Copper binding by the cystatin C fragment. The role of histidine residues.

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Streszczenie

Human cystatin C (hCC) is one of the amyloidogenic molecules involved in neurodegeneration processes. Fragment 85–94, with the FHDQPHLKRK sequence, is interesting from the point of view of coordination as histidine and aspartic acid residues are potential copper(II) ion donors. Our previous studies showed that two potential binding sites are possible within this peptide chain. Therefore, the coordination abilities of each of these two metal ion binding sites have been checked. We have analysed two analogues of the native peptide, where particular histidine residues were substituted with alanine – an amino acid without a coordinating side chain: **Ac-H2A** (with alanine in position 2) and **Ac-H6A** (with alanine in position 6). NMR, potentiometric titration, UV–Vis, CD, EPR and MS studies were carried out. Obtained results showed that both ligands finally form the 4 N copper(II) complexes in a basic range of pH. However, their coordination properties are slightly different. The copper(II) binding efficiency is also different in both cases. Up to pH 6–6.5, AcH2A is more effective, but the situation is quite reversed under more basic conditions. Considering the results obtained, it can be concluded that in the unmodified peptide, the N-terminal binding site seems to be more favourable than the C-terminal.

Słowa kluczowe

Peptide, Copper(II), Bioinorganic complex, Binding site, Histidine

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