Structural characterization and biological activity of Crabrolin and isoforms with different positive charge

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The spreading of bacterial resistance to conventional antibiotics actually in use to combat and defeat the majority of infectious microorganisms, requires the identification and setting up of new compounds able to overcome the resistance. To this purpose, antimicrobial peptides (AMPs) are a possible effective alternative to conventional antibiotics [1].
Typically AMPs have short amino acidic sequence and their mode of action consists in the interaction with bacterial membranes through their positive charge, subsequent folding in amphipathic structures and disruption of the membrane [2].
In this work we analyze a short peptide, Crabrolin, consisting of 13 amino acids (sequence FLPLILRKIVTAL-NH_2), originally found in the venom of European hornet *Vespa crabro* [3], with a net positive charge of +2/+3 at neutral pH, rich in hydrophobic amino acids and two Crabrolin synthetic isoforms whose positive charge was increased (Crabrolin Plus, FLP**K**ILRKIV**R**AL-NH_2) or decreased (Crabrolin Minus, FLPLIL**FW**IVTAL-NH_2) in order to gain further insights on the role of the net positive charge in interacting with bacterial cell membrane.
Peptides were assayed for their ability to inhibit bacterial growth and to bind model bacterial membranes or lipopolysaccharide (LPS). Structural analysis of both peptides by means of CD, NMR and Molecular Dynamics was also performed and correlated to the biological data.
Our results show that although native Crabrolin (WT) displays smaller efficacy than other antibacterial peptides with similar length, Crabrolin Plus exhibits a significant antimicrobial activity while Crabrolin Minus is fully inactive, thus confirming the key role of the positive charges for interacting with the bacterial membrane [4,5].

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