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Abstract

Bioinspired Interactions of Zn (II) and Cu (II) with the Antimicrobial Peptide Holothuroidin: Discovering the Action Mechanism †

Nikolas Tsaggari, Yiannis Sarigiannis and Manos Vlasiou

Department of Life and Health Sciences, University of Nicosia;
tsaggari.n@live.unic.ac.cy (N.T.); sarigiannis.i@unic.ac.cy (Y.S.);
vlasiou.m@unic.ac.cy (M.V.)

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Abstract: The dramatic increase in antimicrobial resistance has led to active research for new treatments. Antimicrobial peptides (AMPs) are small 7 to 100 amino acids [1, 2]. One discovered mode of action of AMPs is membrane disruptive activity, associated with the interaction with membrane phospholipids [3]. Another way of action of AMPs is intracellular targeting. Some AMPs can cross the cell barriers and reach targets in the cytoplasm [2]. For some AMPs, the occurrence of bivalent metal ions (such as Zn2+ and Cu2+) affects their activity or mode of action either because of binding metal ions, so that microbes cannot get enough nutrients essential for their life and virulence [4] or because AMPs need the metal ion as a booster of their antimicrobial activity, affecting the charge or the structure of the peptide [5]. Here, we discuss the action mechanism of Holothuroidin I (HLGHHALDHLLK) [6], a natural derived peptide from Mediterranean Sea cucumber Holothuria tubulosa, of the interactions with important metal ions located in mammals (such as Zn2+ and Cu2+). Zinc (II), is the second most abundant transition metal in living organisms, [7] and present in superoxide dismutases, central enzymes in bacteria and fungi, associated with the detoxification of ROS generated by host cells during host-pathogen interactions [8]. Copper is another essential metal ion, which can switch between oxidized (Cu2+) and reduced (Cu+) states. It is essential for enzymes involved in cellular respiration, iron transport, and superoxide dismutation. Besides, the redox activity of copper may also contribute to its toxicity to microbes (and mammals) through classic copper-catalyzed Fenton chemistry and an increase in reactive oxygen species [9].
The action mechanism evaluation was performed using potentiometric titrations, conductivity studies, UV-Vis studies, voltammetric methods, and density function theory studies, giving valuable inside into the mechanism of interactions of Holothuroidin I with copper and zinc.

References

1. D. Łoboda,a H. Kozłowskib and M. Rowinska-Z˙yrek, 2018, NewJ.Chem., 42, 7560.
2. F. H. Waghu, R. S. Barai, P. Gurung and S. Idicula-Thomas, Nucleic Acids Res., 2016, 44, D1094–D1097.
3. J. D. F. Hale and R. E. W. Hancock, Expert Rev. Anti-Infect. Ther., 2007, 5 (6), 951–959.
4. J. Wa˛tły, S. Potocki and M. Rowinska-Z˙yrek, Chem. – Eur. J., 2016, 22, 15992–16010.
5. A. Som, L. Yang, G. C. L. Wong and G. N. Tew, J. Am. Chem. Soc., 2009, 131 (42), 15102–15103.

6. Domenico Schillaci, Maria Grazia Cusimano, Vincenzo Cunsolo, Rosaria Saletti, Debora Russo, Mirella Vazzana, Maria Vitale and Vincenzo Arizza, AMB Express 2013, 3:35.
7. M. Vasak and D. W. Hasler, Curr. Opin. Chem. Biol., 2000, 4, 177–183.
8. C. S. Hwang, G. Rhie, J. H. Oh, W. K. Huh, H. S. Yim and S. O. Kang, Microbiology, 2002, 148, 3705–3713.
9. J. A. Lemire, J. J. Harrison and R. J. Turner, Nat. Rev. Microbiol., 2013, 11(6), 371–381.