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## **Insect Venom of Social Hymenoptera**

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### **Abstract**

The venoms of the social Hymenoptera evolved to be used as defensive tools to protect the colonies of these insects from the attacks of predators. Generally they do not cause lethal effects but cause mainly inflammatory and/or immunological reactions in the victims of their stings. However, sometimes it is also possible to observe the occurrence of systemic effects like respiratory and/or kidney failure. Meanwhile, the venoms of solitary Hymenoptera evolved mainly to cause paralysis of the preys in order to permit egg laying on/within the prey's body; thus, some components of these venoms cause permanent/ transient paralysis in the preys, while other components seem to act preventing infections of the food and future progenies. In addition to these peptides, the Hymenopteran venoms also may contain a few neurotoxins that target Na<sup>+</sup> and/or Ca<sup>2+</sup> channels or even the nicotinic ACh receptor.

### **Introduction**

The remarkable dominance of insects and other arthropods on land can be attributed, at least partially, to the extraordinary diversity of their chemical defense mechanisms. In addition to the glandular defensive secretions, some arthropods developed sophisticated offensive/ defensive chemical weaponry. In this regard, the development of venoms and its injection apparatus among the Insecta represented evolutionary attributes that contributed to adaptation of the insects to the many different terrestrial environments. Thus, different orders of the Insecta developed their self-chemical weaponry, particularly the Hymenoptera (bees, wasps, and ants) that evolved into their venoms and stinging apparatuses according to their biology and behavior. The species with a solitary life history evolved their venoms to be used as paralytic tools in order to keep their prey alive for feeding and reproduction. The many wasp species taking this evolutionary way include the solitary aculeate wasps belonging to the superfamilies Bethyloidea, Scoliidea, Pompiloidea, Sphecoidea, and Vespoidea. This last superfamily is considered as a single family, the Vespinae, and contains the solitary families Massarinae and Eumeninae as well as the social Vespinae. Members of this group of solitary wasps are seasonal, spending the cooler periods as diapausing larvae in nests provided by the mother-wasp. In the most cases, the food provided consists of arthropod prey paralyzed by injection of venom into their bodies. The immobilized prey is then carried to the nest, where the eggs are laid on the prey and the larval development takes place.

Another group of solitary wasps, the Terebrant, which include the superfamilies Ichneumoidea, Cynipoidea, and Chalcidoidea evolved in the direction of parasitic behavior i.e., their venom evolved to promote short/ long-lasting transient paralysis of

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the prey in order to permit egg-laying on/within the prey's body. In this case, after the egg laying, the prey recovers from the paralysis and carries the eggs of the parasitic wasps. In this situation, the venom of these solitary wasps evolved to cause prey paralysis and seem to be constituted of high molecular-mass proteins and low-molecular-mass compounds, generally presenting neurotoxicity. Meanwhile, those species that evolved in the direction of social behavior developed the formation of castes and established the hierarchic relationship among nest mates of different castes. Generally the social species built large nests containing many workers and larvae, in addition to storage of a reasonable amount of pollen, honey, or nectar dew, attracting many different types of predators to their nests.

## Peptides from the Venoms of Social Hymenoptera

The peptide components of venoms from social Hymenoptera are spread over the molar mass range of 1400 to 7000 kDa and together comprise up to 70% of the weight of freeze-dried Hymenoptera venoms. Most of these peptides have polycationic amphipathic components, presenting a high content of  $\alpha$ -helices in their secondary structures; these peptides generally account for cell lysis, hemolysis, antibiosis, and sometimes promote the delivery of cellular activators/ mediators. In addition to this, the Hymenopteran venoms also may contain a few neurotoxic peptides.

## Peptide Toxins from Honeybee Venom

Honeybee (*Apis mellifera*) venom contains well known peptides such as: melittin, apamin, tertiapin, secapin, and peptide. Some of these peptides present a detergent-like action on plasma membranes, causing cell lysis, while others are neurotoxins. Some aspects of the primary sequences, secondary structures and the biological actions will be emphasized.

## Melittin

Melittin is the major component of honeybee venom, representing about 50% of the total honeybee venom. It consists of 26 amino acid residues, mostly with hydrophobic or at least uncharged side chains, except for the C-terminal region. Melittin can aggregate into a tetrameric form into the venom reservoir, being apparently inactive under this condition. This peptide lowers the surface tension of water at the level of the plasma membrane, acting mainly by its natural detergent-like effect on the plasma membrane, causing cell lysis (specially of mast cells), followed by histamine delivery. Due to this lytic effect on

cell membranes, this peptide may be considered as a venom diffusion factor, facilitating the entry of venom into the blood stream of the stung victims. X-ray crystallography of melittin indicated that the residues 1 to 10 and residues 13 to 26 form  $\alpha$ -helices aligned about  $120^\circ$  to each other, while the proline in position 14 was suggested to be the cause of a bend in the middle of the rod structure. Thus, a single polypeptide chain has the conformation of a bent  $\alpha$ -helical cylinder. When packed, the tetramer does so in a double planar layer. In order to achieve tight hydrophobic interactions, the hydrophobic residues of all four chains extend toward the center of the tetramer. Due to its surfactant properties melittin is considered a direct hemolytic factor, acting synergistically with phospholipase A<sub>2</sub>, activating this enzyme.

## Apamin

The honey bee venom also contains apamin, a peptide of 18 amino acid residues. Apamin is permeable to the blood-brain barrier, causing its effects on the CNS by several routes of administration. It causes neurotoxic effects in the spinal cord of mammals, producing hyperactivity and convulsions in rats. When peripherally applied, apamin seems to selectively and potently affect the potassium permeability's of certain membranes, such as the smooth muscle of the gut. At very low levels, it appears that apamin treatment can convert the normal hyperpolarizing response to epinephrine into a calcium dependent depolarization. The peripheral effects of apamin suggest that the central action may be also due to decreased potassium fluxes, since this would broadly reduce inhibitory tone and increase the excitability.

## Conclusion

The venoms of the social Hymenoptera evolved to be used as defensive tools to protect the colonies of these insects from the attacks of predators. Generally they do not cause lethal effects but cause mainly inflammatory and/or immunological reactions in the victims of their stings. However, sometimes it is also possible to observe the occurrence of systemic effects like respiratory and/or kidney failure.

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