Probing the Effect of Gomesin and Its Linear Analogue on Giant Unilamellar Vesicles Via Optical Microscopy

Domingues, T.M.[1], Braga, L.F.[1], Riske, K.A.[1], Miranda, A.[1]
[1]Departamento de Biofísica, Universidade Federal de São Paulo, São Paulo, Brazil.

The antimicrobial peptide gomesin (*Gm*), isolated from the hemocytes of the tarantula spider *Acanthoscurria gomesiana*, is a potent agent against Gram-positive and Gram-negative bacteria, protozoa and fungi. This peptide, which contains 18 amino acids (pGlu-CRRLCYKQRCVTYCRGR-NH_2) and two disulfide bridges (2/15 and 6/11), adopts a ß-hairpin-like structure, as determined by 2-D nuclear magnetic resonance studies. Gomesin and its linear analogue, [$Ser^{2,6,11,15}$]-*Gm*, were manually synthesized by solid-phase methodology using the *t*-Boc strategy. In order to better understand their mechanisms of action, we performed studies on the interactions of both peptides with large unilamellar vesicles (GUVs) composed of POPC or POPC:POPG by using optical and fluorescence microscopy. On these studies we evaluated: (a) when the POPC:POPG GUVs (1:1 and 4:1 molar ratio) are exposed to 0.3 µM of gomesin or [$Ser^{2,6,11,15}$]-*Gm*, the lytic activity of both peptides was higher than 90% after 15 min; and (b) in the case of POPC GUVs, the observed effect on the lytic activity were around 90% with 3 µM gomesin and with 10 µM of [$Ser^{2,6,11,15}$]-*Gm*. As control, in the absence of peptide, the GUVs were never spontaneously disrupted. This fact leads us to speculate that the gomesin forms a critical structure that disrupts the membrane via carpeting mode. From our results we conclude that both peptides strongly interact with phospholipids vesicles and induce leakage of their content in a surface charge-dependent manner. These results corroborates with previous studies that the first step of the gomesin killing mechanism on bacteria is an electrostatic interaction with the lipid bilayer causing the disruption of the internal membrane.

Palavras Chaves: *gomesin*, *antimicrobial peptide*, *GUV*, *mechanism of action*.
Supported by FAPESP and CNPq.