Ant venoms

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Purpose of review

The review summarizes knowledge about ants that are known to sting humans and their venoms.

Recent findings

Fire ants and Chinese needle ants are showing additional spread of range. Fire ants are now important in much of Asia. Venom allergens have been characterized and studied for fire ants and jack jumper ants. The first studies of *Pachycondyla* venoms have been reported, and a major allergen is Pac c 3, related to Sol i 3 from fire ants. There are very limited data available for other ant groups.

Summary

Ants share some common proteins in venoms, but each group appears to have a number of possibly unique components. Further proteomic studies should expand and clarify our knowledge of these fascinating animals.

Keywords

ant, fire ant, jack jumper ant, phospholipase, sting, venom

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Introduction

Ants are among the most biodiverse organisms on earth. Currently there are 22 recognized subfamilies, 299 genera and about 14 095 described species [1]. In some tropical areas in South America and Africa ants and termites make up a third of the total biomass. Some of the more common ants in temperate regions belong to the subfamily Formicinae. These include carpenter ants, sugar ants, red ants and many other species common in inhabited areas. These ants cannot sting but spray a venom comprising primarily formic acid, which burns and irritates. Although many other species can sting humans, few do with regularity. Only a handful of species are known to cause allergic reactions to venom, and only members of three genera cause allergic reactions commonly enough to be important medical problems. The subfamilies of ants and the placement of the genera discussed in this review are listed in Table 1.

Stinging ants

Most ants are not aggressive and rarely sting large organisms. The most medically important aggressive ants are fire ants of the genus *Solenopsis* [2]. The most important species are *S. invicta*, *S. richteri*, *S. geminata* and *S. saevissima*, but reactions are occasionally seen to stings from *S. xyloni* and *S. aurea* [3].

Another group of aggressive ants are the ponerine ants of the genus *Pachycondyla*, including *P. chinensis* in the far east [4] and *P. sennaarensis* in the middle east [5]. These two species are commonly referred to as Chinese needle ants and samsum ants.

In Australia the large ants of the genus *Myrmecia*, especially *M. pilosula*, are important causes of sting allergy [6].

A number of species of myrmicine ants, especially certain harvester ants of the genus *Pogonomyrmex* will sting, especially in the southwestern North American desert [7]. A number of other species of ponerine ants are known to sting humans including *Odontomachus bauri*, *Hypoponera punctissima* and *Dinoponera gigantea* [8,9]. Several species of ants from the subfamily pseudomyrmicinae, including *Pseudomyrmex ejectus* [8] and a Brazilian species [10] have been reported to cause problems. In Queensland Australia 17 allergic reactions were reported to have been caused by greenhead ants, *Rhytidoponera metallica*, of the subfamily ectatomminae [11].

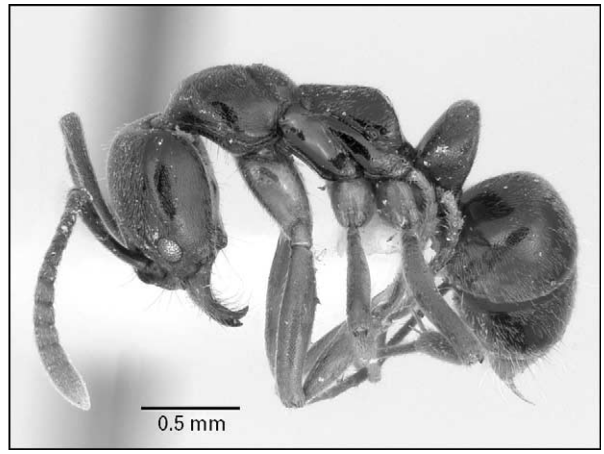
Global spread of stinging ants

Several of the more important stinging ant species have permissive environmental and dietary requirements. These ants are carried on items in international commerce and are spread as tramp species [3,12]. A documented example is the finding of red imported fire ants, *S. invicta*, in a wood cargo delivered from South America to Spain [12]. The red imported fire ant is now well established in southern China and southeast Asia [13,14] and can be found around Brisbane Australia [15]. Spread

Table 1 Subfamilies of ants and the genera discussed

Subfamily	Genus
Myrmicinae	
	Solenopsis
	Tetramorium
	Pogonomyrmex
Formicinae	
	Lasius
Ectatomminae	
	Rhytidoponera
Heteroponerinae	
Dolichoderinae	
Aneuretinae	
Pseudomyrmecinae	
	Pseudomyrmex
Myrmeciinae	
	Myrmecia
Aenictinae	
Dorylinae	
Ectoninae	
Cerapachyinae	
Leptanilioidinae	
Ponerinae	
	Pachycondyla
	Odontomachus
	Hypoponera
	Dinoponera
Agroecomyrmecinae	
Paraponerinae	
Amblyoponinae	
Proceratiinae	
Leptanillinae	

