XANES/EXAFS Study of Sulfur Ligand-Binding with Copper Metal Complexes for Mechanisms Relevant to β-amyloid Oxidation and Alzheimer's Disease

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Recently, some reports have provided sufficient evidence that toxic metal ions (e.g. Cu(II)) are critically involved in the etiopathogenesis of Alzheimer's disease (AD) as well as in other neurodegenerative diseases. The deposition of β-amyloid peptide (βAP) into senile plaque is an important factor in the pathogenesis of AD. A hallmark ofβAP is its pronounced tendency to aggregate, ultimately forming fibrils in which βAP adopts a β-sheet conformation. BAP aggregation has been considered the key parameter by which βAP formation influences the progression of AD. However, increasing experimental evidence is mounting that aggregation may not be the only mechanism of βAP action but that oxidative stress associated with metal-catalyzed transformations of βAP represents an important pathway of the pathology.

The valency and fine structure of S species bound with Cu atom catalyzed transformations of βAP for AD have not been well studied. By EXAFS/XANES spectroscopies, the valency and fine structure of these toxic heavy metals in the catalytic transformations of βAP for AD has been widely investigated. Thus, the main objective of the present work was to investigate the fine structures and oxidation states of S species bound with Cu atoms accumulated in the catalytic transformations of βAP for AD by EXAFS and XANES spectroscopies. The binding sites of Cu(II) metal ions with S ligands and that the mechanism through which metal ions participate in fibrillization events were also studied.

The EXAFS/XANES spectra were collected at the TXR BL16A1 at the NSRRC of Taiwan. An electron storage ring was operated with an energy of 1.5 GeV and a current of 100-150 mA. A Si(111) DCM was used for providing highly monochromatized photon beams with energies of 0.9 to 9 keV and resolving power (E/ΔE) of up to 7000. Data were collected in fluorescence or transmission mode with a Lytle ionization detector for S (2472 eV) K edge experiments at room temperature. The EXAFS data will be analyzed by using the UWXAFS 3.0 program and FEFF 8.0 codes.

The surface of βAP might consist of biopolymer such as polysaccharides, proteins, and lipids, which act as a basic binding site of copper ions. The functional groups within the wall of βAP provided the sulfate (SO_4^{2-}), thiol (mercaptan) or sulfhydryl (mercapto, R-SH) groups that can bind copper ions. Especially, thiol or sulfate functional groups are stronger sites bound with copper ions and may form Cu-SH or $CuSO_4$ complex. The binding sites of Cu(II) metal ions with S ligands and that the mechanism through which metal ions participate in fibrillization events may be evaluated by EXAFS spectroscopy. The Cu and S EXAFS spectra indicating the Cu-S species with bond distances of 1.99 Å and 2.04 Å, respectively were found in Figure 1. Coordination numbers (CN) of the Cu-S species from Cu and S EXAFS spectra were 2.2 and 2.4, respectively. The uptake of copper ions can take place by entrapment in the βAP structure and subsequent sorption onto the binding sites present in the structure in the catalytic transformations of βAP for AD. However, by using the XANES and EXAFS spectra, highly significant correlation occurred between the individual heavy metal on its available percentage in the catalytic transformations of βAP for AD may be further determined and studied.

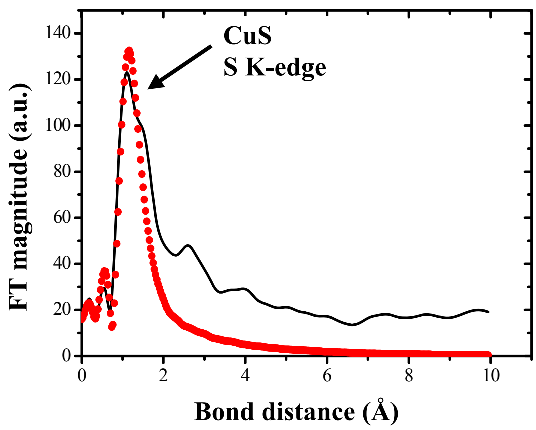

Figure 1. Fourier transform of CuS for sulfur K edges EXAFS that the S species bound with Cu atom catalyzed transformations of βAP for AD. The best fitting of the EXAFS spectra are expressed by the circle lines.