Phenylhydrazine-oxidized red blood cells, an *in vitro* model of thalassemia, were also able to reduce artemisinin activity. This inactivation mechanism allows ineffective artemisinin to be present in *P. falciparum*-infected α-thalassemic individuals which may be a cause of recrudescence of malaria during artemisinin treatment, and might possibly produce artemisinin-resistant parasites in the future .