

Small Peptide Oxidation and Metal Ion Complexation

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Oxidative stress has been shown to have a hand in the development of Alzheimer's and other neurodegenerative diseases. Oxidative stress is typically caused by mitochondrial malfunctions, which most commonly change tyrosine amino acid residues into dopa amino acid residues through the production of superoxide radicals. Metal ions interact with dopa residues exceptionally well through chelation. To assess the binding characteristics of metal ions to small peptides, factors were stripped from the system of the brain down to bare bones, that is, only the operating parties were involved: the metal ion in question and a representative six amino acid peptide, suspended in water. The peptides were specifically six amino acids long to induce a (beta)-hairpin loop; six is the smallest number of amino acids required to form a hairpin. First, peptides were synthesized using single amino acid additions, forming the chain (L)dopa-Valine-(D)Proline-Glycine-Ornithine-(Variable). The variable position was either tyrosine, tryptophan, histidine, glycine, 1-naphthyl-D-alanine, or 2-naphthyl-D-alanine to give proper representation to different types of interpeptide interactions.

After these peptides were synthesized, they were purified using HPLC and characterized using MALDI mass spectrometry. Metal ions were added to the peptide to allow for complexation and mass spectrometry was reanalyzed. Molecular weights evidenced complexation with both one copper ion to one peptide and two copper ions with one peptide. Beyond conformation through molar mass, NMR was used to characterize and assign the heteroatoms of the peptides to confirm the complete formation of the target peptide. Ultra-violet/visible light (UV-vis) spectroscopy was also used to assess binding of metal ions to the synthetic peptides. Peptides were titrated into metal ion solutions, providing raw spectral data. These data were then reconstructed using the Calvin developed program called Sivvu, in which raw data is reconstructed to assess statistical fits and residuals within the data sets. These assessments provided the best fitting model for the system in question, in which metal ion, raw peptide, one metal ion complexed with one peptide, two metal ions complexed with one peptide, and one metal ion complexed with two peptides are present.

This research has provided me with unique opportunities to work with varying techniques, such as NMR and mass spectroscopy, to assess the validity of heteroatom synthetic products. It has allowed me to explore chemical systems that function in a higher order biological system that causes a devastating range of neurodegenerative diseases.