Figure 1 ***Pachycondyla chinensis*, the Chinese needle ant, collected in Pickens, South Carolina**



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in North America continues, although some infestations in western states have been eliminated. *S. geminata*, the tropical fire ant, is a well known tramp species and has become a serious problem in many Asian islands including Indonesia [16] and Taiwan [17], following its spread across many Pacific islands. The black imported fire ant, *S. richteri*, has been carried to Saudi Arabia [18].

The Chinese needle ant, *P. chinensis*, shown in Fig. 1 was introduced into North America over 75 years ago and has now become established in Virginia, North and South Carolina and Georgia [19]. About 8% of sting victims report sting reactions varying from large local reactions to systemic anaphylaxis.

Ant venoms

There have been studies of the protein contents of very few ant venoms, primarily those involved in causing allergic reactions in humans. Recent genomic and proteomic studies of a model wasp, *Nasonia vitripennis* [20,21], should stimulate more studies on insect venom compositions.

Myrmecia

The venoms of the primitive Australian ants of the genus *Myrmecia* have significantly different protein expression from other ants and wasps [22,23]. A review of the clinical aspects of *Myrmecia* allergy was previously published [24]. The allergenic proteins in the venom include several peptides that are found as heterodimers and some as homodimers with molecular weights around 8–9 kDa. The most important is pilosulin 3 or Myr p 2. Additional IgE binding bands were seen in immunoblots at 25.6 and 90 kDa and bands reactive with only a few sera at 6.6, 22.8, 30.4, 32.1 and 34.4 kDa. These larger-molecular-weight proteins have not been characterized. It would be particularly interesting to determine if any of the IgE-binding proteins, especially the one at 25.6 kDa, was a member of the antigen 5/Sol i 3 family.

Solenopsis

The venom of the red imported fire ant, *S. invicta*, is the most thoroughly investigated ant venom. About 95% of the venom consists of water-insoluble piperidine alkaloids, which are responsible for the immediate hive formation and the development of the sterile pustule at the sting site. In recent studies the alkaloid compositions have been reinvestigated and found to be much more complex than previously thought [25,26]. Alkaloid compositions vary among species of fire ants.

The protein compositions of fire ant venoms have been extensively investigated [27,28]. *S. invicta* contains four characterized protein allergens. Two Sol i 2 and 4 are proteins that have not been found in other venoms and are not similar to other characterized proteins [28,29]. These two proteins are related to each other. It has not been possible to obtain a crystal structure yet, although suitable crystals of Sol i 2 have been prepared. Neither allergen contains carbohydrate. Sol i 3 is a member of the antigen 5 family [28,30] and the natural form does not contain carbohydrate. Sera from patients sensitized to Sol i 3 do not cross-react with wasp antigen 5 [31]. The crystal structure has been determined [32••] and very little of the surface is conserved relative to Ves v 5, although the fold is very similar with only variations in loop length. Sol i 1, the fourth allergenic protein, is a phospholipase A_1B similar to the wasp venom enzymes [33]. It contains N-linked common carbohydrate determinant, but there is evidence that some of the IgE reactivity is against protein determinants [34]. Sol i 1 exhibits cross-reactivity with wasp venom phospholipases [31].

Other species of fire ants including *S. richteri*, *S. geminata*, *S. aurea*, and *S. xyloni* have venoms that are highly cross-reactive with *S. invicta* [3,35]. The Sol 2 antigens are most variable among species and may exhibit species specific epitopes, whereas the Sol 1 and 3 antigens appear to be more conserved. *S. richteri* does not express a Sol 4 antigen, but *S. geminata* does.

Recombinant allergens in native conformation have been produced for Sol i 2, 3 and 4 [30,36,37].

