

Structure of $[\text{Cu}(\text{DAPTA})_4]^+$ complex in extremely diluted aqueous solution

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Water soluble copper(I) complexes with phosphine ligands have been proposed as alternative anticancer drugs to the cisplatin reference drug [1]. While structural information of these complexes are generally available for the solid samples, the local structural site of the Cu(I) is not determined in solution, especially at low concentration, in the micromolar domain. The use of the X-Ray Absorption Spectroscopy (XAS) technique will allow an in depth study of the coordination site of copper at variable concentration. A pioneering study of the Cu(I) complex $[\text{Cu}(\text{thp})_4][\text{PF}_6]$, (thp = tris(hydroxymethyl)phosphine) at concentration down to the micromolar domain is available in the literature [2]. Here we present the investigation on the $[\text{Cu}(\text{DAPTA})_4][\text{BF}_4]$ complex, where DAPTA = 3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1] nonane from millimolar concentration down to 66 μM , thus reaching concentration levels that can be correlated with those relevant for biological applications. Acquisition of XAS data on such a dilution level is very challenging and unusual.

XAS spectra at the Cu K-edge have been recorded at GILDA-BM08 beamline (now LISA) of the European Synchrotron Radiation Facility, ESRF (Grenoble, France). The storage ring was operated at 6 GeV in uniform mode with a maximum electron current of 200 mA. Aqueous solutions of 10 mM, 1.0 mM, 165 μM and 66 μM of $[\text{Cu}(\text{DAPTA})_4]^+$ have been measured. Data were recorded in fluorescence mode using a 13-elements high purity Ge detector. Three to four scans were collected for each solution, using a fresh sample each time.

The selectivity of the XAS probe for the atomic species allowed gaining a clear understanding of the local structure arrangements of Cu(I) at different concentrations. Both XANES (X-ray Absorptions Near Edge Structure) and EXAFS (Extended X-ray Absorption Fine Structure) have provided relevant information. A comparison of the normalized XANES curves displays a different shape of spectra at lowest concentration respect to the highest. In addition, an increase of the 1s-4p electronic transition upon dilution (a clear fingerprint feature of the Cu(I) coordination [3]) suggests a decrease of the local coordination number of Cu(I), which is four in the solid [4] and at higher concentration. The comparison of the experimental Fourier Transform curves of the corresponding EXAFS signals shows a dramatic decrease of the first peak upon dilution, a fact that can be explained by the loss of a phosphine ligand. This has further corroborated by the EXAFS fitting analysis.

Summarizing, XANES-EXAFS analyses suggest a decrease of the Cu-P coordination number coupled with a higher structural disorder in lower concentrated solutions of the $[\text{Cu}(\text{DAPTA})_4]^+$ complex in aqueous solution.

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