J Appl Biotechnol Rep. 2021 September;8(3):193-202

Journal of
Applied Biotechnology Reports

doi 10.30491/JABR.2020.236075.1242

Review Article

Insect Antimicrobial Peptides – Therapeutic and Agriculture Perspective

Habeeb Shaik Mohideen [1*], **Henry Pearl Louis** [1]

[1] Bioinformatics & Entomoinformatics Lab, Department of Genetic Engineering, SRM Institute of Science & Technology, Kattankulathur, Tamilnadu–603202, India

Corresponding Author: Habeeb Shaik Mohideen, PhD, Associate Professor, Bioinformatics & Entomoinformatics Lab, Department of Genetic Engineering, SRM Institute of Science & Technology, Kattankulathur, Tamilnadu–603202, India. Tel: +91-9940051100, E-mail: Habeeb_skm@yahoo.co.in, habeebm@srmist.edu.in

Received June 21, 2020; **Accepted** November 3, 2020; **Online Published** April 25, 2021

Abstract

Antimicrobial resistance (AMR) has become a menace for humanity. Several antibiotics have become ineffective, and there is a need for a novel route or approach to find solutions. Antimicrobial peptides (AMPs) have already generated a lot of noise for over four decades. However, insect-based AMPs offer not only novel sources but also provide effective measures, as the insects are known to be exposed to extreme environments. Plenty of insect-based AMPs have been identified from different orders of insect taxonomy. This review concentrates on the world of insect-based AMPs, their known targets and their applications in agriculture and medical fields. Transgenic induction of AMPs in different hosts has been successfully studied in plant systems. By identifying new AMPs, it will also help in the field of agriculture to increase the production rate of the crops by eliminating the disease-causing pathogens, microbes, and pests. In the present review, we have discussed recent knowledge, and several essential medical and agricultural importance of AMPs identified from insects.

Keywords: Insect, Antimicrobial Peptides, Antimicrobial Resistance, High Throughput Screening, Plant-microbe Interaction, Crop Protection

Citation: Mohideen HS, Louis HP. Insect Antimicrobial Peptides–Therapeutic and Agriculture Perspective. J Appl Biotechnol Rep. 2021;8(3): 193-202. doi:10.30491/JABR.2020.236075.1242

Introduction

Antimicrobial resistance (AMR) has become a universal threat, rendering antibiotics ineffective and useless, thereby resulting in severely infected individuals and higher mortality rates.[1] The World Health Organization (WHO) predicted the need for innovative solutions against the AMR nearly two decades ago.[2] The menace is so disturbing that several hundred thousand deaths are being recorded every year across the world due to AMR.[3] These are reported from post-operative/transplantation procedures, neonatal intensive care,[4] failed chemotherapy,[5] replacement surgeries etc. Annually, AMR is estimated to enforce the loss of about €9 billion [6] in Europe and $20 billion in the USA.[3] Due to these reasons, it is imperative to find solutions for better control that is not only viable but also has a broad-spectrum effect with less or no side effects.[7]

Antimicrobial peptides (AMPs) are peptide-based effector molecules that are discovered for the treatment of various human diseases. AMPs are mostly formed naturally by the host innate immune system of all the organisms.[8,9] One of the first AMP was reported in 1947 from *Lactococcus lactis*.[10] Thousands of AMPs have been reported from different forms of life mainly the eukaryotes such as plants, animals, and fungi. The AMPs act as the first line of defense in these organisms and have a unique potential to attack microbes, including the resistant ones[11]

The AMPs that are being used universally have similar characteristics. For example, they are cationic (net +ve charge +2 to +9) and amphipathic. Certain factors like hydrophobicity, a combination of charge and peptide length, are essential for their antimicrobial property, whereas any change in peptide chain position will affect their fundamental secondary structure.[12,13] According to Boman's classification of antimicrobial peptides, they are differentiated into four families based on their secondary structures. They are (a) α-helical structure due to coiled conformation, (b) β-sheet or stranded, (c) both α-helix /β-stranded mixed, and (d) extended chains respectively.[14]

Naturally, these AMPs consist of about 12 – 50 amino acid residues and based on their structure and composition, are divided into several subgroups. Some AMPs are longer in a structure consisting of 100 amino acid residues. Further, AMPs from eukaryotes can be categorized into cationic and also some anionic peptides like Maximin and Dermcidin. More than 3050 AMPs have been discovered from various species, such as bacteria, fungi, plants, and also animals. These peptides will be a stable alternative for antibiotics

used traditionally based on easy concepts of modification and extraction. Recent developments in the field of bioinformatics and biotechnology have made it possible for AMP identification/ synthesis. Novel AMPs have been discovered based on the peptide homology by identifying the presence of protease cleavage sites and focusing on high immune resistant tissues and cells by their expression profiles.[15,16] In general, based on the experimental evidence, these peptides disrupt the cell membrane of microorganisms through different mechanisms. Most studies shown that disrupting the integrity of the cell membrane is the main mechanism of action of these peptides for killing microorganisms (Figure 1).

Mostly identified AMPs are inactive precursor proteins generated by low proteolysis level known as active peptides (20-50 residues). In fruit fly, about seven classes of AMPs have been identified till now, and gene regulation of those identified AMPs have been well studied for better understanding.[17,18] Although many insect AMPs have been reported from recent research, there are only a few reviews about them.

Insect Antimicrobial Peptides

Globally, about 10 quintillion insects are estimated, and the largest group of insect families are Beetles, which comprise about 350,000 to 400,000 species.[19] While comparing with other species, insects are potential sources of various proteins, fats, and some other essential nutrients.[20] Insects habituating in densely populated regions are likely more resistant to various infectious pathogens when compared to low population density, and this may also affect host-pathogen interaction stability.[19,21] It is all about the threats faced by an individual species in the environment to survive from the pathogens during the evolution. For example, when the species gets highly exposed to the pathogenic environment with various types of them, it is expected that the species will produce a more qualitative and quantitative amount of defensive molecules or macromolecules like AMPs.[18,22]

The insect innate immune response mainly consists of humoral immunity and cellular immunity. The advantage is a broad spectrum of combat, and they physically disrupt microbial cell membranes, which are considered as the primary target of AMPs. The AMPs eliminate microorganisms like bacteria and fungi by the formation of transmembrane pores or ion channels, then showing the unique characteristics of killing other viruses and protozoa. They can bind and neutralize endotoxins and then regulate the immune responses. They also affect several processes together in the pathogens such as synthesis of the membrane and fatty acid, regulation of membrane, and chemotaxis.[23] AMPs also show properties like the Antineoplastic effect, healing of wounds, and skin regeneration. They have also shown cytotoxic effects on Leukemia, Mouse myeloma, Lymphoma, Lung cancer, Breast cancer, etc.[24-27]

Recently, these AMPs have also been identified more in numbers from transcriptomes of insects. Therefore, transcriptomic profiling provided various types of insect-based AMPs, namely, Lebocins, Drosomycin, Cecropins, Attacins, Defensins, Drosocins, Diptericins, Metchnikowin, and Ponericin; and plenty of them have not yet been identified. Insect AMPs are highly potent due to their inhibitory concentration, which ranges in low molar level. However until now, no insect AMPs have been available in the market, but there is no doubt soon these insect AMPs may dominate the existing therapeutic antibiotics.[28] The insect ladybird *Harmonia axyridis* is identified to produce about 50 types of AMPs.

