Hematin loses its membranotropic activity upon oligomerization into malaria pigment

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Abstract
Malaria is an infectious disease caused by Plasmodium type parasites transmitted by the bites of infected female anopheles mosquitoes. The malaria parasite multiplies in red blood cells where it degrades hemoglobin. This degradation of hemoglobin proteins releases hematin, an iron-containing porphyrin, which provokes membrane disruption and lysis. The malaria parasite blocks hematin-induced lysis by biocrystallization, a process that converts hematin into insoluble and chemically inert crystals. Hematin molecules are especially prone to self-assembly as dimers, oligomers and aggregates depending on environmental conditions (pH, solvent, temperature, concentration, ionic
strength). Considering the different forms of hematin-based assemblies, it is still unclear which are the ones able to interact with membranes. We have prepared hematin under different conditions to form hematin-based assemblies and to measure their ability to interact and to disorganize membranes. Our results show that different forms of hematin molecules are able to penetrate lipid membranes. Interestingly, this membrane activity is spontaneously inhibited at acidic pH and it can be restored under neutral pH. By contrast, the oligomers of beta-hematin were found to be completely harmless toward lipid membranes. Finally, the AFM visualization of hematin interaction with supported lipid bilayers showed for the first time its preferential interaction with defaults in membranes, at the boundaries between two distinct lipid phases. The superficial adsorption of aggregates on membranes and the absence of effect due to oligomers were also confirmed with AFM. (C) 2015 Elsevier B.V. All rights reserved.

Keywords

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