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Unraveling the unexplored biochemical complexity of ant venoms

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Venoms are sophisticated chemical weapons employed by ants to subdue prey, defend against predators and pathogens and to communicate. Peptides are major components in most animal venoms; among the ca. 9,000 ant species that sting, most possess peptide-rich venoms. However, ant venoms, particularly peptidic toxins, remain largely unexplored. In light of the enormous chemical, taxonomical and ecological diversity of ants, their venoms represent a promising source of still unknown molecules. We studied the biochemical diversity and complexity of ant venoms from a threefold perspective: chemical vs. specific, chemotaxonomical and ecological. The MALDI-TOF mass spectrometry of whole venoms demonstrated that ant venoms are mostly constituted of small peptides, although larger peptides have been detected in a few subfamilies. Although previous studies showed the occurrence of mainly linear, non-reticulated peptides, an in-depth exploration permitted us to reveal peptides structured by disulfide bonds in most of the species studied, thus highlighting the extensive complexity of the toxins in ant venoms. Mass spectrometry-based venom fingerprinting also successfully demonstrated the potential of venom peptides as chemotaxonomical markers. Venom profiling is an easy-to-use tool for both species identification and the elucidation of cryptic diversity within species complexes. In a case study using species from the genus *Pseudomyrmex* as models, we show that contrasting ecological preferences, such as nesting mode and foraging strategy, act on the evolution of venom composition. Moreover, we were able to isolate a new class of dimeric peptides structured by disulfide bonds with potentially novel properties. Overall, our results demonstrate that ant venoms display a much higher range of structural complexity than previously thought and that such complexity could be useful in answering evolutionary and ecological questions. Ant venoms also emerge as unique sources of original and potentially valuable molecules with a probable broad array of pharmacological targets.