On the mechanisms of chemical and biological heme crystallization

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Hemozoin is a heme crystal produced by several blood-feeding organisms as a way to detoxify heme derived from hemoglobin digestion. This crystal when produced synthetically, called β-hematin, is identical to hemozoin. Recent evidence have pointed out that hemozoin formation occurs under physiological conditions near synthetic or biological hydrophilic-hydrophobic interfaces. This would require a heme dimer acting as a precursor of the hemozoin crystal that would be formed spontaneously in the absence of the competing water molecules bound to the heme iron. In addition, several works indicate that hemozoin formation is associated to structures that provide hydrophilic-hydrophobic interfaces such as perimicrovilar membranes (PMM) in the blood sucking insect *Rhodnius prolixus* and in lipid droplets of the fluke *Schistosoma mansoni*. Here we investigated the mechanism by which total lipids extracted from PMM promote heme crystallization in *R. prolixus* midgut. Our first result showed that reduction in medium polarity, by using dimethylsulfoxide or polyethyleneglycol, increased heme solubilization in acidic medium, assessed by alkaline pyridine method. Interestingly, both solvents accelerated spontaneous heme crystallization *in vitro*, probably acting in changes of the dieletric constatnt of water on β-hematin prodution. β-hematin production in this system was confirmed by typical FTIR, XRD and SEM. Total lipids extracted from *R. prolixus* midgut were able to induce hemozoin formation in water-lipid interface, detected by FTIR. The data presented here support the notion that heme crystallization seems to require a reduction in water content in order to induce the removal of axial water bound to heme-iron, and that this may be promoted by the PMM in *R. prolixus* midgut. **Support: WHO-TDR-SSI, CAPES, FAPERJ (JCNE), ICGEB, CNPq.**

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