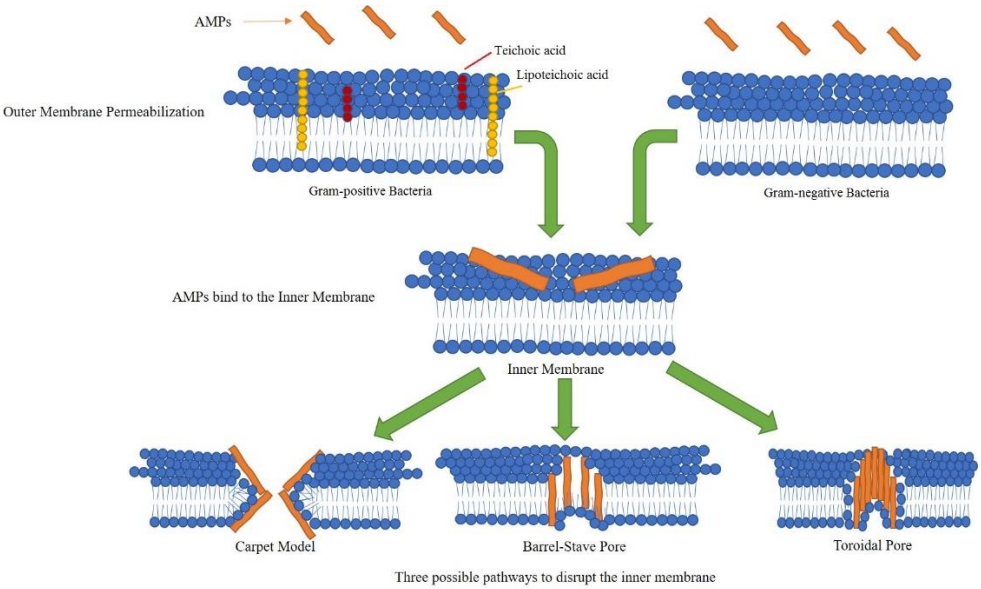

Figure 1. The Schematic Structures of the Gram-negative and -Positive Bacteria Cell Membranes and the Mode of Action of Antimicrobial Peptides on the Cell Membrane.[23]

Types of Insect Antimicrobial Peptides

AMPs are divided into three groups: (a) Cecropins, definite peptides having only α–helices, (b) Defensins having 6-8 continuous cysteine amino acids, and (c) peptides with a high representation of specific amino acids.

(a) Cecropins

Cecropins are small proteins belonging to the family of cationic AMPs ranging in length from 35-38 non-cysteine residues. They were first discovered in the vaccinated hemolymph of *Hyalophora cecropia* pupae from which the term Cecropins was derived. They have also been identified from other insect families like Lepidoptera, Diptera, and Coleoptera. These are highly active on both gram-positive and gram-negative bacteria and also in some fungi.[29] Cecropins from insects are also called as Sarcotoxin, lepidopteran, and Bactericidin. These classes of AMPs will have an N-terminal tryptophan residue and amidated C-terminal.[30] The cecropins are classified into several types based on their structure, namely, (Cecropin-A, Cecropin-B, Cecropin-C, Cecropin-D). All these types have been previously explained in detail.[31]

(b) Defensins

Defensins are the second primary structural class of insect AMPs. Host defense is the vital role of defensins as effectors and regulators. They are classified into two types, namely α-Defensins and β- Defensins. They are cationic peptides with arginine residues having antibiotic activity against vast microorganisms.[33] They have a predominant β-sheet globular structure, are stabilized by intramolecular disulfide bridges, and are widely distributed across insect orders.[34] The first of the defensins were discovered in the flesh fly *Phormia terranovae* containing six cysteine residues. It was found to be most active against gram-positive bacteria primarily and few gram-negative bacteria. Defensins from insects are isolated from various insect orders, namely Coleoptera, Hemiptera, Diptera, Trichoptera, Hymenoptera, and Odonata.[35] A few insect defensins can act against filamentous fungi species also, e.g., Gallerimycin from *Galleria mellonella*, a greater wax moth.[35–38]

Table 1. Cecropins Identified from Insects, their Amino Acid Sequences and their Sources[31,32]

Name	Amino Acid Sequence	Source
Cecropin A	GGLKKLGKKLEGVGKRVFKASEKALPVAVGIKALG-NH2	*Aedes albopictus*
Cecropin B	KWKVFKKIEKMGRNIRNGIVKAGPAIAVLGEAKAL-NH2	*Antheraea pernyi*
Cecropin B1	KWKVFKKIEKMGRNIRNGIVKAGPKWKVFKKIEK-NH2	*Antheraea pernyi*
Cecropin B3	AIAVLGEAKALMGRNIRNGIVKAGPAIAVLGEAKAL-NH2	*Antheraea pernyi*
Cecropin C	GWLKKLGKRIERIGQHTRDATIQGLGIAQQAANVAATAR-NH2	*H. Cecropia*
Cecropin D	WNPFKELEKVGQRVRDAVISAGPAVATVAQATALAK-NH2	*H. Cecropia*
Cecropin P1	SWLSKTAKKLENSAKKRISEGIAIAIQGGPR-NH2	*Ascaris suum*
Lucilin	GWLKKLGKKIERVGQHTRDATIQTIGVAQQAVNVAATLKG	*Lucilia eximia*

Table 2. Defensins Identified from Insects, their Amino Acid Sequences and their Sources[33,36]

Name	Amino Acid Sequence	Source
Heliomicin	DKLIGSCVWGAVNYTSDCNGECKRRGYKGGHCGSFANVNCWCET	*Heliothis virescens*
Insect defensin	GFGCPLDQMQCHRHCQTITGRSGGYCSGPLKLTCTCYR	*Aeschna cyanea*
Phormicin	ATCDLLSGTGINHSACAAHCLLRGNRGGYCNGKGVCVCRN	*Phormia terranovae*
Sapecin A	ATCDLLSGTGINHSACAAHCLLRGNRGGYCNGKAVCVCRN	*Sarcophaga peregrina*
Sapecin B	LTCEIDRSLCLLHCRLKGYLRAYCSQQKVCRCVQ	*Sarcophaga peregrina*
Sapecin C	ATCDLLSGIGVQHSACALHCVFRGNRGGYCTGKGICVCRN	*Sarcophaga peregrina*
Tenecin 1	VTCDILSVEAKGVKLNDAACAAHCLFRGRSGGYCNGKRVCVCR	*Tenebrio molitor*
Termicin	ACNFQSCWATCQAQHSIYFRRAFCDRSQCKCVFVRG	*Pseudacanthotermes spiniger*
Drosomycin	DCLSGRYKGPCAVWDNETCRRVCKEEGRSSGHCSPSLKCWCEGC	*Drosophila melanogaster*
Galleria defensin	DTLIGSCVWGATNYTSDCNAECKRRGYKGGHCGSFLNVNCWCE	*Galleria mellonella*
Hymenoptaen	EFRGSIVIQGTKEGKSRPSLDIDYKQRVYDKNGMTGDAYGGLNIRPGQPSR QHAGFEFGKEYKNGFIKGQSEVQRGPGGRLSPYFGINGGFRF	*Apis mellifera*
Dichotoma defensin	VTCDLLSFEAKGFAANHSLCAAHCLAIGRRGGSCERGVCICRR	*Allomyrina dichotoma*

(c) Peptides with a High Representation of Specific Amino Acids

This section of the review highlights a more significant number of AMPs identified until now. Those peptides with a high content of certain residues, like glycine, tryptophan, arginine, and histidine-rich residues are Attacins, Drosocins, Moricins, Lebocines, Diptericines, Metchnikowin, Ponericins, and Jelleines.[17,31]

Attacins

Attacins rich in glycine residues were first identified in the hemolymph of *H. cecropia*. It has a molecular mass of about 20-23 kDa and isoelectric point 5.7-8.3. It is more effective against gram-negative bacteria. It is distinguished into several types from A-F and classified into two major categories acidic and basic Attacins. They are also reported from various insects, namely *Helicoverpa armigera*, *Glossina morsitans*, *Heliothis virescens*, *Trichoplusia ni*, *Musca domestica*, and *Manduca sexta*.[39,40]

Table 3. Attacins Identified from Insects, their Amino Acid Sequences and their Sources[17]

Name	Amino Acid Sequence	Source
Attacins A-D	AGALTINSDGTSGAVVKVP	*Hyalophora cecropia*
Attacins E-F	DAHGALTLNSDGTSGAVV KVPFAGNDLNI	*Hyalophora cecropia*

