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Impact of *C*- and *N*-terminal protection on the stability, metal chelation and antimicrobial properties of calcitermin

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Streszczenie

The main limitation to the use of antimicrobial peptides (AMPs) as regular drugs, against antibiotic and antifungal resistance, mainly relates to their rapid degradation by proteolytic enzymes. The introduction of suitable structural changes in the peptide chain can make the peptide less susceptible to the action of proteases, thus overcoming this problem. To improve the plasma stability of calcitermin, a metal-chelating AMP present in the human respiratory tract and investigated in the present study, *C*- and/or *N*- terminal modifications have been introduced in the native sequence. Evaluation of peptide stability has been performed to determine the half-life times in human plasma of both native calcitermin and its derivatives. However, the protection of the peptide termini can also affect its metal coordination behaviour. Thus, the characterization of Zn^{2+} and Cu^{2+} complexes has been performed by means of several techniques, including potentiometry, high-resolution mass spectrometry, UV–Vis, circular dichroism and EPR. On the basis of the obtained results, it was possible to compare the biological activity of the studied systems, taking into account both the metal-binding ability and the peptide stability to search for a link among them. A significant result of this study is that the *N*-terminal protection increases the calcitermin half-life over seven times and the formation of metal complexes confers resistance towards degradation almost doubling its half-life.

Słowa kluczowe

Antimicrobials, Coordination chemistry, Metals, Peptides

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