

Copper(II) complexes of neuropeptide gamma mutant (H4A) products of metal-catalyzed oxidation.

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Streszczenie

The point mutation in the sequence of neuropeptide gamma (H4A, H4ANPG, Asp¹-Ala-Gly-Ala⁴-Gly-Gln-Ile-Ser-His⁹-Lys-Arg-His¹²-Lys-Thr-Asp-Ser-Phe-Val-Gly-Leu-Met²¹-NH₂) was introduced to observe the influence of histidine H⁴ residue on the acid–base properties of the peptide and coordination abilities to copper(II) ions. The potentiometric studies of neuropeptide gamma were only performed in pH 2.5–7.4 pH range. At higher pH than 7.4 additional deprotonations of the neuropeptide gamma were observed. The potentiometric measurements for both peptides (H4ANPG and Ac-H4ANPG, Ac-Asp¹-Ala-Gly-Ala⁴-Gly-Gln-Ile-Ser-His⁹-Lys-Arg-His¹²-Lys-Thr-Asp-Ser-Phe-Val-Gly-Leu-Met²¹-NH₂) without copper(II) ions were performed in whole 2.5–10.5 pH range. It means that H⁴ residue in neuropeptide gamma has influence on its acid–base properties and it's most likely that this residue takes place in hydrogen bond formation. The acetylation of the N-terminal amino group changes the acid–base properties of the H4ANPG. The potentiometric study for the Ac-H4ANPG peptide suggests in the 5.7–7 pH range four additional deprotonations. It may support the tend to amyloid-like fibril formation by tachykinin neuropeptides and as it is suggested the presence of the hydrogen bonds (labile protons) in tiny fibrils. The potentiometric, spectroscopic (UV–Vis, CD and EPR) and mass spectrometric (ESI-MS) results for the Cu(II)–H4ANPG system clearly indicate the stabilization of the 2N {NH₂,β-COO[−]–Asp¹,N_{im}–H⁹,OH–S⁸} complex by the coordination of the amine and β-carboxylate groups of the D¹ residue and most likely by the OH and imidazole nitrogen of the Ser⁸ and His⁹ residues, respectively. The additional deprotonations of the Ac-H4ANPG do not have any influence on its coordination abilities in comparison to those containing two histidine residues in the peptide chain. To elucidate the products of the copper(II)-catalyzed oxidation of the H4ANPG and Ac-H4ANPG, the liquid

chromatography–mass spectrometry (LC–MS) method and Cu(II)/hydrogen peroxide as a model oxidizing system were employed. For both peptides in the Cu(II)–peptide–hydrogen peroxide in 1:1:4 M ratio systems, oxidation of two histidine (H^9, H^{12}) residues to 2-oxohistidines was observed. Under experimental conditions the metal-catalyzed oxidation both peptides undergo fragmentations by cleavage of the S^8-H^9 , H^9-K^{10} , $H^{12}-K^{13}$ peptide bonds supporting the participation of the H^9 and H^{12} residues in the coordination of copper(II) ions.

Słowa kluczowe

Neuropeptide gamma mutant, Copper(II) complexes, Stability constants, Copper(II)-catalyzed oxidation, Acid–base properties

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