Supplementary Material (ESI) for Chemical Communications

Supplementary information

Substrate Mediated Reduction of Copper-Amyloid-β Complex of Alzheimer's Disease

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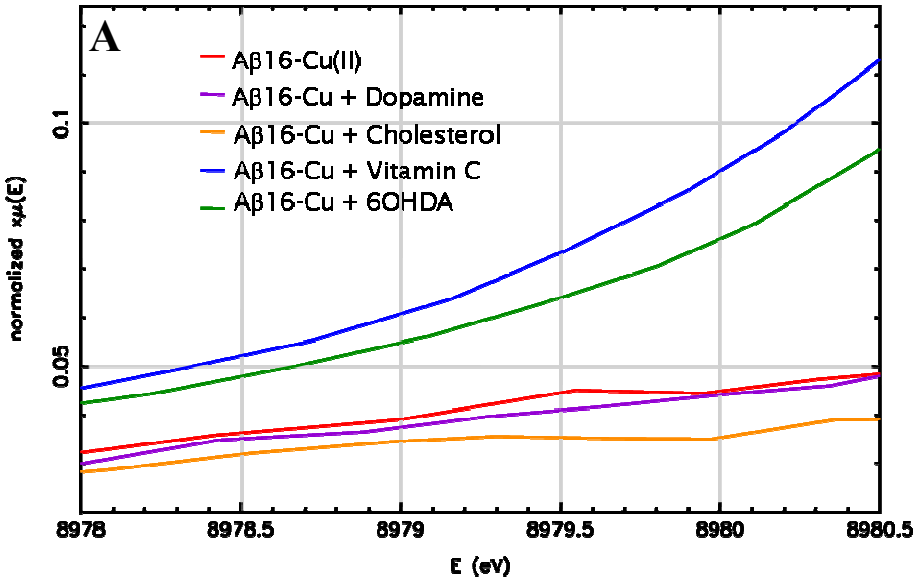
Sample preparation- The Aβ(1-16) peptide was obtained from Auspep Pty Ltd. The Aβ-Cu^{2+} complex samples were freshly prepared before the data collections. Known quantities of Aβ(1−16) peptides were dissolved in common isotonic phosphate saline (PBS). Freshly prepared solution of $CuCl_2$ was added to peptide solutions to the concentration ratio 1:1 of metal to peptide. Prepared Aβ(1-16)-Cu^{2+} complexes were mixed them with 10-fold molar ratio of substrates dissolved in water except cholesterol which was dissolved in chloroform and added with 5-fold molar ratio. The Aβ/Cu concentration was 1.1mM in the reference oxidized Aβ-Cu^{2+} sample and about 2.2.mM in all other samples with substrates. Finally, 17% of glycerol was added to the sample solution as a cryoprotectant. Glycerol is an accepted cryoprotectant in protein crystallography, EPR and XAS spectroscopy. Immediately after the preparation the samples were injected into 230 µL Teflon cells made with two Kapton windows (approx. 4 x 25 mm), rapidly frozen in liquid nitrogen.

X-ray absorption data collection- A series of Cu *K*-edge (8980.4 eV) X-ray absorption spectrum scans were obtained from the sample in a fluorescence mode at low T using a helium displex cryostat. The experiments were conducted at the Pacific Northwest Consortium Collaborative Access Team (PNC-CAT) 20BM bending magnet beamline at the Advanced Photon Source (APS) of Argonne National Laboratories, USA. The beamline optical setup was equipped with a double crystal Si(111) monochromator and a 5 milliradian rhodium coated harmonic-rejection mirror. To increase sensitivity with millimolar concentration solutions a 12-element liquid-N2-cooled Ge detector was used. The beam size was (ver x horiz) 1 x 15 mm. The incident X-ray intensity was monitored using an ionization chamber. The stability of the monochromator energy was checked for all spectra by simultaneously accumulating by transmittance a Cu foil spectrum. The energy was calibrated with reference to the lowest energy inflection point of a Cu foil spectrum which was assumed to be 8980.4 eV. The enlarged XANES regions of 8078-8980 eV (**A**), 8980-8986 eV (**B**), and 8995-9055 eV (**C**) of normalized absorption amplitude *vs* energy E are shown in Figure SI below.