Moricins

These were first identified from *B. mori* by bacterial injection. They do not have amino acid residue modifications like α-amidation of C-termini present in cecropins and the hydroxylation of lysine residues.[41] They actually have a high permeability ratio of the bacterial membrane due to the amphipathic N-terminal segment of α-helix. Moricins have shown positive results in inhibiting the growth of both gram-positive and gram-negative bacteria (gram-positive bacteria to a large extent).[42,43]

Table 4. Moricin and its Amino Acid Sequences with the Source of Identification[42]

Name	Amino Acid Sequence	Source
Moricin	AKIPIKAIKTVGKAVGKGLRAINIAST ANDVFNFLKPKKRKA	*Bombyx mori*

Drosocins

These were first identified from *Drosophila melanogaster* and were conserved in the entire Drosophila genus (19 amino acid residues).[31] Drosocins have high resistance to gram-negative bacteria, and some proline-rich drosocin i.e., glycosylated drosocin shows potential activity against *E. coli*.[44] They are highly capable against bacteria and fungi due to certain pore-forming peptides, which help in their entry into the cell membrane.[9] Apidaecin produced by honeybee is a homolog to drosocin.[45]

Table 5. Drosocin and its Amino Acid Sequences with the Source of Identification[18]

Name	Amino Acid Sequence	Source
Drosocin	GKPRPYSPRPTSHPRPIRV	*Drosophila melanogaster*

Lebocins

Lebocins were first discovered in *B. mori* (silkworm) that was inoculated with *E. coli.* They are naturally rich in proline peptide with O-glycosylated 32 residues.[41] They are highly reactive on both gram-positive and gram-negative bacteria and fungi. This AMP has been reported from other lepidopteran species, namely, *Manduca sexta, Trichoplusia ni, Pseudoplusia includens, S.cynthia, Pieris rapae,* and *Antheraea pernyi.* Lebocin has 41% sequence homology to *Apis mellifera* produced Abaecin.[29,46-49]

Table 6. Lebocin and its Amino Acid Sequences with the Source of Identification[41]

Name	Amino Acid Sequence	Source
Lebocin	DLRFLYPRGKLPVPTPPPFNPKPIYIDMGNRY	*Bombyx mori*

Diptericin

This family consists of glycine-rich antibacterial peptide weighs about 8kDa with 82 amino acid residues. It has been identified from insects of various families, namely *Phormia terranovae*, *Mayetiola destructor*, *Sacrophaga peregrina*, and also in *Drosophila melanogaster*. It is more active against specific gram-negative bacteria (*Erwinia carotovora*, *E.coli* K12, *Erwinia nericola* T).[35]

Table 7. Diptericin and its Amino Acid Sequences[50]

Name	Amino Acid Sequence	Source
Diptericin	DEKPKLILPTPAPPNLPQLVGGGGG NRKDGFGVSVDAHQKVWTSDNGR HSIGVTPGYSQHLGGPYGNSRPDYR IGAGYSYNF	*Sarcophaga peregrina*

Jelleines

Jelleines are a type of insect antimicrobial peptide isolated from the Royal jelly of *Apis mellifera.* They consist of 8-9 amino acid residues with a charge of +2.[51,52] Four types of AMPs have been identified and isolated from royal jelly, namely Jelleines 1, Jelleines 2, Jelleines 3, and Jelleines 4. These were active against both gram-positive and gram-negative bacteria and also fungi.[23]

Table 8. Jelleines Identified from *Apis mellifera* and their Amino Acid Sequences[52]

Name	Amino Acid Sequence	Source
Jelleines 1	PFKLSLHL	*Apis mellifera*
Jelleines 2	TPFKLSLHL	
Jelleines 3	EPFKLSLHL	
Jelleines 4	TPFKLSLH	

Metchnikowin

It has been named after the Russian scientist Elie Metchinikoff. It is a proline-rich peptide with 26 amino acid residues identified from *D. melanogaster*. Metchnikowin is active against gram-positive bacteria and fungi and shows no activity against gram-negative bacteria. It can bind to ribosomes of microbes, which prevents protein translation.[53] This peptide also interacts against an important fungal cell wall synthesizing enzyme called β-(1,3) glucanosyl transferase Gel 1. According to the study of Moghaddam et al., it has inhibited around 52% SDH activity of *Fusarium graminearum*.[54]

Table 9. Metchnikowin and its Amino Acid Sequences[53,54]

Name	Amino Acid Sequence	Source
Metchnikowin	HRHEGPIFNTRPSPFNPNEPR PGPIY	*Drosophila melanogaster*

Ponericins

They were first identified and isolated from the predatory ant venom of *Pachycondyla goeldii*, which is from the subfamily Ponerinae.[55] Based on the primary structure similarities, they are divided into three families, namely Ponericins G, Ponericins L, and Ponericins W. The cell membrane of Ponericins have an α-helical structure.[56]

Insect AMPs in the Field of Therapeutics and Medicine

Due to various modes of action of AMPs, they are more potent than conventional antibiotics which makes them an ideal candidate for new antibiotics.[57,58] AMPs neutralize endotoxin ability, considerably low Minimum Inhibitory Concentration (MIC) and show that they are highly capable of killing bacteria. They show potential activity against biofilms, which also showed resistance to traditional antibiotics. In addition to that, the potential AMPs have

Table 10. Ponericins Identified from *Pachycondyla goeldii* and their Amino Acid Sequences[31,56]

Name	Amino Acid Sequence	Source
Ponericins W1	WLGSALKIGAKLLPSVVGLFKKKKQ	*Pachycondyla goeldii*
Ponericins W2	WLGSALKIGAKLLPSVVGLFQKKKK	
Ponericins W3	GIWGTLAKIGIKAVPRVISMLKKKKQ	
Ponericins W4	GIWGTALKWGVKLLPKLVGMAQTKKQ	
Ponericins W5	FWGALIKGAAKLIPSVVGLFKKKQ	
Ponericins W6	FIGTALGIASAIPAIVKLFK	
Ponericins G1	GWKDWAKKAGGWLKKKGPGMAKAALKAAMQ	
Ponericins G2	GWKDWLKKGKEWLKAKGPGIVKAALQAATQ	
Ponericins G3	GWKDWLNKGKEWLKKKGPGIMKAALKAATQ	
Ponericins G4	DFKDWMKTAGEWLKKKGPGILKAAMAAAT	
Ponericins G5	GLKDWVKIAGGWLKKGPGILKAAMAAATQ	
Ponericins G6	GLVDVLGKVGGLIKKLLP	
Ponericins G7	GLVDVLGKVG GLIKKLLPG	
Ponericins L1	LLKELWTKMKGAGKAVLGKI	
Ponericins L2	LLKELWTKIKGAGKAVLGKIKGLL	

shown a wide range of anticancer and antiviral properties. There are several hindrances for the activity of AMPs on humans, like some synthetic degradation pathways, namely β-elimination, hydrolysis, oxidation, isomerization, and deamination.

