THE EFFECT OF CHLOROQUINE ON IRON DISTRIBUTION IN *PLASMODIUM FALCIPARUM*

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Antimalarial drugs such as chloroquine (CQ) have been shown to interact with Fe(III)PPIX and suggested to prevent haemozoin formation *in vivo* causing a build-up of toxic Fe(III)PPIX or its complex with CQ. Several morphological changes including vacuolar swelling, pigment clumping, loss of haemozoin granules, increase in undigested haemoglobin and a build-up of vesicles containing electron-dense material have been observed by transmission electron microscopy (TEM). No study has previously reported the effect of chloroquine on the overall distribution of iron in the malaria parasite. This study investigated this distribution of iron in *Plasmodium falciparum* using electron spectroscopic imaging (ESI) and TEM. Major changes were observed mainly in the trophozoite-stage. These parasites contained significant amounts of iron in the parasite cytosol and a large number of transport vesicles containing iron. It is clear that significant quantities of iron accumulate not only in the transport vesicles, but also in the parasite cytosol, which is almost free of iron in untreated parasites. The results obtained in this study support the hypothesis that the drug accumulates primarily inside the food vacuole where it interacts with Fe(III)PPIX released from haemoglobin, resulting in formation of potentially toxic Fe(III)PPIX or Fe(III)PPIX-chloroquine complex inside the food vacuole causing membrane damage. The toxic Fe(III)PPIX is transported from the food vacuole into the parasite cytosol resulting in a radical redistribution of iron in the parasite, where it disrupts membranes altering their properties and inhibiting vesicle fusion with the food vacuole resulting in an increase in transport vesicles inside the parasite cytosol.