

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office via the User Portal:

<https://www.esrf.fr/misapps/SMISWebClient/protected/welcome.do>

Reports supporting requests for additional beam time

Reports can be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.



Experiment title: Probing the mode of action of 4-aminoquinoline antimalarials by X-ray spectroscopies

Experiment number:
CH5490

Beamline: ID26	Date of experiment: from: May 30, 2018 to: June 5, 2018	Date of report: June 08, 2018
Shifts: 18	Local contact(s): Rafał Baran	<i>Received at ESRF:</i>

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Report:

In the experiment CH5490, we investigated the chemical state of hematin-Fe(III) and phthalocyanine-Fe(II) biologically active centres by means of X-ray absorption (XAS) and emission (XES) spectroscopies. We explored up to an unprecedented level of accuracy how 4-aminoquinoline (4-AQ) compounds bind organic Fe. Sample solutions (Table 1) were freshly prepared by mixing the mother solutions of the two components a few minutes before each spectral acquisition. Both CH₂Cl₂ and DMSO solvents degrade kapton[®] (Figure 1a), but the reaction with DMSO was slow enough to allow mounting of DMSO-containing solutions in a kapton[®]-covered plastic holder without sensible effects (Figure 1b).

Table 1. Samples studied at ID26

ID	Solution ^a	ID	Solution ^a
B1	Hematin in DMSO, 10 mmol/L	S3	B6+PIP in CH ₂ Cl ₂ , 40 mmol/L
B2	Fe-phthalocyanine in DMSO, 30 mmol/L	S4	B2+BQ, 60 mmol/L
B3	Hematin in DMSO/water ^b , 10 mmol/L	S5	B3+CQ in DMSO/water ^b , 20 mmol/L
B4	FeCl ₂ in DMSO, 30 mmol/L	S6	B4+BQ, 60 mmol/L
B5	Fe-phthalocyanine in DMSO/water ^b , 20 mmol/L	S9	B4+BP 60 mmol/L
B6	Fe-phthalocyanine in CH ₂ Cl ₂ , 20 mmol/L	S10	B5+CQ in DMSO/water ^b , 20 mmol/L
B7	FeCl ₃ in DMSO, 30 mmol/L	S12	B7+BQ, 60 mmol/L
S2	B1+BQ, 20 mmol/L	S13	B7+BP, 50 mmol/L

^a DMSO: dimethylsulfoxide; BQ: 4,7-dichloroquinoline; CQ: chloroquine; PIP: piperazine.; BP: 7-chloro-4-(4-methyl-1-piperazinyl)quinoline.

^b Aqueous citrate/phosphate buffer at pH = 5.

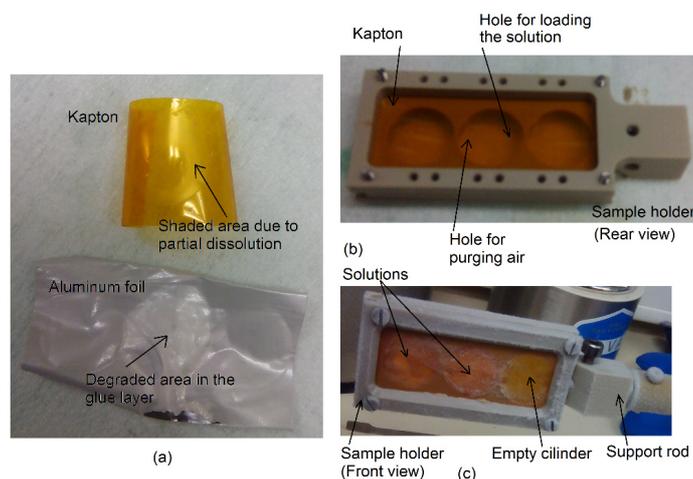


Figure 1. Sample preparation. (a) Damage to kapton® and glue on the rear of an Al foil due to exposition to CH_2Cl_2 . (b) Sample holder, rear view. (c) Sample holder, front view.

The sample was flash-frozen by immersing the sample holder in liquid nitrogen and then mounted on the closed circle He-cryostat at the ID26 spectrometer. HERFD-XANES, XES and valence-to-core signals were recorded while keeping the specimen in the 20-30 K T range.

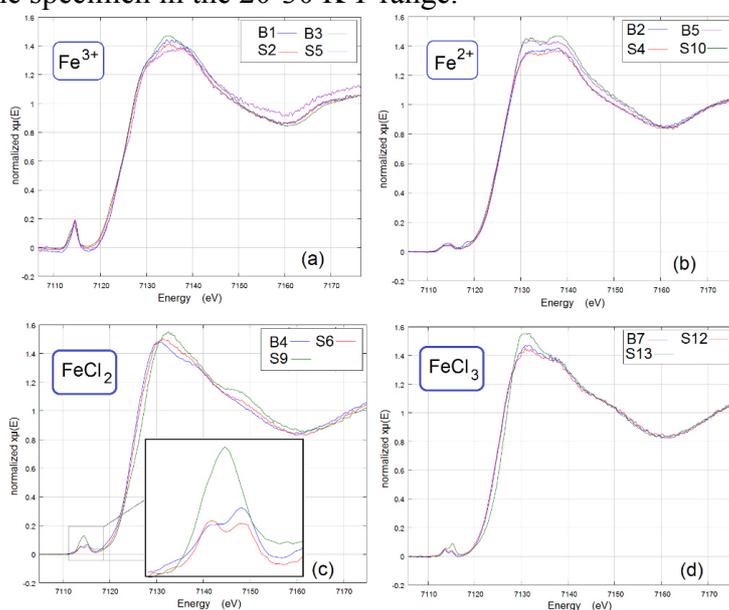


Figure 2. Comparison of relevant spectral features in representative samples here examined. (a) Hematin Fe(III) solutions. (b) Phthalocyanine Fe(II) solutions. (c) FeCl_2 solutions. (d) FeCl_3 solutions.

Organic Fe(II) compounds show a different shape of the XANES signal, already in the pre-edge region (Fig. 2b). Addition of BQ to Fe-phthalocyanine (B2/S4) causes the high-E pre-edge peak at 7118 eV to disappear, while the signal at ~ 7.14 keV splits into two neatly distinguishable components. Other parameters, including E_0 , $K\beta$ splitting and position of the ν_{tc} transitions, are not affected. Analogously to hematin solutions, addition of CQ (B2/S10) to Fe-phthalocyanine implies a + 3 eV shift of the absorption edge. On the contrary, addition of water changes (B2/B5) the signal of Fe-phthalocyanine in the pre-edge region and causes the E_0 inflection to shift by +2 eV. The interaction of BQ with iron (II) chloride (B4/S6) implies detectable differences in the relative weight of the resonant peaks in the pre-edge region (Fig. 2c, inset), a small but detectable reduction (-0.4 eV) of the $K\beta$ doublet separation, and a neat shift (+1.1 eV) toward higher energies of the ν_{tc} feature. These detected changes in the spectral features will be interpreted with reference to the current Literature, with the aid of high-grade quantum simulations.

It is also important to note how the use of different solution conditions has allowed to obtain a clear evidence of the solvent effect on the iron cation properties.