To overcome hindrances, AMPs are now produced in pharmaceutical industries as L and D amino acids, which helps them to withstand proteolytic degradation.[24] The cancer cell has a resisting property called Multidrug Resistance (MDR), which makes them more drug-resistant. Some AMPs are also capable of killing cancer cells rapidly and have easier absorption with lower side effects. However, it has a greater disadvantage in the form of toxicity, permeability, stability, and route of drug administration.[59]

To screen potential AMP libraries, high throughput sequencing is being used, which was first used in the process of drug development in the late 1980s. As to the United Kingdom's five-year antimicrobial strategy 2013-2018, the number of highly resistant pathogens are rapidly increasing which will become increasingly difficult to maintain the public and animal health welfare. There is an urgent need for the development of new antibiotics, diagnostic methods, and novel therapies by promoting innovation and investment in the development of new resistant drugs. The AMPs were identified as alternatives for antimicrobials.[30,32,60] One of the AMP identified from the mosquito *Aedes aegypti* namely (BR003-Cecropin A), is effective against gram-negative bacteria. Recently, antimicrobial agents were identified using high throughput sequencing approaches, that are found to target *Pseudomonas aeruginosa*, *Candida albicans*.[61,62]

Table 11 gives a hint of few insect AMPs reported to have therapeutic properties. Some AMPs have shown the effect of immune-stimulation by provoking the process of chemokines, cell migration, and cell proliferation. Currently, there are more insect derived AMPs which are effective against pathogens affecting humans, namely, *Citrobacter freundii*, *Euterobacter aerogenes*, *K.pneumonia*, and *Legionella dumoffei*.[18,36,63-65] Some of the fungal species that are prone to some types of insect antimicrobial peptides include *Pichia pastoris*, *Trichoderma viridae*, and *Aspergillus fumigatus.* Various insect AMPs have been identified, including Mellitin derived from honeybee, which is effective against *Herpus simlex virus* and two types of alloferons identified from blowfly that are effective against type A and type B *Human influenza* virus.[30,66,67] The need for developing AMPs as a tool against AMR [68] and their resistance mechanisms has been also well documented.[69]

Table 11. Few Insect-based AMPs with Therapeutic Properties

S. No	Name/Class of AMP	Source/Order	Application	Reference
1	Cecropin A	*G. mellonella*	Destroys planktonic and sessile biofilm-forming UPEC cells	[79]
2	Cec B	*H. cecropia*	Improved the survival of mice bearing malignant ascites/antitumor activity	[80]
3	Cec XJ	*B. mori*	Antitumor activity proved in mouse models	[81]
4	Cec XJ	*B. mori*	Inhibits the proliferation of human gastric cancer cells and induces cell death both in vitro and in vivo	[81]
5	Cec XJ	*B. mori*	Induces cytoskeleton disruption in esophageal carcinoma cells	[82]
6	CSαβ - DLP2 and DLP4	*H. illucens*	Antibacterial and immunomodulatory activities of insect defensins-DLP2 and DLP4 against multidrug-resistant *S. aureus*	[83]
7	Defensin	Diptera, Hymenoptera, Coleoptera,Lepidoptera, Hemiptera, Isoptera, Odonata	Effective against *M. luteus, A. viridians, B. megaterium, B. subtilis, B. thuringiensis* and *S aureus.*	[84]
8	Tenecin - 1 & 3	*T. molitor*	Antineoplastic therapy. Inhibits proliferation of leukaemia cells	[84]
9	Hecate (Derivative of melittin)	*A. mellifer*	Active against Herpes simplex virus 1 (HSV-1)	[85]
10	Alloferons	*C. vicina*	Active against Human influenza viruses A and B	[86]

Table 12. Few Insect-based AMPs with Agriculture Significance

S. No	Name/Class of AMP	Source	Application	Reference
1	Attacin E	*H. cecropia*	Gets secreted into hemolymph upon bacterial infection; Phytopathogenic bacteria control of fire blight disease in Pear	[87]
2	Apidaecins	*A. melifera*	Transgenic potato showed improved activity against plant pathogenic bacteria belonging to Erwinia and Pseudomonas genera. Also active against Salmonella and Shigella species, Rhizobium and Agrobacterium species and	[88]
3	Heliomicin	*B. cinerea*	Transgenic tobacco showed resistance to variety of plant pathogenic bacteria	[89]
4	Drosomycin	*B. cinerea*	Transgenic tobacco showed resistance to variety of plant pathogenic bacteria	[89]
5	Sarcotoxin	*S. peregrina*	Transgenic tobacco effective against *P.syringae* pv. tabaci and *E. carotovora* ssp. carotovora	[78]
6	Cecropins A and B	*B. mori*	Transgenic rice (*Magneporthe grisea, Xanthomonas oryzae*) showed significant rersistance to yield reducing bacterial and fungal species	[90,91]
7	Magainin	Multiple insects	Highly effective against various fungal and bacterial species and significantly boosted the resistance when expressed in tobacco	[72]
8	Cecropin A	*G. mellonella*	Control of larval *Heliothis virescens* via microbial entomopathogens and disrupts the immune response against parasites	[92]
9	Attacin	*H. cecropia*	Resistance to Blackleg and soft rot diseases, caused by the bacterium *Erwinia carotovora* in potato	[93]
10	Tenecin - 1 & 3	*T. molitor*	Important for the feed industry not only because of the protection of animals	[84]

Insect AMPs in the Field of Agriculture

Insects inflict two types of damage to plants, one physical and the other that alters its physiological balance. The production losses in the field of agriculture at both pre- and post-harvest stage is highly immeasurable due to several microbial diseases which reduce the yield of products. About 14% of total loss of all crop production in the entire world is caused exclusively by microbial diseases. The beneficial role of AMPs in agriculture has been well documented. Using AMPs in the field of agriculture has been implemented in the 1980s when they were discovered. Still, they showed low activity against certain pathogens and more toxic effects against animal and human cells, so there is a need for specific AMPs to be designed and used to reduce this cause.[72,73] Transgenic expression of plant based defensin BrD1 exhibited clear insecticidal potential in comparison to the control. Expression of BrD1 in different plants may make them resistant to sucking insects.[74] Similar findings have already been reported on wheat, banana and other crops.[75] The floral defensins, PhDef1 and PhDef2 provide resistance against pathogens of banana.[76] Sarcotoxin-IA isolated from flesh fly, when genetically engineered into tobacco plant; dose dependent resistance to *Erwinia carotovora* subsp. carotovora (causing wild fire disease), *Pseudomonas syringae* pv. tabaci, (causing bacterial soft rot disease), *Rhizoctonia solani*, and *Pythium aphanidermatum*, was reported.[77,78]

D. melanogaster based proline-rich AMP Metchnikowin, when expressed in barley showed resistance to different fusarium spp, species from the phylum Ascomycota and in a dose-dependent manner against Basidiomycota phyla.[94,95] Fusing the active regions of different AMPs have given rise to chimeric AMPs which improved the impact of these AMPs on their target pathogens.[96,97] Commercially important species of *B. mori* has been reported to produce six classes of AMPs which renders immunity against the invading pathogens which include several bacteria [98] Resistance to *Xanthomonas axonopodis* by the transgenic sweet orange has been attributed to insect based Attacin-A gene coded signal peptide.[99,100] Cecropin boosts significant resistance in tomato plants against two major pathogens of tomato causing wilt and spot diseases.[101] A brief description of AMPs expressed in transgenic plants that confer partial resistance to pathogens has been well documented [102] and a list of few insect-based AMPs having applications in the agriculture field are listed in Table 12. Another major class of AMPs defensins, such as drosomycin and heliomicin expressed in tobacco, have proven to be effective against *B. cinerea*.[89] Some of the AMPs from animals have also been analyzed for the plant potential such as Magainin from frog and Cercopin from silk moth, mainly used in *in-vivo* and *ex-vivo* studies against the pathogens.[71] There are some complex factors in the plant micro-environment, which affect the activity between the pathogens and AMPs. AMPs, therefore, could well be the future of pest control.

Scope and Applications of AMPs

Diversity in insects offers an unprecedented scope for exploring human-friendly entities. Various studies, as mentioned earlier, have reported the presence and efficacy of insect-based AMPs.[104] Further mining of insect genomes and transcriptomes may well unearth a treasure of biologically

significant molecules. There is still a long way to go in the field of insect AMPs, and these have the potential to replace the existing drug compounds.

Natural therapeutic peptides have some drawbacks, and these could be overcome by insect AMPs, which could further lead us into peptide mimetics.[105] AMPs can play a more significant role in cancer therapeutics, especially skin cancer,[106] and other infections.[105] Their ability to negate resistance mechanisms and their broad-spectrum activity work in favour of AMPs.[107] Homology to mammalian peptides has been reported, and these could help us understand different human disorders.[108] Different AMPs can act as reference molecules that can be fine-tuned; by synthesizing derivatives of these AMP that will have good absorbance, bioavailability, with the least side effects.

