

Copper(II) complexes of the *Neb*-colloostatin analogues containing histidine residue structure stability biological activity.

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Streszczenie

Neb-colloostatin was discovered during the isolation of Neb-TMOF from the ovary of the grey fleshfly *Neobellieria bullata*. Its amino acid sequence was determined as SIVP4LGLP8VP10IGP13IVVGP18R. The analogues with point mutation P4H and P8H were synthesized and their copper(II) complexes were studied by potentiometry, UV-Vis, circular dichroism (CD), and electron paramagnetic resonance (EPR) spectroscopic and mass spectrometry (MS) methods. To obtain a complete complex speciation 1:1 and 2:1 metal-to-ligand molar ratios for both peptides were studied. At physiological pH (7.4), both peptides form mononuclear the CuH-1L complex with 3N{NH₂,N,NIm} coordination mode. For the P4H and P8H peptides at high pH (11) the binding sites of copper(II) ions are quite different. For the CuH-4L complex of the P4H peptide the 4N{4N} coordination mode is dominant, while for the P8H peptide the 4N{NIm,3N} binding site towards N-termini is formed with (6,5,5) chelate ring. At high pH the P8H peptide cannot form the 4N{NH₂,3N} complex because of the presence of the Pro⁴ residue in the amino acid sequence (a break point in the metal coordination). At pH 7.4 dinuclear the Cu₂H-4L complexes dominate with suggested the 3N{NH₂,2N}3N{NIm,2N} binding sites where the 3N{NIm,2N} coordination mode for the P4H peptide towards C-termini, and for P8H peptide towards N-termini are formed. The induction of apoptosis in vivo in *Tenebrio molitor* cells by the ligands and their copper(II) complexes at pH 7.4 was studied. The systems studied have lower apoptotic properties compared to those of Neb-colloostatin and its copper(II) complex at pH 7.

Słowa kluczowe

copper(II) complexes, Neb -colloostatin analogues, Stability, structure, biological activity

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