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Review Article

Antimicrobial Peptides from Insects: An Overview

Ravi, C., Jeyashree, A. and Renuka Devi, K.

Department of Zoology and Microbiology, Thiagarajar College (Autonomous)
Madurai – 625 009, Tamil Nadu, India
E-mail: ravi_cyril@yahoo.co.in

Bacteria are exceptionally adept at acquiring resistance to antibiotics and antiseptic agents, hence new antibiotics and strategies are therefore needed to deal with this threat. Several authors have reported the inhibitory effect of anti microbial peptides of animal origin on bacteria and research is on the rise about insect antimicrobial peptides. An attempt has been made to have a comprehensive review of the research work carried out on antimicrobial peptides from insects.

Innate immunity is the first line of defense in multicellular organisms against invading microbes such as bacteria, fungi, and viruses (Montano *et al*., 2011). Invertebrates lack an adaptive immune system, yet their innate immunity effectively kills invading microbes, they fight against foreign organisms by humoral and cellular reactions such as nodule formation, and melanization (Ratcliffe, 1985; Iwangwa and Lee, 2005). The insects are by far the most species rich group of animals and effectively exploit a huge range of niches (Dunn, 1986; Bulet *et al*., 1999; Saito *et al*., 2004) and it is necessary for insects to overcome effectively against the impacts of pathogens (Hoffmann and Reichhart, 1997; Lowenberger, 2001). In Insects, the immune system is comprised of innate and humoral defense mechanism, though evidences suggest the presence of adaptive responses as well (Gotz and Boman, 1985; Dunn, 1986; Boman and Hultmark, 1987; Kimbrell, 1991; Watson *et al*., 2005; Dong *et al*., 2006; Sadd and Schmid-Hempel, 2006). The phagocytosis and encapsulation mechanisms are operative in cellular immunity (Rizki and Rizki, 1984; Dularay and Lackie, 1985; Ratcliffe *et al*., 1985; Boman and Hultmark, 1987), whereas humoral responses mainly involve the rapid synthesis and release of different types of Antimicrobial peptides (AMPs) in the insect hemolymph upon microbial infection (Bulet *et al*., 1999). Collectively these AMPs are known to mount effective immune defense against invading pathogens.

AMPs are part of the armament that insects have developed to fight off pathogens, which are low molecular weight heat stable, typically cationic and often made of less than 100 amino acid residues (Wang and Lai, 2010). It was evident that the fat body of insects is mainly responsible for the production of AMPs (Brey *et al*., 1998; Hoffmann *et al*., 1999; Ganz, 2003; Schmid-Hempel, 2005). Large number of AMPs has been identified from insect and mammalian species but first Boman's group purified an AMP from hemolymph of immunized pupae of *Hyalophora cecropia* (Hultmark *et al*., 1980). Although their structures are diverse, most of the AMPs can be assigned to a limited number of families. The most common structures are represented by peptides assuming an alpha-helical conformation in organic solutions or disulfide-stabilized beta-sheets with or without the presence of alpha-helical domains (Bulet and Stocklin, 2005).

Many AMPs that are isolated from different insect species (Cociancich *et al*.,1994a) are categorized by homology as belonging to one of the several families, namely the cecropins (Hultmark *et al*., 1980; Boman and Hultmark, 1987; Kaaya *et al*., 1987; Dickenson *et al*., 1988; Kanai and Natori, 1989; Kysten *et al*., 1990; Samkovlis, *et al*., 1990, 1991), attacins (Hultmark *et al*., 1983; Kockum *et al*., 1984; Casteel *et al*., 1990; Wicker *et al*., 1990; Sun *et al*., 1991), lysozymes (Mohrig and Messner, 1968; Powning and Davidson,1976; Jolles *et al*., 1979; Hultmark *et al*., 1980; Engstrom *et al*., 1985), defencins (Dimarcq *et al*., 1990; Lambert *et al*., 1989), and dipteracins (Dimarcq *et al*., 1990; Wicker *et al*., 1990).All five antibacterial protein groups have been isolated from dipteran insects (Hultmark, 1993). But in *Drosophila*, seven distinct groups of AMPs (cecropins, drosocin, attacins, dipteracins, defensin, drosomycin and metchnikowins) have been identified and characterized by whole genome microarray analysis (Bulet *et al*., 1999; Irving *et al*., 2001).

Cecropins, the polypeptides originally found in cecropia moth, *Hyalophora cecropia* (Steiner *et al*., 1981) were thought to be primarily responsible for antibacterial activity whereas some other insects found to show such activity against many kinds of Gram positive and Gram negative bacteria as well as fungi (Hultmark *et al*., 1982; Qu *et al*., 1982; Teshima *et al*., 1987; Boman *et al*., 1989; Tu *et al*., 1989). Although cecropins have been isolated from several species of lepidopteran and dipteran insects (Cociancich *et al*., 1994 a), they have not been found in other insect orders. In the domesticated silkworms, *Bombyx mori,* cecropins are classified into three subtypes A, B and D. Cecropins contains 2 alpha helices which act on Gram negative bacteria most effectively (Taniai *et al*., 1995; Yamano *al*., 1998; Yang *et al*., 1999). Under physiological conditions, proline rich lebocin was found to have weak anti-bacterial activity which was similar to abaecin isolated from honey bee, but its activity becomes much higher, when lebocin is glycosylated or exists with cercoprin D (Furukawa *et al*., 1997).

