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The role of disulfide bridges in the 3-D structures of the antimicrobial peptides gomesin and protegrin-1: a molecular dynamics study

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ABSTRACT. Some antimicrobial peptides have a broad spectrum of action against many different kinds of microorganisms. Gomesin and protegrin-1 are examples of such antimicrobial peptides, and they were studied by molecular dynamics in this research. Both have a β-hairpin conformation stabilized by two disulfide bridges and are active against Gram-positive and Gram-negative bacteria, as well as fungi. In this study, the role of the disulfide bridge in the maintenance of the tertiary peptide structure of protegrin-1 and gomesin is analyzed by the structural characteristics of these peptides and two of their respective variants, gomy4 and proty4, in which the four cysteines are replaced by four tyrosine residues. The absence of disulfide bridges in gomy4 and proty4 is compensated by overall reinforcement of the original hydrogen bonds and extra attractive interactions between the aromatic rings of the tyrosine residues. The net effects on the variants with respect to the corresponding natural peptides are: i) maintenance of the original β-hairpin conformation, with great structural similarities between the mutant and the corresponding natural peptide; ii) combination of positive Φ and Ψ Ra-

machandran angles within the hairpin head region with a qualitative change to a combination of positive (Φ) and negative (Ψ) angles, and iii) significant increase in structural flexibility. Experimental facts about the antimicrobial activity of the gomesin and protegrin-1 variants have also been established here, in the hope that the detailed data provided in the present study may be useful for understanding the mechanism of action of these peptides.

Key words: Gomesin; Protegrin-1; Antimicrobial peptides; Cysteine-rich peptides; Molecular simulations