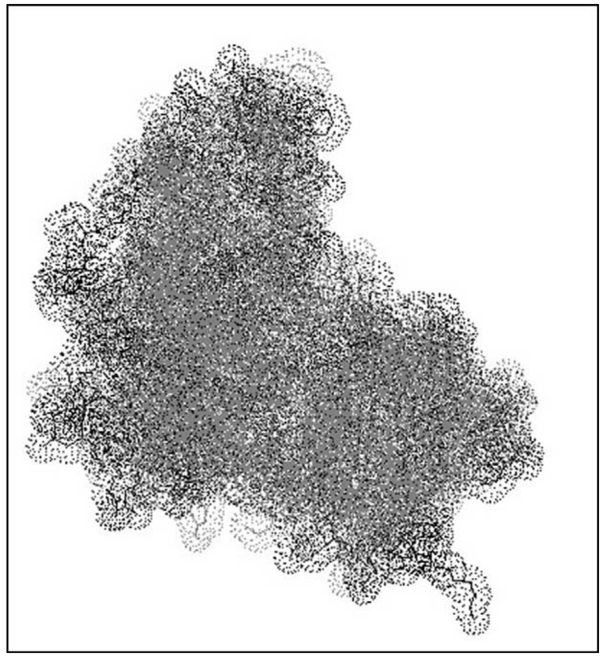
Pogonomyrmex

Harvester ant venom allergy was first described in 1977 [7]. Studies of the venom showed the presence of large amounts of phospholipase A and B activities as well as hyaluronidase, lipase, phosphatase and esterases as well as strong hemolytic activity [38,39]. Harvester ant venom is primarily an aqueous solution and does not contain much water-insoluble material. The types of assays used were not highly specific for the enzyme activities and none of the proteins was isolated. There is probably a phospholipase A_1B, which typically also has some lipase and esterase activity, a phosphatase, some esterases and hemolytic peptides present. Several protein bands were observed that did not correspond to any of the enzyme activities [39]. Venom from *P. badius* was one of the most potent lethal Hymenoptera venoms in mice.

Pachycondyla

There have been some recent investigations of *Pachycondyla* venoms. The venom of the samsum ant contains IgE-binding proteins at 16 and 24 kDa [40]. The16-kDa antigen did not bind IgE from *S. invicta* sensitized patient sera, but the 24-kDa antigen was reactive with all 10 *S. invicta* fire ant sensitized patient sera. The corresponding antigen was isolated, cloned and sequenced from *P. chinesis* venom [41••]. It was found to be a member of the antigen5/Sol i 3 family and showed 54% identity with Sol i 3. Pac c 3 appeared to be the most important allergen in *P. chinesis* venom. We have used the Swiss Model program [42] to construct a three-dimensional model of Pac c 3 and have superimposed it on the crystal structure of Sol i 3 [32••] in Fig. 2. There appears to be limited conservation of the surfaces, but more than is seen between Sol i 3 and Ves v 5. This is consistent with a limited amount on immunologic cross-reactivity as was shown for Samsum ant venom [40]. These ants are not closely related by phylogeny, and myrmecine and ponerine ants are thought to have diverged about 150 million years ago [43].

Figure 2 The modeled three dimensional structure of Pac c 3 in gray dots superimposed on the crystal structure of Sol i 3 from [32••] shown in black dots



Note the limited conservation of surface and the highly conserved fold structure.

Other ants

The venom of the giant hunting ant, *Dinoponera australis*, has recently been reported to contain over 75 proteins and peptides [44]. Included are vasoactive peptides related to kinins and bombesins, antimicrobials and ion channel modifiers.

The venom of *Pseudomyrmex triplarinus* contains 12 proteins from 4.2 to over 100 kDa. These include phospholipase, hemolysins and six anti-inflammatory myrmexins [45].

The venom of the pavement ant, *Tetramorium caespitum*, is primarily an aqueous solution of proteins and free amino acids [46]. The pavement ant is a myrmicine ant, which can be a household pest.

Future studies

As the amount of genomic and proteomic data expands, more studies will be carried out on ant venoms and venom allergens. This will lead to component-resolved diagnosis of allergic reactions [47]. Recent advances include the production of a cDNA library and microarrays for gene expression studies in the imported fire ant, *S. invicta* [48], and the development of Fourmidable, which is a database for studies in ant genomics [49]. There are presently only two species, *S. invicta* and *Lasius niger*, in the database, but others will probably be added in the near future.

Conclusion

Only two groups of stinging ants, imported fire ants and jack jumper ants, have had the allergenic components of their venoms extensively investigated. There are some more limited studies of Chinese needle ants, samsum ants and harvester ants. Ant venoms are heterogeneous with many expressing components unique to each group. Fire ants have Sol i 2 and 4, not described in other venoms as well as a complex mix of piperidine alkaloids. Jack jumper and related ants produce pilosulins, not found in other ant groups. Some enzymes, especially phospholipase A_1B, may be expressed in many, if not most ant venoms. Another group of proteins commonly found are members of the Antigen 5/Sol i 3 family. These proteins are also typical of wasp venoms.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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