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Determination of the role of specific amino acids in the binding of Zn(II), Ni(II), and Cu(II) to the active site of the M10 family metallopeptidase

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Streszczenie

Metallopeptidases are a group of metal-dependent enzymes that hydrolyze peptide bonds. These enzymes found in *Streptococcus pneumoniae* assist the pathogen in infecting the host by breaking down host tissues and extracellular matrix proteins. Considering metallopeptidases' significant role in bacterial virulence, inhibiting this enzyme represents a promising avenue for research. These enzymes are characterized by the presence of Zn(II) in the active site, proper coordination of which is essential for their catalytic function. This work aims to determine the significance of the specific amino acids in the metal binding domain of metallopeptidase from *S. pneumoniae*. For this purpose, we investigated the coordination chemistry of Zn(II), Ni(II), and Cu(II) ions with point-mutated peptide models of the metal-binding domain. Mutations were introduced at His-2 (L1) and Glu-1. Studies have shown that at pH 7.14 (pH of infected lungs by *S. pneumoniae*), point mutation on glutamic acid caused only minor effects on the binding of Zn(II) and Ni(II), while significantly improving Cu(II) binding. The stability of copper complexes is greater with the mutant Glu-1 → Gln-1 than with the original domain due to a hydrogen bonding network created by the Gln backbone with its side chain. Substituting histidine resulted in a significant reduction in metal binding for all metal ions, highlighting the crucial role of His-2 in metal coordination. Introduced mutations at neutral pH did not significantly affect the secondary structure of metal complexes. However, at alkaline pH, the peptides showed a higher percentage of antiparallel β-sheet structures upon the addition of Cu(II), Ni(II) and Zn(II).

Słowa kluczowe

Metallopeptidases, Transition metal ions, Coordination chemistry, Metal binding domain, Point mutations study, Thermodynamic properties, Metal-peptide complexes

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