Magnetic properties of malarial pigments

A. Sienkiewicz[1], J. Krzystek[2], M. Walczak[1], K. Ławniczak-Jabłońska[1], B. Vileno[3], G. Chatain[4], A. J. Kosar[4], D. S. Bohle[4], and L. Forró[3]

[1]Institute of Physics, Polish Academy of Sciences
Lotników 32/46, 02-668 Warsaw, Poland
[2]National High Magnetic Field Laboratory, Florida State University
1800 E. Paul Dirac Dr., Tallahassee, FL 32310, USA
[3]Institute of Physics of Complex Matter, École Polytechnique Fédérale
CH-1015 Lausanne, Switzerland
[4]Department of Chemistry, McGill University, 801 Sherbrooke Street West
Montreal, Quebec H3A 2K6, Canada

Malaria continues to be one of the most common human infections, responsible for 1-2 million deaths per year. Today, over 40% of the world's population, especially in the tropics, is at risk. The most acute form of malaria is caused by a protozoan parasite, *Plasmodium falciparum* (*Pf*). The intraerythrocytic stage of *Pf* involves hemoglobin proteolysis as the primary nutrient source with the concomitant release of free heme. The liberated heme is detoxified by *Pf* into an inert crystalline material, called malarial pigment, or hemozoin. The mechanism of hemozoin formation is not well understood. It is largely accepted, however, that many of traditional anitimalarials prevent the formation of hemozoin. The spread of chloroquine-resistant strains (CQR) of *Pf* and the absence of a suitable replacement for this once effective antimalarial created an urgent need to understand mechanisms behind the drug's action. Recently, the crystal structure of hemozoin and its synthetic analogue, β-hematin, has been solved by X-ray powder diffraction [1].

In this work, we implemented several spectroscopic tools, including the multi-frequency high-field electron paramagnetic resonance (HFEPR), extended X-ray absorption fine structure (EXAFS) and X-ray absorption near edge structure (XANES) techniques to get a better insight into magnetic properties and structural details of both malarial pigments [2, 3]. The EPR spectra of malarial pigments were acquired in an unprecedented wide range of microwave frequencies of 9, 34 and 94 GHz for hemozoin and 9, 27 - 500 GHz for β-hematin, respectively. The results point to the existence of five-coordinate high-spin iron Fe^{III} ($\boldsymbol{S} = 5/2$) with largely axial symmetry in the bulk phase of hemozoin and β-hematin. The XANES and EXAFS spectra of iron K-edge were recorded in the k-range up to 10 $Å^{-1}$ for both malarial pigments. The analysis of the experimental data suggests that radial distributions of atoms around the iron centers in these compounds are very similar. Moreover, the comparison of XANES and EXAFS spectra of malarial pigments with the results gathered for Fe^{III}-containing systems also points to the existence of trivalent iron centers that are embedded in protoporphyrin-IX planes in both hemozoin and β-hematin.

[1] S. Pagola, P. W. Stephens, D. S. Bohle, A. D. Kosar, and S. K. Madsen, Nature, **404** (2000) 307.
[2] A. Sienkiewicz, J. Krzystek, B. Vileno, G. Chatin, A. J. Kosar, D. S. Bohle, and L. Forró, J. Am. Chem. Soc. **128** (2006), in print.
[3] M. Walczak, K. Ławniczak-Jabłońska, A. Sienkiewicz, I. N. Demchenko, E. Piskorska, G. Chatain, and D. S. Bohle, Nucl. Instrum. Meth. Phys. Res. B **238** (2005) 32.

Name of the presenting author (oral): Andrzej Sienkiewicz
e-mail address: sienk@ifpan.edu.pl
url's: http://www.ifpan.edu.pl