HEME BIOCRYSTALLIZATION AS A PREVENTIVE ANTIOXIDANT DEFENSE IN BLOOD FEEDING ORGANISMS

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Blood feeding organisms digest hemoglobin and release high quantities of free heme in their digestive tract. Free heme is very toxic and several mechanisms have been developed to protect these organisms against its deleterious effects. We are currently studying one of these adaptations, which consist on the crystallization of free heme into a pigment named hemozoin (Hz). Currently, Hz has been found in five distinct blood feeding organisms of great medical importance including *Plasmodium*, *Rhodnius* and *Schistosoma*. For these organisms, Hz formation represents the main heme detoxification route as the pro-oxidant effects of heme are drastically reduced upon its crystallization. Also, when heme crystallization is inhibited by quinoline antimalarials, in the kissing bug *Rhodnius prolixus*, heme-induced oxidative stress is established. Several lines of evidence points out that hydrophobic environments would play a key catalytic role in heme crystallization. In *R. prolixus*, extracellular phospholipid membranes lining the midgut epithelial cells are the structures involved in Hz formation, whereas in the blood fluke *Schistosoma mansoni*, heme crystallization is promoted by extracellular lipid droplets found in gut lumen. In both organisms, lipids present in these structures seem to play an essential catalytic role in heme crystallization by allowing association of heme at hydrohylic-hydrophobic interfaces. Further, quinoline antimalarials are able to interfere with heme crystallization in non-*Plasmodium* organisms. Thus, as Hz formation is peculiar to these organisms, but absent in the host, this makes it an exceptionally attractive drug target which could be used to control and/or treat the illnesses transmitted or caused by these blood-feeders.

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