Learning the Science Behind Bacteriocins Through Lacticin 3147; a Promising Lantibiotic

Allison Wan, Cherry Ibarra-Romero, John C. Vederas

Department of Chemistry, University of Alberta, Edmonton Canada

Abstract

- In 2017, antimicrobial resistance was declared a global concern by the WHO.[1]
- It is predicted that in 2050, ten million people around the world will die as a result.[1]
- Antimicrobial resistance is the developed ability of microorganisms to survive against antibacterial solutions.[1]
- Bacteriocins are antimicrobial peptides that are ribosomally synthesized by bacteria which show great promise for use in food preservation as a replacement for antibiotics.[2]
- Lacticin 3147 is a two component (Ltn A1, Ltn A2) lantibiotic, a subclass of bacteriocins, produced by the bacteria *Lactococcus lactis* subsp. DPC 3147.[3]
- Because of its broad activity on a range of Gram-positive bacteria and stability compared to nisin, a broadly used bacteriocin, lacticin 3147 became the focus of many studies.[4]

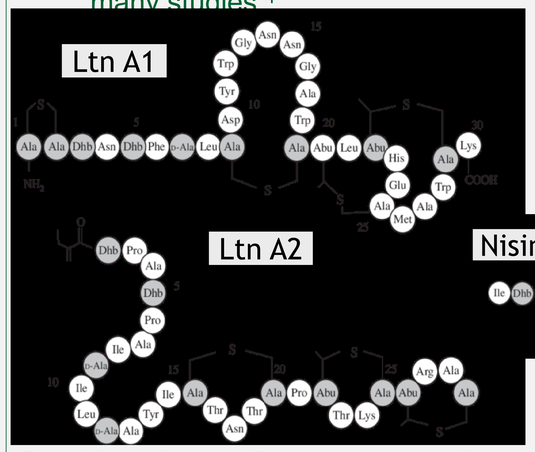
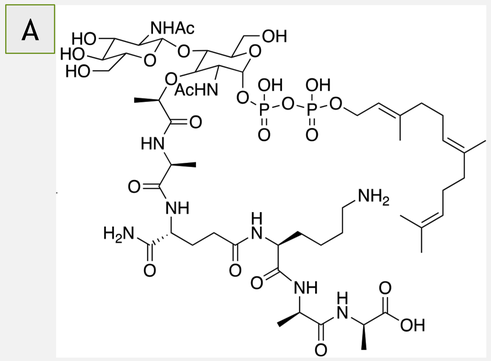


Figure 1, General Structures of Bacteriocins. **A)** Lacticin A1 **B)** Lacticin A2 **C)** Nisin

Lacticin 3147 Mechanism of Action

- Studies suggest Ltn A1 binds to the outer membrane component lipid II and recruits Ltn A2, subsequently lysing the cell.[5]



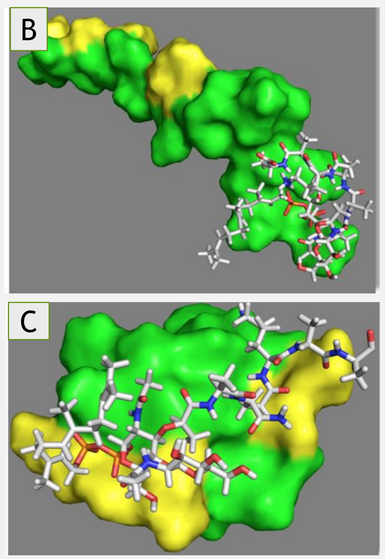


Figure 2, Lipid II and Ltn A1 Interaction. **A)** Chemical Structural of Lipid II **B)** Ltn A1 (3D surface representation) and Lipid II (stick model) Complex **C)** Ltn A1 and Lipid II Complex

