HAEM DETOXIFICATION BY SPONTANEOUS SELF-ASSEMBLY OF HAEMOZOIN AT THE LIPID/WATER INTERFACE

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Recent studies in our laboratories have led to a new paradigm for understanding the biosynthesis of haemozoin in the malaria parasite and other organisms that detoxify ferriprotoporphyrin IX (Fe(III)PPIX) by forming this insoluble biomineral-like solid. Molecular dynamics simulations suggest that dimeric Fe(III)PPIX, present in aqueous solution will rapidly and spontaneously form a haemozoin-like intermolecular precursor in a medium in which hydrogen bonding is absent and in which the dielectric constant is reduced. The prediction was confirmed by showing that synthetic haemozoin (β-haematin) forms rapidly and spontaneously under physiologically appropriate conditions of temperature and pH near the interface of aqueous solutions and long chain alcohols (octanol and pentanol) and at the interface of lipids and water. Product formation was confirmed by infrared spectroscopy, X-ray powder diffraction, scanning electron microscopy and in situ resonance Raman spectroscopy. The rate of reaction suggests that this is the likely mechanism of haemozoin formation. Antimalarials such as chloroquine have been shown to inhibit the process at lipid/water interfaces at low micromolar concentrations.