

**P11: STUDIES OF THE PRO-OXIDANT ACTIVITY OF ARTEMISININ
AND QUINOLINE-CONTAINING DRUGS USING LDL
OXIDATION AS A MODEL**

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ABSTRACT

Artemisinin and quinoline-containing drugs represent for the important classes of antimalarial drugs. The molecular basis of the mechanism of action of these drugs have been widely proposed, and one of them involves the interaction of drugs with ferriprotoporphyrin IX (ferric heme or hemin). The objectives of this study were to study the pro-oxidant activity of artemisinin in comparison with quinoline-containing drugs by using LDL oxidation as a model, and to determine the importance of hemin on the mechanism of drug-induced LDL oxidation. Low density lipoprotein (LDL) was separated from plasma by sequential gradient ultracentrifugation technique. The oxidation of LDL was conducted at 37°C under dark condition for 8 hours. One hundred µg/ml of LDL was incubated in 10 mM phosphate buffer saline (PBS), pH 7.4 with artemisinin and four quinoline-containing drugs (i.e., quinine, chloroquine, mefloquine and primaquine), both in the absence and presence of hemin. The degree of LDL oxidation was determined by the formation of thiobarbituric acid reactive substances (TBARs) and the decrease of tryptophan fluorescence. Artemisinin significantly enhanced hemin-induced TBARs formation. Quinoline-containing drugs also enhanced hemin-induced TBARs formation, but with lesser degree than artemisinin. Artemisinin reduced tryptophan fluorescence intensity of LDL significantly within 2 hours. Other quinoline-containing drugs were shown to have no effect on tryptophan fluorescence of LDL even in the presence of hemin. The results indicated that artemisinin existed a more potent pro-oxidant action than that of quinoline-containing drugs, and the pro-oxidant activity of both artemisinin and quinoline-containing drugs required hemin as the catalyst.

Key words: Artemisinin, Quinoline-containing drugs, pro-oxidant activity, LDL oxidation