The importance of cyclic structure on labaditin activity against a gram-positive bacteria

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Antimicrobial resistance has reached alarming levels in many countries, thus leading to a search for new classes of antibiotics, such as antimicrobial peptides whose activity is exerted by interacting specifically with the microorganism membrane. In this study, we investigated the molecular-level mechanism of action for Labaditin (Lo), a 10-amino acid residue cyclic peptide from Jatropha multifida with known bactericidal activity against Streptococcus mutans. Lo showed to be also effective against Staphylococcus aureus (S. aureus) but this does not apply to its linear analogue (L1). Using polarization-modulated infrared reflection absorption spectroscopy (PM-IRRAS), the secondary structure of Lo has shown to be preserved upon interacting with Langmuir monolayers containing a phospholipid mixture mimicking S. aureus membrane, in contrast to L1. This structure preservation is key for the Lo self-assembly forming peptide nanotubes that induce pore formation (unimeric) in large unilamellar vesicles (LUVs), according to permeability assays and dynamic light scattering measurements. Therefore, the comparison between Labaditin (Lo) and its linear analogue L1 allowed us to infer that the bactericidal activity of Lo is more related to its interaction with the membrane. It does not require specific metabolic targets, which makes cyclic peptides promising for antibiotics without bacteria resistance.

Biography
Simone Cristina Barbosa has completed her PhD at University of Sao Paulo/Brazil focusing in antimicrobial peptides. The postdoctoral studies was done at the UBC – Canada, and now a days at the University of Sao Paulo. The present results are related her last research performed in her postdoc in Brazil.

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