Conclusion

AMPs have been reported from across life-forms and their presence in insects is expected to be much higher than anticipated. Insect-based AMPs predicted to thus-far give a great opportunity to assess their structural, chemical, biological and functional efficacy. Advancements in genomic and proteomic technologies have generated huge data which can be analyzed for the prediction of new class of AMPs and their interaction with the respective host's target. The clinical usage of AMPs is still limited due to high bioavailability, high specificity, potential hemolysis, low toxicity level, and limited drug-drug interaction. The success achieved in fighting blight and other types of bacterial and fungal pathogenic diseases through transgenic expression of attacins, drosocins, cecropins, melittins and defensins class of AMPs in potato, tomato, pear, tobacco could be extended to large-scale field-based assessments and be extended to other types of crops. Similarly, more in-vitro and in-vivo studies involving these AMPs could lead us to finding alternative anti-biotics and peptides of other therapeutic importance.

Acknowledgment

The authors thank the support and motivation provided by the management and administration of the SRM Institute of Science and Technology, India. The authors thank DST – SERB (YSS/2014/000293), India, for supporting them with a grant that led to this review article.

Declaration

The author Habeeb Shaik Mohideen has been publishing scientific articles earlier in the name of S. K. M. Habeeb/ Habeeb. S. K. M.

References

1. Izadpanah M, Khalili H. Antibiotic regimens for treatment of infections due to multidrug-resistant Gram-negative pathogens: An evidence-based literature review. J Res Pharm Pract. 2015;4(3):105-14. doi:10.4103/2279-042X. 162360
2. Najafi M, Lemon SM, Knobler SL, Burroughs T. The resistance phenomenon in microbes and infectious disease vectors: implications for human health and strategies for containment–workshop summary. Washington, DC: National Academies Press; 2003. doi:10.17226/10651
3. de Kraker ME, Stewardson AJ, Harbarth S. Will 10 million people die a year due to antimicrobial resistance by 2050?. PLoS medicine. 2016;13(11):e1002184. doi:10.1371/journal.pmed.1002184
4. Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Pediatrics. 2010;126(3):443-56. doi:10.1542/peds.2009-2959
5. Nesher L, Rolston KV. The current spectrum of infection in cancer patients with chemotherapy related neutropenia. Infection. 2014;42(1):5-13. doi:10.1007/s15010-013-0525-9
6. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathog Global health. 2015;109(7):309-18. doi:10.1179/2047773215Y.0000000030
7. Shrestha P, Cooper BS, Coast J, Oppong R, Thuy ND, Phodha T, et al. Enumerating the economic cost of antimicrobial resistance per antibiotic consumed to inform the evaluation of interventions affecting their use. Antimicrob Resist Infect Control. 2018;7(1):98. doi:10.1186/s13756-018-0384-3
8. Tonk M, Cabezas-Cruz A, Valdes JJ, Rego RO, Chrudimska T, Strnad M, Sima R, Bell-Sakyi L, Franta Z, Vilcinskas A, Grubhoffer L. Defensins from the tick Ixodes scapularis are effective against phytopathogenic fungi and the human bacterial pathogen *Listeria grayi*. Parasit Vectors. 2014;7(1):1-8. doi:10.1186/s13071-014-0554-y
9. Rahnamaeian M, Cytryńska M, Zdybicka-Barabas A, Vilcinskas A. The functional interaction between abaecin and pore-forming peptides indicates a general mechanism of antibacterial potentiation. Peptides. 2016;78:17-23. doi:10.1016/j.peptides.2016.01.016
10. Mattick AT, Hirsch A. Further observations on an inhibitory substance (nisin) from lactic *streptococci*. Lancet. 1947;5:5-8. doi:10.1016/s0140-6736(47)90004-4
11. Jenssen H, Hamill P, Hancock RE. Peptide antimicrobial agents. Clin Microbiol Rev. 2006;19(3):491-511. doi:10.1128/CMR.00056-05
12. Walkenhorst WF, Klein JW, Vo P, Wimley WC. pH dependence of microbe sterilization by cationic antimicrobial peptides. Antimicrob Agents Chemother. 2013;57(7):3312-20. doi:10.1128/AAC.00063-13
13. Ahn MJ, Sohn HI, Nan YH, Murugan RN, Cheong CJ, Ryu EK, et al. Functional and structural characterization of Drosocin and its derivatives linked O-GalNAc at Thr 11 residue. Bull Korean Chem Soc. 2011;32(9):3327-32. doi:10.5012/bkcs.2011.32.9.3327
14. Uccelletti D, Zanni E, Marcellini L, Palleschi C, Barra D, Mangoni ML. Anti-Pseudomonas activity of frog skin antimicrobial peptides in a *Caenorhabditis elegans* infection model: a plausible mode of action in vitro and in vivo. Antimicrob Agents Chemother. 2010;54(9):3853-60. doi:10.1128/AAC.00154-10
15. Yi HY, Chowdhury M, Huang YD, Yu XQ. Insect antimicrobial peptides and their applications. Appl Microbiol Biotechnol. 2014;98(13):5807-22. doi:10.1007/s00253-014-5792-6
16. Hoagland DT, Liu J, Lee RB, Lee RE. New agents for the treatment of drug-resistant *Mycobacterium tuberculosis*. Adv Drug Deliv Rev. 2016;102:55-72. doi:10.1016/j.addr.2016.04.026
17. Imler JL, Bulet P. Antimicrobial peptides in *Drosophila*:

