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The role of side chains in the fine tuning of metal binding ability of peptides

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Peptides have high metal binding affinity, but both the thermodynamic stability and the coordination geometry of peptide complexes are very much influenced by the amino acid sequence of the ligands. One field of our present research work is the synthesis and investigation of polypeptides containing various side chain donor groups, in which the coordination of side chain donor atoms comes to the front and their sequences serve as the models of different metalloproteins. The histidine imidazole nitrogens are frequent side chain donor groups in these metallopoteins and imidazole nitrogen is one ot the most important binding sites of transition metal ions. Such metal ion – protein interaction plays role for example in the function of Cu,Zn superoxide-dismutase enzyme or neurodegenerative diseases.

We synthesized such series of multihistidine peptides in which the systematic change of the amino acid sequence is carried out and the equilibrium, structural and electrochemical parameters of their complexes are determined. These molecules include oligopeptides built up from 4 to 12 amino acid residues containing histidines in different positions and amino acid environments. To understand the specific effects of these side chains lysine, aspartic acid or phenylalanine were systematically inserted into the sequence of the multihistidine peptides: Ac-HDAH-NH_2, Ac-HADH-NH_2, Ac-HXHZH-NH_2 (X, Z = Ala, Phe, Asp, Lys) and Ac-HXHAHXH-NH_2 (X = Asp or Phe). We performed the equilibrium, structural and electrochemical studies of copper(II), nickel(II) and zinc(II) complexes of these multihistidine peptides. The stoichiometry, stability and structure of complexes were studied using pH-potentiometric, UV-vis, CD spectroscopy and ESI-MS techniques. The electrochemical parameters of copper(II) complexes were determined on the basis of CV measurements and these data were completed by SOD activity measurements in some cases.

The results clearly show that the stability of the metal complexes significantly depend on the metal ion and the number and position of histidines in the peptide. The metal binding ability of the peptide is, however, affected by the amino acids which are present in the neighbourhood of the histidine amino acids, also. These conclusions strongly suggest that the thermodynamic and structural properties of the peptide complexes could be finely tuned by the change of quality and sequence of amino acids around the side chain donor atoms of coordinating the metal ions. This means, that the systematic planning of the sequence of peptides could increase the metal binding selectivity of peptides as well.

References

[1] G. Csire, S. Timári, J. Asztalos, J.M. Király, M. Kiss, K. Várnagy, *J. Inorg. Biochem.*, **177,** 198-210 (2017)

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