Copper(II) complexes of terminally free alloferon peptide mutants containing two different histidyl (H^1 and H^6 or H^9 or H^{12}) binding sites structure stability and biological activity.

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Streszczenie

Mono- and dinuclear copper(II) complexes of the alloferon 1 with point mutations H9A/H12A H^1GVSGH^6GQA^{9}GVA^{12}G, H6A/H12A H^1GVSGA^{6}GQH^9GVA^{12}G and H6A/H9A H^1GVSGA^{6}GQA^{9}GVH^{12}G have been studied by potentiometric, UV-visible, CD, EPR spectroscopic, and mass spectrometry (MS) methods. Complete complex speciation at metal-to-ligand molar ratios 1:1 and 2:1 was obtained. For all systems studied in the 5 – 6.5 pH range, the CuL complex dominates with 3 N{NH_2,N_{Im}-H^1,N_{Im}-$H^{6\ or\ 9\ or\ 12}$} binding site. The stability of the CuL complexes for the ligands studied varies according to the H9A/H12A > H6A/H12A > H6A/H9A series. For the dinuclear systems the amine/imidazole nitrogen donor atoms of the histidine residue H^1 and the imidazole nitrogen atoms of H^6 or H^9 or H^{12} can be considered as independent metal-binding sites in the species formed. The stability of the dinuclear complexes is higher when two coordinated copper(II) ions are closer to each other.

The inductions of phenoloxidase activity and apoptosis *in vivo* in *Tenebrio molitor* cells by the ligands and their copper(II) complexes at pH 7.4 have been studied. The H6A/H9A, H6A/H12A peptides displayed lower hemocytotoxic activity compared to that of alloferon 1, while the H9A/H12A analogue was not active. Among the copper(II) complexes, the most active was the Cu(II)-H9A/H12A complex formed at pH 7.4 with 3 N{NH_2,N_{Im}-H^1,N_{Im}-H^6} (CuL) and 3 N{NH_2,N^-,N_{Im}-H^6} and/or 4 N{NH_2,N_{Im}-H^1,N^-,N_{Im}-H^6} (CuH_{-1} L) binding sites. The Cu(II)-H6A/H9A and Cu(II)-H6A/H12A complexes were not active.

Słowa kluczowe

copper(II) complexes, Alloferon analogues, Stability, structure, biological activity