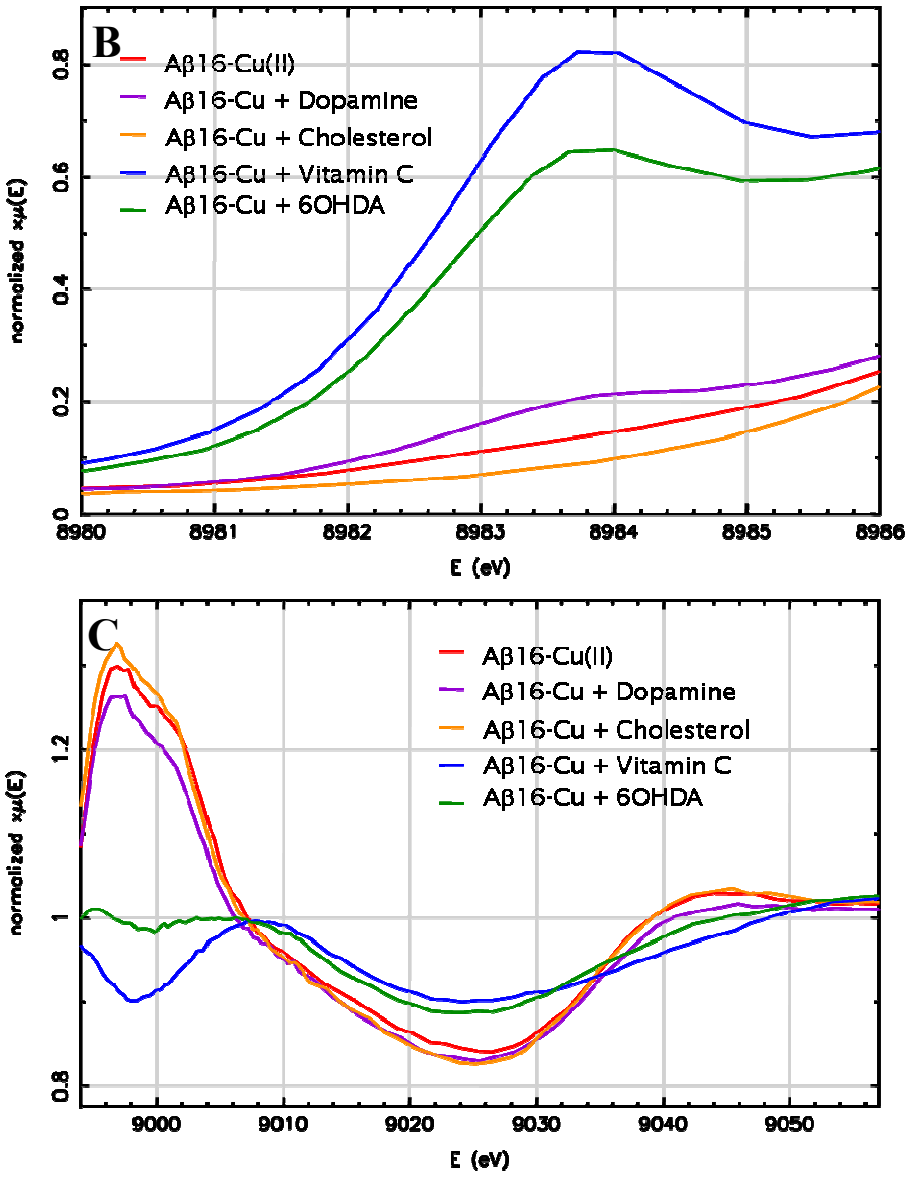


Figure SI. The XANES regions (8078-8980 eV (**A**), 8980-8986 eV (**B**) and 8995-9055 eV (**C**)) of normalized absorption amplitude *vs* energy E for oxidized (Aβ(1–16)–Cu^{2+} - red, with dopamine - purple and with cholesterol - orange) and reduced (Aβ(1–16)–Cu^{1+} with vitamin C - blue and with 6-hydroxyldopamine (6-OHDA) - green) complexes.