Purification General Methods

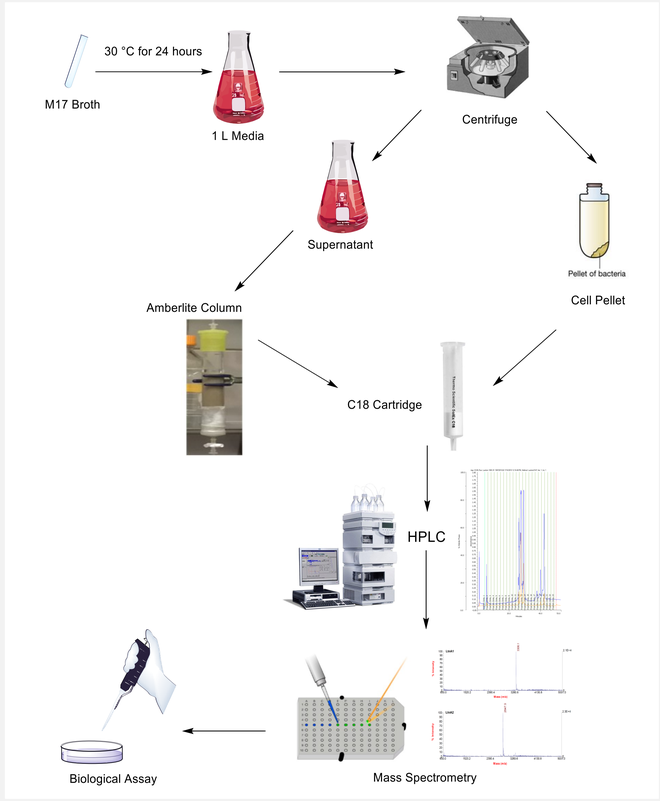


Figure 3, General Lacticin 3147 Guided Purification Process

Conclusion

- Both the A1 and A2 structures found in Lacticin 3147 are active in small concentrations (~μM/mL — nM/mL), and therefore have strong antimicrobial effects
- Further studies being conducted involving isotope labelling of A1 and A2 for deeper mechanism of action studies
- Bacteriocins are a promising field of study to fight against antimicrobial resistance

Results

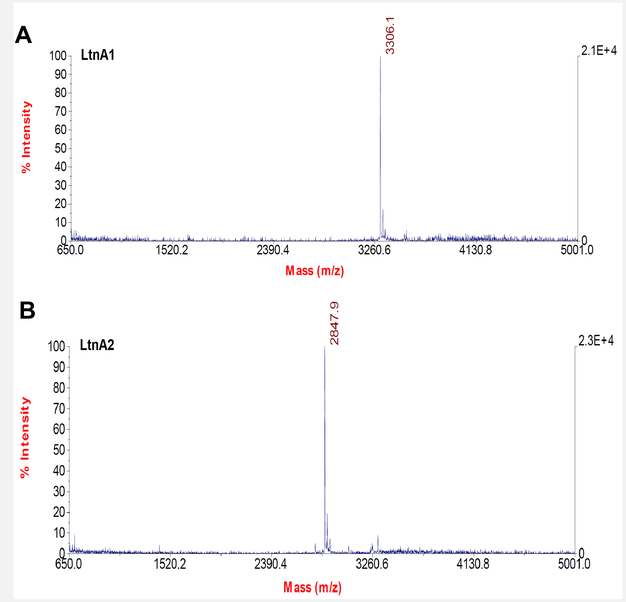


Figure 4, MALDI-TOF spectra. **A)** Ltn A1 **B)** Ltn A2

HPLC chromatogram results suggest that productivity in the cell pellet was greater than the supernatant.

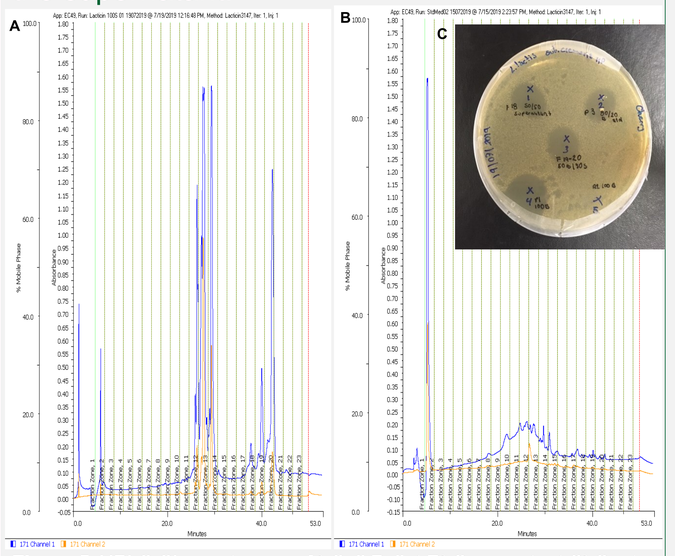


Figure 5, HPLC Chromatogram. **A)** Cell Pellet **B)** Supernatant **C)** Spot on Lawn Assay Against *L. lactis* subsp. cremoris HP

References

(1) https://www.who.int/antimicrobial-resistance/en/

(2) Acedo J. Z.; Chiorean S.; Vederas J. C.; van Belkum M. J. *FEMS Microbiol. Rev.* 2018, 805-811.

(3) Martin, N. I.; Sprules, T.; Carpenter, M. R.; Cotter, P. D.; Hill, C.; Ross, R. P.; Vederas, J. C. *Biochemistry.* 2004, 3049-3056.

(4) Liu, W.; Chan, A. S. H.; Cochrane, S. A.; Vederas, J. C. *J. Am. Chem. Soc.* 2011, 14216-14219.

(5) Bakhtiary, A.; Cochrane, S. A.; Mercier, P.; Mckay, R. T.; Miskolzie, M.; Sit, C. S.; Vederas, J. C. *J. Am. Chem. Soc.* 2017, 17803-17810.

Acknowledgements

I'd like to thank both Ms.Ibarra-Romero for supervising me during the program and Dr.Vederas for allowing me to work in his lab. Finally, I'd like to thank WISEST for providing me with this amazing opportunity.