

Zn-enhanced Asp-rich antimicrobial peptides: N-terminal coordination by Zn(II) and Cu(II), which distinguishes Cu(II) binding to different peptides.

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Rok wydania

2021

Czasopismo

International Journal of
Molecular Sciences

Numer woluminu

22

Strony

6971/1-6971/20

DOI

10.3390/ijms22136971

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

The antimicrobial activity of surfactant-associated anionic peptides (SAAPs), which are isolated from the ovine pulmonary surfactant and are selective against the ovine pathogen *Mannheimia haemolytica*, is strongly enhanced in the presence of Zn(II) ions. Both calorimetry and ITC measurements show that the unique Asp-only peptide SAAP3 (DDDDDDD) and its analogs SAAP2 (GDDDDDD) and SAAP6 (GADDDDD) have a similar micromolar affinity for Zn(II), which binds to the N-terminal amine and Asp carboxylates in a net entropically-driven process. All three peptides also bind Cu(II) with a net entropically-driven process but with higher affinity than they bind Zn(II) and coordination that involves the N-terminal amine and deprotonated amides as the pH increases. The parent SAAP3 binds Cu(II) with the highest affinity; however, as shown with potentiometry and absorption, CD and EPR spectroscopy, Asp residues in the first and/or second positions distinguish Cu(II) binding to SAAP3 and SAAP2 from their binding to SAAP6, decreasing the Cu(II) Lewis acidity and suppressing its square planar amide coordination by two pH units. We also show that these metal ions do not stabilize a membrane disrupting ability nor do they induce the antimicrobial activity of these peptides against a panel of human pathogens.

Słowa kluczowe

metal-antimicrobial peptide interactions, thermodynamics, Zn(II) and Cu(II) bioinorganic chemistry

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Adres publiczny

<http://dx.doi.org/10.3390/ijms22136971>

Strona internetowa wydawcy

<http://www.mdpi.com/journal/metals>