structures, activities and gene regulation. Chem Immunol Allergy. 2005;86:1-21. doi:10.1159/000086648
18. Altincicek B, Vilcinskas A. Analysis of the immune-inducible transcriptome from microbial stress resistant, rat-tailed maggots of the drone fly *Eristalis tenax*. BMC Genomics. 2007;8(1):326. doi:10.1186/1471-2164-8-326
19. Stork NE, McBroom J, Gely C, Hamilton AJ. New approaches narrow global species estimates for beetles, insects, and terrestrial arthropods. Proc Natl Acad Sci U S A. 2015;112(24):7519-23. doi:10.1073/pnas.1502408112
20. Bovera F, Loponte R, Marono S, Piccolo G, Parisi G, Iaconisi V, et al. Use of *Tenebrio molitor* larvae meal as protein source in broiler diet: Effect on growth performance, nutrient digestibility, and carcass and meat traits. J Anim Sci. 2016;94(2):639-47. doi:10.2527/jas.2015-9201
21. Wilson K, Reeson AF. Density-dependent prophylaxis: evidence from Lepidoptera-*baculovirus* interactions?. Ecol Entomol. 1998;23(1):100-1. doi:10.1046/j.1365-2311.1998.00107.x
22. Zhang LJ, Gallo RL. Antimicrobial peptides. Curr Biol. 2016;26(1):R14-9. doi:10.1016/j.cub.2015.11.017
23. Huan Y, Kong Q, Mou H, Yi H. Antimicrobial peptides: classification, design, application and research progress in multiple fields. Front Microbiol. 2020;11:2559. doi:10.3389/fmicb.2020.582779
24. Nagarajan K, Marimuthu SK, Palanisamy S, Subbiah L. Peptide therapeutics versus superbugs: highlight on current research and advancements. Int J Pept Res Ther. 2018;24(1):19-33. doi:10.1007/s10989-017-9650-0
25. Chernysh S, Gordya N, Suborova T. Insect antimicrobial peptide complexes prevent resistance development in bacteria. PLoS One. 2015;10(7):e0130788. doi:10.1371/journal.pone.0130788
26. Shen W, He P, Xiao C, Chen X. From Antimicrobial Peptides to Antimicrobial Poly (α-amino acid) s. Adv Healthc Mater. 2018;7(20):1800354. doi:10.1002/adhm.201800354
27. Brogden KA. Antimicrobial peptides: pore formers or metabolic inhibitors in bacteria?. Nat Rev Microbiol. 2005;3(3):238-50. doi:10.1038/nrmicro1098
28. Kim IW, Lee JH, Subramaniyam S, Yun EY, Kim I, Park Jet al. De novo transcriptome analysis and detection of antimicrobial peptides of the American cockroach Periplaneta americana (Linnaeus). PLoS One. 2016;11(5):e0155304. doi:10.1371/journal.pone.0155304
29. Liu G, Kang D, Steiner H. Trichoplusia ni lebocin, an inducible immune gene with a downstream insertion element. Biochem Biophys Res Commun. 2000;269(3):803-7. doi:10.1006/bbrc.2000.2366
30. Mylonakis E, Podsiadlowski L, Muhammed M, Vilcinskas A. Diversity, evolution and medical applications of insect antimicrobial peptides. Philos Trans R Soc. B Biol. Sci. 2016;371(1695):20150290. doi:10.1098/rstb.2015.0290
31. Wu Q, Patočka J, Kuča K. Insect antimicrobial peptides, a mini review. Toxins. 2018;10(11):461. doi:10.3390/toxins10110461
32. Moy TI, Conery AL, Larkins-Ford J, Wu G, Mazitschek R, Casadei G, et al. High-throughput screen for novel antimicrobials using a whole animal infection model. ACS chem Biol. 2009;4(7):527-33. doi:10.1021/cb900084v
33. Hoffmann JA, Hetru C. Insect defensins: inducible antibacterial peptides. Immunol Today. 1992;13(10):411-5. doi:10.1016/0167-5699(92)90092-L
34. Zhao BC, Lin HC, Yang D, Ye X, Li ZG. Disulfide bridges in defensins. Curr Top Med Chem. 2016;16(2):206-19. doi:10.2174/1568026615666150701115911
35. Lambert J, Keppi E, Dimarcq JL, Wicker C, Reichhart JM, Dunbar B, et al. Insect immunity: isolation from immune blood of the dipteran *Phormia terranovae* of two insect antibacterial peptides with sequence homology to rabbit lung macrophage bactericidal peptides. Proc Natl Acad Sci U S A. 1989;86(1):262-6. doi:10.1073/pnas.86.1.262
36. Poppel AK, Vogel H, Wiesner J, Vilcinskas A. Antimicrobial peptides expressed in medicinal maggots of the blow fly *Lucilia sericata* show combinatorial activity against bacteria. Antimicrob Agents Chemother. 2015;59(5):2508-14. doi:10.1128/AAC.05180-14
37. Tonk M, Knorr E, Cabezas-Cruz A, Valdes JJ, Kollewe C, Vilcinskas A. *Tribolium castaneum* defensins are primarily active against Gram-positive bacteria. J Invertebr Pathol. 2015;132:208-15. doi:10.1016/j.jip.2015.10.009
38. Matsuyama K, Natori S. Purification of three antibacterial proteins from the culture medium of NIH-Sape-4, an embryonic cell line of *Sarcophaga peregrina*. J Biol Chemi. 1988;263(32):17112-6. doi:10.1016/S0021-9258(18)37505-7
39. Dushay MS, Roethele JB, Chaverri JM, Dulek DE, Syed SK, Kitami T, et al. Two attacin antibacterial genes of *Drosophila melanogaster*. Gene. 2000;246(1-2):49-57. doi:10.1016/S0378-1119(00)00041-X
40. Lu D, Geng T, Hou C, Huang Y, Qin G, Guo X. Bombyx mori cecropin A has a high antifungal activity to entomopathogenic fungus *Beauveria bassiana*. Gene. 2016;583(1):29-35. doi:10.1016/j.gene.2016.02.045
41. Hara S, Yamakawa M. Moricin, a Novel Type of Antibacterial Peptide Isolated from the Silkworm, *Bombyx mori* (*). J Biol Chem. 1995;270(50):29923-7. doi:10.1074/jbc.270.50.29923
42. Hemmi H, Ishibashi J, Hara S, Yamakawa M. Solution structure of moricin, an antibacterial peptide, isolated from the silkworm *Bombyx mori*. FEBS lett. 2002;518(1-3):33-8. doi:10.1016/S0014-5793(02)02637-6
43. Iwasaki T, Ishibashi J, Tanaka H, Sato M, Asaoka A, Taylor D, et al. Selective cancer cell cytotoxicity of enantiomeric 9-mer peptides derived from beetle defensins depends on negatively charged phosphatidylserine on the cell surface. Peptides. 2009;30(4):660-8. doi:10.1016/j.peptides.2008.12.019
44. Bluhm ME, Schneider VA, Schafer I, Piantavigna S, Goldbach T, Knappe D, et al. N-terminal Ile-Orn-and Trp-Orn-motif repeats enhance membrane interaction and increase the antimicrobial activity of apidaecins against *Pseudomonas aeruginosa*. Front Cell Dev Biol. 2016;4:39. doi:10.3389/fcell.2016.00039
45. Gobbo M, Biondi L, Filira F, Gennaro R, Benincasa M, Scolaro B, et al. Antimicrobial peptides: synthesis and antibacterial activity of linear and cyclic drosocin and apidaecin 1b analogues. J Med Chem. 2002;45(20):4494-504. doi:10.1021/jm020861d
46. Tamez-Guerra P, Valadez-Lira JA, Alcocer-Gonzalez JM, Oppert B, Gomez-Flores R, Tamez-Guerra R, et al. Detection of genes encoding antimicrobial peptides in Mexican strains of *Trichoplusia ni* (Hubner) exposed to *Bacillus thuringiensis*. J invertebr Pathol. 2008;98(2):218-27. doi:10.1016/j.jip.2008.02.008
47. Rao XJ, Xu XX, Yu XQ. Functional analysis of two lebocin-related proteins from *Manduca sexta*. Insect Biochem Mol Biol. 2012;42(4):231-9. doi:10.1016/j.ibmb.2011.12.005
48. Bao Y, Yamano Y, Morishima I. A novel lebocin-like gene from eri-silkworm, *Samia cynthia* ricini, that does not encode the antibacterial peptide lebocin. Comp Biochem Physiol B Biochem Mol Biol. 2005;140(1):127-31. doi:10.1016/j.cbpc.2004.09.022
49. Rayaprolu S, Wang Y, Kanost MR, Hartson S, Jiang H. Functional analysis of four processing products from multiple precursors encoded by a lebocin-related gene from *Manduca sexta*. Dev Comp Immunol. 2010;34(6):638-47. doi:10.1016/j.dci.2010.01.008

