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Honey BEE Venom and ITS Composition: Focusing on Different *Apis* Species - A Review

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Abstract—*Bee venom is synthesized in the venom glands of worker bees and queen. It is stored in the venom sac. Venom is a unique weapon possessed by honey bees in the animal kingdom and has a prime role of defense for the bee colony. It is a complex mixture containing simple organic molecules, proteins, peptides, phospholipids, physiologically active amines, amino acids, sugars, volatile pheromones, minerals and other bioactive elements. Toxicity of these compounds is known to man since ages and these are responsible for many toxic or allergic reactions such as local pain, itching, irritation, moderate to severe allergic reactions and from mild inflammation to death. A perusal of work previously done on the venom of honey bee reveals that the best studied proteins (enzymes) are phospholipase A2- responsible for cleaving the membrane phospholipids; phospholipase B- responsible for cleavage of the toxic lysolecithin; hyaluronidase- which degrades the matrix component hyaluronic acid into non-viscous segments and acid and alkaline phosphatase acting on organic phosphates. Small proteins and peptides include melittin, apamine, MCD peptide (mast cell degranulating peptide), adolapine, protease inhibitor, tertiapine, cardiopep, procamine A,B and small peptides of less than 5 amino acids are secapine, pamine and minimine. Amines include histamines, dopamine, noradrenalin and neurotransmitters. Sugars are glucose and fructose. Volatile pheromones are complex ethers, isopentyl acetate, n-butyl acetate and (2)-11-eicosen-1-ol. Last but not the least are some of minerals which include P, Ca and Mg.*

Keywords*: bee venom, enzymes, peptides, Apis spp*

1. INTRODUCTION

Defending the colony with the sting which is believed to have evolved from the egg laying apparatus of the female is characteristic feature of all insects that belong to the order Hymenoptera including ants, wasps and bees. Since it is a modification of the ovipositor so only the females can sting. The anatomy of the sting (venom apparatus) reveals the presence of two important associated exocrine glands *i.e*. venom gland (acidic) and dufors gland (alkaline). The secretions of both glands are apocrine and are released into the lumen to be stored in the venom sac. The production of bee venom increases during the first two weeks of the adult worker's life and reaches a maximum when the worker bee becomes involved in hive defense and foraging. It diminishes as the bee gets older. The queen bee's production of venom is highest on emergence, probably because it must be prepared for immediate battles with other queens. Hymenoptera venom is responsible for the toxic or allergic reactions which are mostly caused by low molecular weight compounds which can result in pain, local inflammation (Hider, 1988), itching and irritation as the immediate response that get attenuated after some hours (Golden,1989). The most prominent compound responsible for these allergic reactions is a peptide called Melittin, however a combination of mastocytes with IgE by triggering a cascade of mediators including histamines, leucotrienes, platelet activating factors, enzymes, peptides and other chemicals (Hider, 1981 and 1988) are also responsible for the allergic reactions.

2. THE COLLECTION METHODS AND PHYSICAL CHARACTERISTICS OF BEE VENOM

Bee venom is odorless, colorless, clear watery liquid with ornamental pungent smell, a bitter taste and basic pH (4.5 to 5.5). (Krell, 1996; Schmidt and Buchmann, 1999) that is used by bees for defense. The dried form is of yellow color and some commercial preparations are brown due to oxidation of some of their proteins. Honey bee venom comprises a number of volatile compounds which are easily lost during collection. Venom causes burning and irritation to the eyes and the mucous membrane if come on contact.

The composition of bee venom depends on the different extraction and collection methods. Pence (1981) revealed from his studies that venom collected under water to avoid the evaporation of some very volatile compounds seemed to yield the most potent venom. Kumar and Devi (2014a, b), Kumar *et al,* (2014 a,b,c,d) observed differences in the composition of venom gland and venom sac secretion by surgical removing the poison gland and poison sac of the worker honey bees of different *Apis* species

Hsiang and Elliott (1975) concluded from their studies that the venom collected by surgically removing the venom sac showed different protein content than that collected by electric shock method. A standard electro-shock collecting apparatus

with cooling system is used by Gunnison (1966) for preserving the more volatile compounds. However Morse and Benton (1964a, b) recommended that this electro shock method cannot be used for the Africanized honey bees and also for some other defensive races. Galuszka (1972) confirmed that electroshock method was the most efficient collection method with slight modification involving 15 minute stimulation at intervals of three days, repeated after 2 to 3 weeks. This increased the collection efficiency greatly and the hive remained undisturbed.

