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Review

Wasp venomic: Unravelling the toxins arsenal of *Polybia paulista* venom and its potential pharmaceutical applications

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ABSTRACT

Polybia paulista (Hymenoptera: Vespidae) is a neotropical social wasp from southeast Brazil. As most social Hymenoptera, venom from *P. paulista* comprises a complex mixture of bioactive toxins ranging from low molecular weight compounds to peptides and proteins. Several efforts have been made to elucidate the molecular composition of the *P. paulista* venom. Data derived from proteomic, peptidomic and allergomic analyses has enhanced our understanding of the whole envenoming process caused by the insect sting. The combined use of bioinformatics, *-omics-* and molecular biology tools have allowed the identification, characterization, *in vitro* synthesis and recombinant expression of several wasp venom toxins. Some of these *P. paulista* - derived bioactive compounds have been evaluated for the rational design of antivenoms and the improvement of allergy specific diagnosis and immunotherapy. Molecular characterization of crude venom extract has enabled the description and isolation of novel toxins with potential biotechnological applications. Here, we review the different approaches that have been used to unravel the venom composition of *P. paulista*. We also describe the main groups of *P. paulista* - venom toxins currently identified and analyze their potential in the development of component-resolved diagnosis of allergy, and in the rational design of antivenoms and novel bioactive drugs.

Contents

Abbreviations: PLA1, phospholipase A1; PLA2, phospholipase A2; Poly p 1, phospholipase A1 from *Polybia paulista* venom; Poly p 2, hyaluronidase from *Polybia paulista* venom; Poly p 5, antigen-5 from *Polybia paulista* venom; HPLC, high-performance liquid chromatography; HVA, Hymenoptera venom allergy; SIT, specific immunotherapy; PMNLs, polymorphonuclear leukocytes; CRD, component resolved diagnosis.

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1. Introduction

Sting accidents caused by social Hymenoptera represent one of the three major causes of anaphylaxis among human population worldwide [1]. Venoms from these insects are mixtures of unique natural weapons evolved to ensure the defense of the colony against predators and prey capture [2]. Venom toxin cocktails include low molecular weight compounds – terpenes, biogenic amines –, highly abundant peptides, and allergenic proteins – phospholipases A1, A2, hyaluronidases, acid phosphatase and antigen 5 – [3]. Low molecular weight compounds, and peptides are often involved in toxic reactions causing pain, inflammation, tachycardia/bradycardia and cardiac arrhythmia [4]. Meanwhile, allergenic proteins are related to local and/or systemic allergic reactions including life-threatening anaphylaxis related to the occurrence of HVA.

More than 20,000 species of bees (Apoidea) and ants (Formicidae) along with 15,000 species of wasps and yellow jackets (Vespoidea) have been identified as clinically relevant [5]. To date, systemic analyses based on the use of biomolecule databases, bioinformatic tools and *-omics-* approaches including genomic, transcriptomic, proteomic, peptidomic and glycomics have been successfully used to unravel the toxins arsenal from these venomous animals [6,7]. Venomic analyses of bioactive molecules from social Hymenoptera have enabled the rational design of novel antitoxins [8], and the evaluation of venom components for potential biotechnological applications. Furthermore, detection and molecular characterization of allergenic proteins from Hymenoptera venoms have enabled the production of recombinant allergens then allowing the development of component resolved diagnosis (CRD) and molecular-defined immunotherapy (IT) of HVA [9]. Unlike traditional methods based on the use of crude venom extracts that showed an extremely variable composition [10], these novel alternatives for allergy diagnosis and SIT use defined panels of standardized and highly purified allergens with characterized physiochemical and immunologic profiles. Consequently, the use of recombinant allergens as the allergenic materials significantly improves the reliability of the diagnosis and the safety profile of the immunotherapy [3,7].

Brazil hosts nearly 320 species of social wasps which represent 57% and 33% of the species currently described in Latin America (552) and worldwide (974), respectively [11]. The close coexistence between social wasps and the human populations (Fig. 1) causes a high number of medically important stinging accidents, due to the highly aggressive behavior of these insects [12]. The victims may experience local toxic and/or immunological life-threatening reactions, depending on the number of wasps involved in the accident, the amount of venom

Fig. 1. Distribution of *P. paulista* wasp in South America.