

Phyllomelittins: novel antimicrobial peptides from the Brazilian treefrog *Phyllomedusa hypochondrialis*

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Capillary chromatography on-line with MS and MS/MS experiments led to the identification of six novel antimicrobial peptides from the legs' skin of the treefrog *Phyllomedusa hypochondrialis*. These peptides were found to be structurally-related among them (56-92% identity), constituted by 12-17 amino acid residues, and showed a C-terminus sequence motif that resemble bee venom and *Rana* genus melittin-related peptides (27-77% identity), hence the named phyllomelittins. Imaging mass spectrometry was used to assess the unique spatial distribution of phyllomelittins in frog skin fragments, since the peptides could only be detected in dorsal region of the hind legs of the frog. In common with other antimicrobial peptides from Phyllomedusinae frogs, (e.g., dermaseptins, phylloseptins), phyllomelitin-1 ([M+H]⁺ = 1509.9 Da) showed micromolar ranges of activities against Gram-negative (*Escherichia coli*), Gram-positive (*Staphylococcus aureus*), and protozoan (*Trypanosoma cruzi*), despite exhibiting at the same time, 14% hemolytic activity at 64 µg/mL. The role of the particular anatomical localization of phyllomelittins and possible exclusive gene expression of this family of peptides in the legs' skin of *P. hypochondrialis* merit further investigation in itself as well as in other *Phyllomedusa* species.

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