XANES AND EXAFS STUDIES OF MALARIAL PIGMENT'S SUBSTITUTES IN REACTION WITH ANTIMALARIAL DRUG

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Malaria remains the world's most prevalent vector-borne disease, which causes severe health problem particularly in African and Asiatic countries. Today, over 40% of the world's population, especially in the tropics, is at risk [1, 2]. The most severe form of malaria is caused by a protozoan parasite, *Plasmodium falciparum* (*Pf*), which lately has become resistant to traditional therapies. The intraerythrocytic stage of *Pf* involves hemoglobin proteolysis as the primary nutrient source and detoxify heme into an inert crystalline material, called malarial pigment, or hemozoin [3]. The crystal structure of hemozoin has been solved by X-ray powder diffraction [4] in the last years and its synthetic analogue, β-hematin was synthesized. The X-ray absorption spectroscopy (XAS) measurements performed on solid hemozoin and β-hematin samples confirmed that the radial distributions of atoms around the iron centers in these compounds are very similar but differ in the level of ordering. These studies also pointed to the presence of the trivalent iron atoms (FeIII) in both materials [5].

Understanding of all possible interactions and chemical structures related to malarial pigments become now critically important in respect the commonly used drugs based on chloroquine are not longer effective on many tribes of parasite.

In presented work we are especially interested in drug-induced perturbations of the dimer structures of soluble β-hematin-like compounds, iron(III) (meso-porphyrin-IX anhydride) and iron(III) (deuteron-porphyrin-IX anhydride). Similarly to their insoluble parent compound, β-hematin, *i.e.* Iron(III) (protoporphyrin-IX anhydride), these compounds are also built of dimers.

The XAS measurements were performed at ESRF (station ID26). The high resolution XANES and EXAFS spectra enabled us to reveal the differences in local environment of Fe atoms before and after drug addition. The results of EXAFS χ–function analysis for hemozoin' substitutes as compare to monomeric reference compounds, will be presented. The indicated changes in 1*s*-3*d* preedge feature of XANES spectra point on symmetry changes in nearest iron neighborhood and degree of bonds covalency. The shape of that feature depends strongly on used solvent. In solution of dimethyl sulfoxide (DMSO) differences after adding antimalarial drug to dimmer as well as to corresponding monomer are well noticeable.

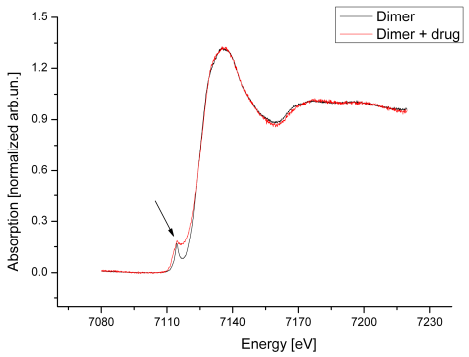

Figure 1. Comparison of XANES spectra of dimer before and after interaction with antimalarial drug in solution of DMSO.

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References

[1] L.H. Miller, D.I. Baruch, K. Marsch, O.K. Duombo, *Nature* **415** (2002) 673-679.

[2] World Health Organization, The World Malaria Report 2005, http://www.who.int/malaria.

[3] A. Dorn, R. Stoffel, H. Matile, A. Bubendorf, R.G. Ridley, *Nature* **374** (1995) 269-271.

[4] S. Pagola, P.W. Stephens, D.S. Bohle, A.D. Kosar, S.K. Madsen, *Nature* **404** (2000) 307-310.

[5] M. Walczak, K. Ławniczak-Jabłońska, A. Sienkiewicz, I.N. Demchenko, E. Piskorska, G. Chatain, D.S. Bohle, *Nucl. Instrum. Meth. Phys. Res. B* **238** (2005) 32-38.