50. Reichhart JM, Essrich M, Dimarcq JL, Hoffmann D, Hoffmann JA, Lagueux M. Insect immunity. Isolation of cDNA clones corresponding to diptericin, an inducible antibacterial peptide from *Phormia terranovae* (Diptera) Transcriptional profiles during immunization. Eur J Biochem. 1989;182(2):423-7. doi:10.1111/j.1432-1033.1989.tb14848.x
51. Romanelli A, Moggio L, Montella RC, Campiglia P, Iannaccone M, Capuano F, et al. Peptides from Royal Jelly: studies on the antimicrobial activity of jelleins, jelleins analogs and synergy with temporins. J Pept Sci. 2011;17(5):348-52. doi:10.1002/psc.1316
52. Fontana R, Mendes MA, De Souza BM, Konno K, Cesar LM, Malaspina O, et al. elleines: A family of antimicrobial peptides from the Royal Jelly of honeybees (*Apis mellifera*). Peptides. 2004;5:919-28. doi:10.1016/j.peptides.2004.03.016
53. Levashina EA, Ohresser S, Bulet P, Reichhart JM, Hetru C, Hoffmann JA. Metchnikowin, a novel immune-inducible proline-rich peptide from *Drosophila* with antibacterial and antifungal properties. Eur J Biochem. 1995;233(2):694-700. doi:10.1111/j.1432-1033.1995.694_2.x
54. Levashina EA, Ohresser S, Lemaitre B, Imler JL. Two distinct pathways can control expression of the gene encoding the *Drosophila* antimicrobial peptide metchnikowin. J Mol Biol. 1998;278(3):515-27. doi:10.1006/jmbi.1998.1705
55. Orivel J, Redeker V, Le Caer JP, Krier F, Revol-Junelles AM, Longeon A, et al, new antibacterial and insecticidal peptides from the venom of the ant *Pachycondyla goeldii*. J Biol Chem. 2001;276(21):17823-9. doi:10.1074/jbc.M100216200
56. Johnson SR, Copello JA, Evans MS, Suarez AV. A biochemical characterization of the major peptides from the venom of the giant neotropical hunting ant *Dinoponera australis*. Toxicon. 2010;55(4):702-10. doi:10.1016/j.toxicon.2009.10.021
57. Akbari R, Hakemi-Vala M, Pashaie F, Bevalian P, Hashemi A, Pooshang Bagheri K. Highly synergistic effects of melittin with conventional antibiotics against multidrug-resistant isolates of *acinetobacter baumannii* and *pseudomonas aeruginosa*. Microb Drug Resist. 2019;25(2):193-202. doi:10.1089/mdr.2018.0016
58. Lee JK, Luchian T, Park Y. New antimicrobial peptide kills drug-resistant pathogens without detectable resistance. Oncotarget. 2018;9(21):15616-34. doi:10.18632/oncotarget.24582
59. Hutchings CJ, Koglin M, Olson WC, Marshall FH. Opportunities for therapeutic antibodies directed at G-protein-coupled receptors. Nat Rev Drug Discov. 2017;16(11):787-810. doi:10.1038/nrd.2017.91
60. Segalat L. Drug discovery: here comes the worm. ACS Chem Biol. 2006;1(5):277-8. doi:10.1021/cb600221m
61. Breger J, Fuchs BB, Aperis G, Moy TI, Ausubel FM, Mylonakis E. Antifungal chemical compounds identified using a *C. elegans* pathogenicity assay. PLoS Pathog. 2007;3(2):e18. doi:10.1371/journal.ppat.0030018
62. Desalermos A, Muhammed M, Glavis-Bloom J, Mylonakis E. Using *Caenorhabditis elegans* for antimicrobial drug discovery. Expert Opin Drug Discov. 2011;6(6):645-52. doi:10.1517/17460441.2011.573781
63. Rajamuthiah R, Jayamani E, Conery AL, Fuchs BB, Kim W, Johnston T, et al. A defensin from the model beetle *Tribolium castaneum* acts synergistically with telavancin and daptomycin against multidrug resistant *Staphylococcus aureus*. PLoS One. 2015;10(6):e0128576. doi:10.1371/journal.pone.0128576
64. Vonkavaara M, Pavel ST, Holzl K, Nordfelth R, Sjostedt A, Stoven S. *Francisella* is sensitive to insect antimicrobial peptides. J Innate Immun. 2013;5:50-9. doi:10.1159/000342468
65. Ursic-Bedoya R, Buchhop J, Joy JB, Durvasula R, Lowenberger C. Prolixicin: a novel antimicrobial peptide isolated from *Rhodnius prolixus* with differential activity against bacteria and *Trypanosoma cruzi*. Insect Mol Biol. 2011;20(6):775-86. doi:10.1111/j.1365-2583.2011.01107.x
66. Langen G, Imani J, Altincicek B, Kieseritzky G, Kogel KH, Vilcinskas A. Transgenic expression of gallerimycin, a novel antifungal insect defensin from the greater wax moth *Galleria mellonella*, confers resistance to pathogenic fungi in tobacco. Biol Chem. 2006;387(5):549-57. doi:10.1515/BC.2006.071
67. Imamura M, Wada S, Ueda K, Saito A, Koizumi N, Iwahana H, et al. Multipeptide precursor structure of acaloleptin A isoform, antibacterial peptides from the Udo longicorn beetle, *Acalolepta luxuriosa*. Dev Comp Immunol. 2009;33(10):1120-7. doi:10.1016/j.dci.2009.06.004
68. Moghaddam MM, Aghamollaei H, Kooshki H, Barjini KA, Mirnejad R, Choopani A. The development of antimicrobial peptides as an approach to prevention of antibiotic resistance. Rev Med Microbiol. 2015;26(3):98-110. doi:10.1097/MRM.0000000000000032
69. Moravej H, Moravej Z, Yazdanparast M, Heiat M, Mirhosseini A, Moosazadeh Moghaddam M, et al. Antimicrobial peptides: features, action, and their resistance mechanisms in bacteria. Microb Drug Resist. 2018;24(6):747-67. doi:10.1089/mdr.2017.0392
70. Lay FT, Anderson MA. Defensins-components of the innate immune system in plants. Curr Protein Pept Sci. 2005;6(1):85-101. doi:10.2174/1389203053027575
71. Broekaert WF, Terras FR, Cammue BP, Osborn RW. Plant defensins: novel antimicrobial peptides as components of the host defense system. Plant physiol. 1995;108(4):1353-58. doi:10.1104/pp.108.4.1353
72. Alan AR. Sensitivity of bacterial and fungal plant pathogens to the lytic peptides, MSI-99, magainin II, and cecropin B. Mol Plant-Microbe Interact. 2002;15(7):701-8. doi:10.1094/MPMI.2002.15.7.701
73. Wang G, Li X, Wang Z. APD2: the updated antimicrobial peptide database and its application in peptide design. Nucleic Acids Res. 2009;37:D933-7. doi:10.1093/nar/gk n823
74. Choi MS, Kim YH, Park HM, Seo BY, Jung JK, Kim ST, Kim MC, Shin DB, Yun HT, Choi IS, Kim CK. Expression of BrD1, a plant defensin from *Brassica rapa*, confers resistance against *Brown planthopper* (*Nilaparvata lugens*) in transgenic rices. Mol Cells. 2009;28(2):131-7. doi:10.1007/s10059-009-0117-9
75. Li Z, Zhou M, Zhang Z, Ren L, Du L, Zhang B, et al. Expression of a radish defensin in transgenic wheat confers increased resistance to *Fusarium graminearum* and *Rhizoctonia cerealis*. Funct Integr Genomics. 2011;11(1):63-70. doi:10.1007/s10142-011-0211-x
76. Ghag SB, Shekhawat UK, Ganapathi TR. Petunia floral defensins with unique prodomains as novel candidates for development of *Fusarium* wilt resistance in transgenic banana plants. PLoS One. 2012;7(6):e39557. doi:10.1371/journal.pone.0039557
77. Mitsuhara I, Matsufuru H, Ohshima M, Kaku H, Nakajima Y, Murai N, et al. Induced expression of sarcotoxin IA enhanced host resistance against both bacterial and fungal pathogens in transgenic tobacco. Mol Plant-Microbe Interact. 2000;13(8):860-8. doi:10.1094/MPMI.2000.13.8.860
78. Ohshimax M, Mitsuhara I, Okamoto M, Sawano S, Nishiyama K, Kaku F, et al. Enhanced resistance to bacterial diseases of transgenic tobacco plants overexpressing sarcotoxin IA, a bactericidal peptide of insect. The Journal of Biochemistry. 1999;125(3):431-5.

