Modulating Copper(II) Coordination and Antimicrobial Activity: Effects of d-Amino Acid Substitution and *Retro-Inverso* Modification in Human Saliva MUC7 Peptide

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Streszczenie

Fragments of MUC7, a salivary protein involved in nonimmune defense, arise from proteolytic cleavage in saliva and exhibit antimicrobial properties. However, their therapeutic use is limited by low stability due to further degradation. To address this, a native MUC7 fragment was modified using D-amino acids and the retro-inverso strategy. Given the role of metal ions in enhancing antimicrobial peptides, we analyzed the bioinorganic chemistry of these systems with Cu(II) and assessed their antimicrobial activity against fungal and bacterial strains. This study is the first to explore the correlation between metal binding mode, structure, stability, and antimicrobial activity of retro-inverso peptides as well as Cu(II) coordination in such systems. A combination of experimental techniques (potentiometry, mass spectrometry, UV−vis, circular dichroism, electron paramagnetic resonance, and nuclear magnetic resonance spectroscopy) and density functional theory calculations characterized their coordination chemistry. Our results demonstrate that the “standard” enantiomeric exchange and retro-inverso modifications of the MUC7 fragment have a minimal effect on the secondary structure and biological activity of the studied peptides and their Cu(II) complexes. However, these modifications significantly influence on the thermodynamic stability of studied systems.

Słowa kluczowe

Electron paramagnetic resonance spectroscopy, Ions, Ligands, Monomers, Peptides and proteins

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