Insect defensins are highly effective against Gram-positive bacteria (Hetru *et al*., 2003), including human pathogenic bacteria such as *Staphylococcus aureus*, whereas they do not exhibit strong activity against Gram-negative bacteria and its antibacterial mechanism have well been studied (Okada and Natori, 1984, 1985; Christensen *et al*., 1988; Matsuyama and Natori, 1990; Cociancich *et al*., 1993; Yamada and Natori, 1994). Contrary to cecropins, insect defensins are isolated from several insect orders such as dipteran, hymenopteran, coleopteran, trichopteran, hemipteran, and odonata (Hoffmann and Hetru, 1992; Cociancich *et al*., 1994 b). Apart from the insect defensins, all types of antibacterial proteins have been reported in lepidopteran insects (Boman *et al*., 1991; Hara and Yamakawa, 1995).

Attacin is active against Gram negative bacteria by inhibiting the synthesis of its outer membrane protein whereas moricin increases their membrane permeability thereby kills Gram positive and negative bacteria (Sugiyama *et al*., 1995; Hara *et al*., 1995). Several other antibacterial factors have been reported from *B. mori*, including lysozyme and two lectins (Yamakawa and Tanaka, 1999).

Lysozymes are muramidases that hydrolyse the β-1, 4- glycosidic linkage in the N-acetyl glucosamine and N-acetyl muramic acid residues in the peptidoglycan layer of the bacterial cell and cause their lysis. These polypeptides are up regulated upon infection in the lepidopteran insects (Daffre *et al*., 1994). From the domesticated and wild silk moths, *B. mori* and *Antheraea mylitta*, respectively A C-type lysozyme has been characterized (Lee and Brey, 1995; Jain *et al*., 2001).

Due to the result of fast developing pathogenic bacteria that are resistant to classical antibiotics (Moellering, 1998) in recent years, intensive studies have been undertaken towards more effective antimicrobial drugs. Particularly interesting are AMPs discovered as components of unspecific innate mechanisms of infection fighting in humans and animals (Andreu and Rivas, 1999). It was evident that antimicrobial peptides are highly conserved across a wide range of taxa including bacteria, plants, invertebrates and vertebrates (Yeaman and Yount, 2003). This reveals that they can be a useful tool to investigate the evolution of immune systems (Hultmark, 1994; Gillespie *et al.,* 1997; Mushegian and Medzhitov, 2001). The knowledge and the continuing study on these immune peptides will continue to shed light on many important issues spanning across many different fields of research. Insect AMPs are also likely to have vital applications in disease control (Lowenberger, 2001).

AMPs are an essential component of innate immunity which can rapidly respond to diverse microbial pathogens. Insects, as a rich source of AMPs, attract great attention of scientists in both understanding of the basic biology of the immune system and searching molecular templates for anti-infective drug design. Despite a large number of AMPs have been identified from different insect species, little information in terms of these peptides is available regarding their applications (Tian *et al*., 2010). With several desirable properties, such as heat-tolerance, relatively broad antimicrobial spectrum and low toxicity to eukaryotic cells, AMPs, especially the "food-derived antimicrobial peptides" may serve as a potentially significant group of food preservatives (Zhao *et al*., 2010). Insects are vectors of a wide range of animal and human parasites like malaria, yellow fever, dengue fever and sleeping sickness, all of which are major causes of mortality (Ham *et al*., 1994), many of these parasites are exposed to the action of antimicrobial peptides at some point during their life cycle (Lowenberger, 2001). This has led to research which ultimately aims to produce transgenic forms of insect vectors which will kill the parasite, thereby preventing the transmission to humans (Lowenberger, 2001).

The silkworm *B. mori* whose genome sequence is available (Xia *et al*., 2004), with 18510 predicted genes and about 400 mutant lines (Hoffmann, 2003; Kanost *et al*., 2004). *B. mori*, is an economically important insect, acts as a host for different pathogenic microorganisms (Chitra *et al*., 1975) with varying degree of tolerance to different pathogens (Chitra *et al*., 1975). Although earlier workers have characterized cecropin-like antibacterial proteins (Morishima *et al*., 1990) and lysozymes (Powning and Davidson, 1973), to what extent they are involved in the humoral response in silkworm remains to be understood. With a relatively large body size, *B. mori* may serve as a good model for genetic and biochemical study of insect immune responses. It could be used as a bioreactor for the production of AMPs that act on the deadly human pathogens in the near future.

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