3. THE COMPOSITION OF VENOM

3.1 Venom of the European honey bee, *Apis mellifera*

A. mellifera is the most commonly domesticated species of honey bees. *Apis* venom especially *Apis mellifera* is considered to be the best characterized venom in the Hymenoptera (Edstrom, 1992). The stinging behavior is characterized by pheromone secretion and is most commonly observed near the colony to defend the colony from other insects (Banks and Shipolini, 1986). The description of venom complex as revealed by Peak (1986) in his studies covers the morphology of the venom apparatus, the collection of venom, the pharmacological effects of bee venom and allergies to the hymenoptera venom of bees, wasps and ants. Crane (1990), Dotimas and Hider (1987) and Banks and Shipolini (1986) gave a very clear overview of the venom composition, effects, harvesting and use of *A.mellifera* and other species.

3.2 Venom of other *Apis* species

The venom from all other *Apis* species is similar in composition and quality but there are slight differences in their production and toxicity based on their size and physiological differences. *A.florea* is the smallest of all the species of honey bees, while *A. dorsata* has the largest individual body size of all honey bees (Michener, 2000) *A. cerana* and *A. mellifera* are of medium size. As reported by Benton and Morse (1968) the toxicity of *Apis cerana* venom is twice as high as that of *Apis mellifera.* Kumar and Devi (2014 a, b), Kumar *et al* (2014 a, b) observed that there were considerable differences in the composition of venom gland and venom sac secretion and concluded that the concentration of lipids, proteins, activity of acid phosphatase and hexokinase was found to be more in case of venom gland of *A. dorsata* followed by *A. cerana, A. mellifera* and then by *A. florea*. Cholesterol, glucose, free amino acids, and activity of alkaline phosphatase were more in venom sac of *A. dorsata* followed by *A. cerana, A. mellifera* and then by *A. florea*. Glycogen was absent in both Venom gland and Venom sac of *Apis* species as confirmed by the absence of glucose-6- phosphatase activity.

3.3 Summary of venom composition (Banks and Shipolini, 1986; Dotimas and Hider, 1987; Shkenderov and Ivanov, 1983; Urtubey, 2005).

A). Small proteins and Peptides

1. Melittin; biologically most active peptide
2. Apamine; biologically active peptide
3. MCD peptide; mast cell degranulating peptide
4. Adolapine; biologically active peptide
5. Protease Inhibitor; biologically active peptides
6. Tertiapine, Cardiopep, Procamine A,B
7. Small peptides of less than 5 amino acids are Secapine, Pamine, Minimine

B). Proteins (Enzymes)

1. Phospholipase A2 (PLA2); enzyme hydrolysing phospholipids.
2. Phospholipase B; enzyme doing cleavage of the toxic lysolectin
3. Acid phosphomonoestrase
4. Hyluronidase enzyme; catalyzes hydrolysis of hyaluronic acids, the tissue cement.
5. Phosphatase (acid and alkaline phosphatase)
6. α-Glucosidase and Lysophospholipase.

C) Phospholipids

D) Physiologically active amines including Histamine, dopamine, noradrenalin, and neurotransmitters

E) Amino acids: γ-amino-butyric acids and α- amino acids

F) Sugars: Glucose and Fructose.

G) Volatile pheromones are complex ethers, iso-pentyl acetate; n-butyl acetate; iso-pentanol; n-hexyl acetate; N-octyl acetate; 2-nonanol; n-decyl acetate; benzyl acetate; benzyl alcohol; (2)-11-eicosen-1-ol. Complex ethers.

H) Minerals like P.Ca and Mg.

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