Coordination abilities of α-synuclein fragments modified in the 30th (A30P) and 53rd (A53T) positions and products of metal-catalyzed oxidation.

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Streszczenie

A potentiometric and spectroscopic (UV-Vis, CD and EPR) study of Cu(II) binding to the M^{26}-D^{27}-56 (A30P, A53T) and Ac-M^{26}-D^{27}-56 (A30P, A53T) fragments of α-synuclein was carried out. Mutations in the 30th (A30P) and 53rd (A53T) positions in these fragments do not change the binding mode of copper(II) ions but the stabilities of the 3N and 4N complexes formed for M^{26}-D^{27}-56 are lower compared to those of the M^{29}-D^{30}-56 peptide. At physiological pH 7.4 the 3N {NH_2, N^-, β-COO^-, N_{Im}} coordination mode dominates. The Ac-M^{26}-D^{27}-56 (A30P, A53T) fragment displays higher tendencies to aggregation than that of Ac-M^{29}-D^{30}-56. The high performance liquid chromatography (HPLC) and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) methods and Cu(II)–hydrogen peroxide as a model oxidizing system to elucidate the products of copper(II)-catalyzed oxidation of the M^{26}-D^{27}-56 (A30P, A53T) fragment of α-synuclein were employed. A peptide solution (0.50 mM) was incubated at 37 °C for 24 h with a metal–peptide–hydrogen peroxide 1 : 1 : 4 molar ratio in a phosphate buffer, pH 7.4. Reaction of hydrogen peroxide with this fragment led to the oxidation of methionine to methionine sulfoxide. For the Cu(II)–peptide–hydrogen peroxide 1 : 1 : 4 molar ratio system oxidation of the histidine residue to 2-oxohistidine, asparagine and 5-hydroxy-2-oxohistidine was observed. Under experimental conditions the M^{26}-D^{27}-56 (A30P, A53T) fragment undergoes the fragmentations by cleavage of the V^{49}–H^{50}, H^{50}–G^{51}, G^{31}–K^{32}, T^{33}–K^{34} and K^{43}–T^{44} peptide bonds supporting the participation of the His and Lys residues in the coordination of copper(II) ions.