doi:10.1093/oxfordjournals.jbchem.a022304
79. Kalsy M, Tonk M, Hardt M, Dobrindt U, Zdybicka-Barabas A, Cytrynska M, et al. The insect antimicrobial peptide cecropin A disrupts *uropathogenic Escherichia coli* biofilms. NPJ Biofilms Microbiomes. 2020;6(1):1-8. doi:10.1038/s41522-020-0116-3
80. Moore AJ, Devine DA, Bibby MC. Preliminary experimental anticancer activity of cecropins. Pept Res. 1994;7(5):265-9.
81. Xia LJ, Wu YL, Ma J, Zhang FC. Therapeutic effects of antimicrobial peptide on malignant ascites in a mouse model. Mol Med Rep. 2018;17(5):6245-52. doi:10.3892/mmr.2018.8691
82. Xia L, Wu Y, Kang S, Ma J, Yang J, Zhang F. CecropinXJ, a silkworm antimicrobial peptide, induces cytoskeleton disruption in esophageal carcinoma cells. Acta Biochim Biophys Sin. 2014;46(10):867-76. doi:10.1093/abbs/gmu 070
83. Li Z, Mao R, Teng D, Hao Y, Chen H, Wang X, Wang X, et al. Antibacterial and immunomodulatory activities of insect defensins-DLP2 and DLP4 against multidrug-resistant *Staphylococcus aureus*. Sci Rep. 2017;7(1):1-6. doi:10.1038/s41598-017-10839-4
84. Jozefiak A, Engberg RM. Insect proteins as a potential source of antimicrobial peptides in livestock production. A review. J Anim Feed Sci. 2017;26(2):87-99. doi:10.22358/jafs/69998/2017
85. Kruse T, Kristensen HH. Using antimicrobial host defense peptides as anti-infective and immunomodulatory agents. Expert Rev Anti Infect Ther. 2008;6(6):887-95. doi:10.1586/14787210.6.6.887
86. Chernysh S, Kim SI, Bekker G, Pleskach VA, Filatova NA, Anikin VB, et al. Antiviral and antitumor peptides from insects. Proc Natl Acad Sci U S A. 2002;99(20):12628-32. doi:10.1073/pnas.192301899
87. Reynoird JP, Mourgues F, Norelli J, Aldwinckle HS, Brisset MN, Chevreau E. First evidence for improved resistance to fire blight in transgenic pear expressing the attacin E gene from *Hyalophora cecropia*. Plant Sci. 1999;149(1):23-31. doi:10.1016/S0168-9452(99)00139-9
88. Casteels P, Ampe C, Jacobs F, Vaeck M, Tempst PJ. Apidaecins: antibacterial peptides from honeybees. EMBO J. 1989;8(8):2387-91. doi:10.1002/j.1460-2075.1989.tb08368.x
89. Banzet N, Latorse MP, Bulet P, Francois E, Derpierre C, Dubald M. Expression of insect cystein-rich antifungal peptides in transgenic tobacco enhances resistance to a fungal disease. Plant Sci. 2002;162(6):995-1006. doi:10.1016/S0168-9452(02)00053-5
90. Coca M, Bortolotti C, Rufat M, Penas G, Eritja R, Tharreau D, et al. Transgenic rice plants expressing the antifungal AFP protein from *Aspergillus giganteus* show enhanced resistance to the rice blast fungus *Magnaporthe grisea*. Plant Mol Biol. 2004;54(2):245-59. doi:10.1023/B:PLAN.0000028791.34706.80
91. Sharma A, Sharma R, Imamura M, Yamakawa M, Machii H. Transgenic expression of cecropin B, an antibacterial peptide from *Bombyx mori*, confers enhanced resistance to bacterial leaf blight in rice. FEBS lett. 2000;484(1):7-11. doi:10.1016/S0014-5793(00)02106-2
92. Shelby KS. Induction of antimicrobial peptides in infected tissues of larval *Heliothis virescens* (*Lepidoptera*: *Noctuidae*). Fla Entomol. 2014:921-7. doi:10.1653/024.0 97.0350
93. Arce P, Moreno M, Gutierrez M, Gebauer M, Dell'Orto P, Torres H, et al. Enhanced resistance to bacterial infection by *Erwinia carotovora* subsp. atroseptica in transgenic potato plants expressing the attacin or the cecropin SB-37 genes. Am J Potato Res. 1999;76(3):169-77. doi:10.1007/BF02853582
94. Rahnamaeian M, Langen G, Imani J, Khalifa W, Altincicek B, Von Wettstein D, et al. Insect peptide metchnikowin confers on barley a selective capacity for resistance to fungal ascomycetes pathogens. J Exp Bot. 2009;60(14):4105-14. doi:10.1093/jxb/erp240
95. Rahnamaeian M, Vilcinskas A. Defense gene expression is potentiated in transgenic barley expressing antifungal peptide metchnikowin throughout powdery mildew challenge. J Plant Res. 2012;125(1):115-24. doi:10.1007/s10265-011-0420-3
96. Yevtushenko DP, Romero R, Forward BS, Hancock RE, Kay WW, Misra S. Pathogen-induced expression of a cecropin A-melittin antimicrobial peptide gene confers antifungal resistance in transgenic tobacco. J Exp Bot. 2005;56(416):1685-95. doi:10.1093/jxb/eri165
97. Khademi M, Varasteh-Shams M, Nazarian-Firouzabadi F, Ismaili A. New Recombinant Antimicrobial Peptides Confer Resistance to Fungal Pathogens in Tobacco Plants. Front Plant Sci. 2020;11:1236. doi:10.3389/fpls.2020.01236
98. Nesa J, Sadat A, Buccini DF, Kati A, Mandal AK, Franco OL. Antimicrobial peptides from *Bombyx mori*: a splendid immune defense response in silkworms. RSC Adv. 2020;10(1):512-23. doi:10.1039/C9RA06864C
99. Cardoso SC, Barbosa-Mendes JM, Boscariol-Camargo RL, Christiano RS, Bergamin Filho A, Vieira ML, Mendes BM, Mourro Filho FD. Transgenic sweet orange (Citrus sinensis L. Osbeck) expressing the attacin A gene for resistance to *Xanthomonas citri* subsp. citri. Plant Mol Biol Rep. 2010;28(2):185-92. doi:10.1007/s11105-009-0141-0
100. Boscariol RL, Monteiro M, Takahashi EK, Chabregas SM, Vieira ML, Vieira LGet al. Attacin A Gene from *Tricloplusia ni* Reduces Susceptibility to *Xanthomonas axonopodis* pv. citri in Transgenic *Citrus sinensis'Hamlin'*. J Am Soc Hortic Sci. 2006;131(4):530-6. doi:10.21273/JASHS.131.4.530
101. Jan PS, Huang HY, Chen HM. Expression of a synthesized gene encoding cationic peptide cecropin B in transgenic tomato plants protects against bacterial diseases. Appl Environ Microbiol. 2010;76(3):769-75. doi:10.1128/AEM.00698-09
102. Montesinos E. Antimicrobial peptides and plant disease control. FEMS microbiol lett. 2007;270(1):1-11. doi:10.1111/j.1574-6968.2007.00683.x
103. Bechinger B, Lohner K. Detergent-like actions of linear amphipathic cationic antimicrobial peptides. Biochim Biophys Acta-Biomembr. 2006;1758(9):1529-39. doi:10.1016/j.bbamem.2006.07.001
104. Wojda I, Cytryńska M, Zdybicka-Barabas A, Kordaczuk J. Insect Defense Proteins and Peptides. Vertebrate and Invertebrate Respiratory Proteins, Lipoproteins and Other Body Fluid Proteins. Subcell Biochem. 2020;94:81-121. doi:10.1007/978-3-030-41769-7_4
105. Tonk M, Vilcinskas A. The medical potential of antimicrobial peptides from insects. Curr Top Med Chem. 2017;17(5):554-75. doi:10.2174/1568026616666160713123654
106. Tonk M, Vilcinskas A, Rahnamaeian M. Insect antimicrobial peptides: potential tools for the prevention of skin cancer. Appl Microbiol Biotechnol. 2016;100(17):7397-405. doi:10.1007/s00253-016-7718-y
107. Wang S, Zeng X, Yang Q, Qiao S. Antimicrobial peptides as potential alternatives to antibiotics in food animal industry. Int J Mol Sci. 2016;17(5):603. doi:10.3390/ijms17050603
108. Chowanski S, Adamski Z, Lubawy J, Marciniak P, Pacholska-Bogalska J, Slocinska M, et al. Insect peptides–perspectives in human diseases treatment. Curr Med Chem. 2017;24(29):3116-52. doi:10.2174/0929867324666170526120218