

Electronic Structure of Drugs in Water Solution Studied Using RIXS

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Beamline(s): X1B

Introduction: So far the electronic structure and dynamics in biological systems has been little investigated. Synchrotron based X-ray diffraction is used to determine the *molecular geometry* that in many cases can determine the biological function of the molecule. The electronic structure determines the properties of matter, and it is therefore natural to anticipate that a description of the *electronic structure* of biological systems will lead to a progress in molecular biology.

When studying biological systems it is necessary to be able to perform the experiments in their natural environment i.e. in water/liquid. Among the different spectroscopic tools which could be used, resonant inelastic soft X-ray scattering (RIXS) has several advantageous properties: First, it is a photon-in photon-out experiment; The large photon penetration depth makes it a bulk sensitive method which makes it possible to study the electronic structure of liquids and molecules in solution. Second, it probes the electronic structure at specific atomic sites, which is useful when studying macromolecules. And third, the dipole selection rules, governing the soft X-ray transitions, gives information about the symmetry of the bonds.

Methods and Materials: The experiment on liquid samples was carried out at beam line X1B. The X-ray emission spectra were recorded using a high-resolution grazing-incidence X-ray fluorescence spectrometer [1] with a resolution better than 0.6 eV. To be able to run the liquid samples under high vacuum conditions a liquid cell was constructed with a thin window (1000Å Si_3N_4) with an estimated transmission of 60% for the incident and emitted radiation.

Results: A series of β -adrenoreceptors were studied in solid phase (crystal) and in water solution. The O K absorption and emission (figure 1) reflects the electronic structure around oxygen atoms. When the incoming beam energy is above ~ 534 eV we excite the water molecules and the emission spectra mimics the pure water spectrum [2]. When the excitation energy is 532 eV we are below the water threshold and the emission spectra reflects the local electronic structure at the oxygen sites of the atenolol molecule. The comparison with the solid phase spectra highlights changes of electronic structure upon solvation. These changes are related to how the surrounding water molecules form hydrogen bonds with the oxygen atoms in the drug molecule.

Conclusions: This experiment shows that it is possible to study solvation with the RIXS technique. We are presently working with the theoretical analysis of the spectra. The study will be augmented with investigation of the molecules in gas phase and also try to resolve the different oxygen sites in the molecule.

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References: [1] J. Nordgren and R. Nyholm, *Nucl. Instr. Methods A* **246**, 242, 1986; J. Nordgren, G. Bray, S. Cramm, R. Nyholm, J.-E. Rubensson, and N. Wassdahl, *Rev. Sci. Instrum.* **60**, 1690, 1989. [2] J.-H. Guo, et al, to be published.

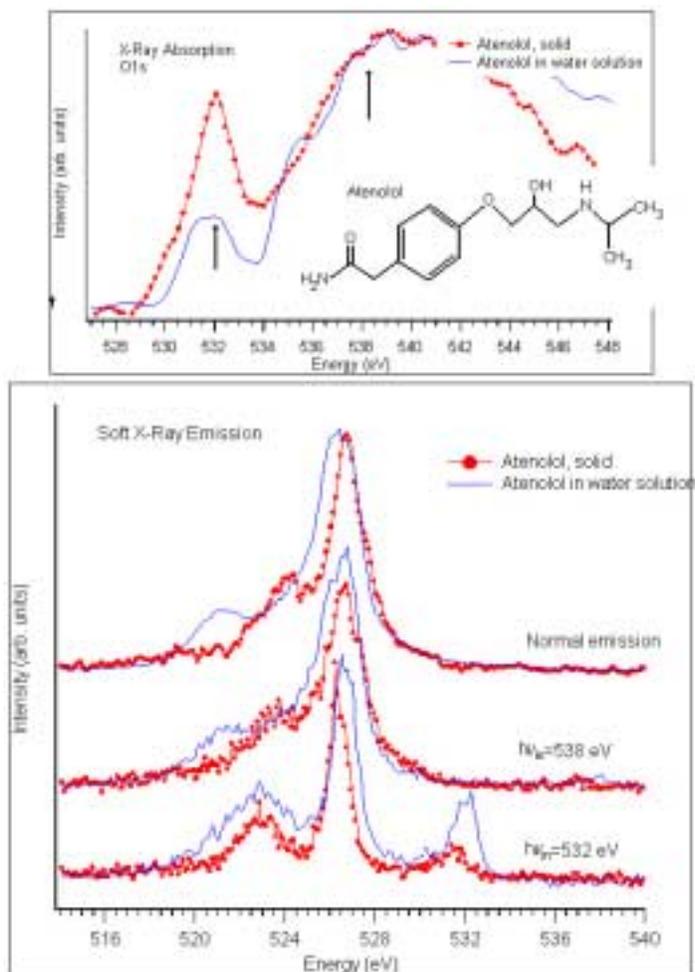


Figure 1 X-ray absorption and RIXS spectra of the β -adrenoreceptor atenolol in solid form and as a solute in water.