FRONTIERS IN CURRENT ASPECTS OF ANTIMICROBIAL PEPTIDES FROM INSECTS AND THEIR THERAPEUTIC PERSPECTIVES

Abstract

The abuse of antibiotics leads to antibiotic resistance, a major clinical challenge. The demand for better antibiotics is growing in the era of rogue microbes with a sophisticated mechanism to evade the immune system and equipped with improved drug resistance mechanisms. The search and development of new antimicrobial compounds and the evolution of drug-resistant microbes is a cat and mouse game. Nevertheless, with the discovery of antimicrobial peptides (AMPs), new hope is emerging for effective combat against drug-evasive microbes. AMPs with a broad-spectrum antibacterial activity are expected to become the alternative antibiotics through the development of AMPs-based therapies. Antimicrobial peptides are short unique peptides of either basic or amphipathic character, having a length between 12 to 50 residues. They are predominantly found to be membrane proteins but also have few cytoplasmic targets. Nisin is the first AMP identified from bacteria found to kill other bacteria in a competitive, nutritional environment. Since then, the DRAMP database has reported 3791 antimicrobial peptides, including 431 from bacteria, 4 from archaea, 7 from protozoa, 6 from fungal, 824 from plants and 2519 from animals. They also possess other pharmacological activities besides antimicrobial activity, such as immune modulation, antiangiogenic, and wound healing activity. We review the historical developments in antimicrobial peptide drug discovery, their classification, mechanism of action, molecular biology and their application.

Keywords: Antimicrobial peptides (AMPs), Mechanism of action, Classification, AMP applications

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I. INTRODUCTION

The relationship between the eukaryotic and prokaryotic organisms in the historical and ecological niche has been raised since the appearance of these microns. They exhibit a symbiotic relationship with each other like parasitism, mutualism and commensalism to play an important role in the evolutionary criteria. Insects are considered the most successfully evolved animal taxon on earth. These insects exhibit the highest capacity to produce peptide proteins against the activity of bacteria, fungus and viral infections that are regarded as antimicrobial peptides. Antimicrobial peptides provide a potential strategy for the recovery of threats like bacterial, viral and fungal infections. They are considered the highly conserved molecule or immune effectors across the life tree. Protein peptides known as antimicrobial peptides are a type of naturally occurring first line of defense against diseases, including those that affect both bacteria and mammals. Of the 3087 antimicrobial peptides reported in the antimicrobial peptide database (APD), only 305 have been obtained from insects [1].

Antimicrobial peptides can be designated as a novel pharmaceutical candidate that is used to treat pathogenic microorganisms, antibiotic resistance microbial species and even cancers. Exhibition of cytotoxic effects against diverse cancer cell lines is a significant property of insect antimicrobial peptides. These peptides are effective against several types of cancer; they may be mouse myeloma, melanoma, lymphoma, leukemia, breast cancer and lung cancer [2]. The varied mechanisms of action (MOA) of antimicrobial peptides encompass several actions such as membrane disruption, suppression of DNA and protein synthesis, and impairment of cellular functions, including metabolism and cell wall formation. This peptide significantly promotes adaptability and survival during antagonistic competition with other bacteria found in a related ecological niche. Comparing the antimicrobial peptides to the current anticancer medicines, they represent a promising next-generation medication with many modes of action. Peptides' antibacterial action is cell-specific. Positively charged amino acids, notably arginine (R) and lysine (K), and negatively charged phospholipids in the bacterial membrane interact electrostatically to cause the interaction between peptides and the cell membrane. Such as zwitter ionic phosphatidyl ethanolamine and phosphatidyl glycerol (PG)[3]. The antibacterial repertoire also contains a few smaller proteins. A prepo mode or form of an antimicrobial peptide is actually created nearly 130 times more quickly than Igm [4]. Since ancient times, these antimicrobial peptides have been life-saving treatments for several infectious disorders. The entry of germs into the host body is controlled and prevented. When multidrug-resistant organisms emerged and spread over time, these antimicrobial medicines' actions or discoveries steadily reduced. The World Health Organization has recently listed the necessary antimicrobial peptides. According to how urgently new antibiotics are needed, they have divided the developing antibiotics into three groups: critical, high, and medium priority. Although numerous gram-positive bacteria species are on the high priority list, the gram-negative bacteria species have the highest priority. Numerous studies targeting new antibiotics against multi-drug resistant bacteria (MRD) and new anticancer treatments have focused on antimicrobial and anticancer peptides. Antimicrobial peptides often contain hydrophobic and hydrophilic moieties with a significantly positive net charge. They are also cationic and amphipathic. They can be effective against a variety of pathogens and can exhibit potent antibacterial effects against bacteria resistant to antibiotics [5].

This chapter explains the structure, description and molecular biology and biological properties of insect antimicrobial peptides with their application. Several insect antimicrobial peptides are explained here, they are cecropin, defensin, attacin, melittin, metchnikowin, apisimin, moricin, gloverin, diptericin, coprisin, papiliocin, abaecin, drosocin, lebocin, pyrrrhocoricin, jelliene, ponericin and persulcatusin.

II. BRIEF HISTORY OF ANTIMICROBIAL PEPTIDES

The middle of the 20th century focused on these antimicrobial peptides for research [6]. Since then, numerous types of molecules with antibiotic action have been discovered in animals, insects, plants, and bacteria, and their usage has transformed clinical medicine [7]. Moths, bees, and frogs, along with some butterflies, are among the most common eukaryotic animals [6]. Lysozyme was the first naturally occurring antibiotic to be extracted from our bodies, and Alexander Fleming identified its antibacterial action about 90 years ago [8]. The "Golden Age of Antibiotics" then began, which resulted in a decline in interest in natural host antibiotics and the increased importance of immune defense strategies. In the 1960s, multidrug-resistant microbial infections emerged after the "golden age of antibiotics". They were injecting bacteria into pupae allowed to demonstrate the inducible cationic antimicrobial proteins from the Hylophora cacropia moth. Based on similarities in sequences, strictures, and modes of action, as well as the inter functionality of these peptides from other kingdoms, all defensins developed from a single precursor [6]. Since 1939, when Gramicidin's and other antimicrobial compounds were discovered, prokaryotic cells have included antimicrobial peptides [8]. Today's world health organization considers antibiotic resistance one of the main dangers to global public health due to the misuse and overuse of antibiotics in recent years due to the diversity of insects, the biggest group of organisms in the animal kingdom [5]. Understanding the intricacy of the human immune system is improved by research on the natural immune systems of insects. There is mounting proof that insects' natural immune systems are significantly more complicated than one might anticipate [9].

III. INSECT POLYPEPTIDES REPORTED AS ANTIMICROBIAL AGENTS

Always insect's innate immune system is composed of cellular and humoral mechanisms. The cellular mechanism relies on enzymatic activation that consists of phagocytosis and is encapsulated by haemolymph. But like humoral response is associated with producing a broad spectrum of molecules, including cationic antimicrobial peptides. Till now, venom from bees is considered a microbial agent against coronary illness, cancer therapy and skin disorders.

1. **Structure-activity of antimicrobial peptides from insects:** These antimicrobial peptides are always categorized based on amino acid substitutions. It consists of around 7 to 100 amino acids and is sub-grouped on the criteria of amino acid structure and composition [10]. These have secondary structures, majorly based on 4 themes; 1) α-helical, 2) β-stranded, 3) β-hairpin and 4) extended conformation. Single drugs are always used to treat or clear infections in antibiotics treatment. Bacteria develop a better resistance against several ubiquitous antimicrobial peptides. These insect antimicrobial peptides can kill bacteria in various ways, including bacterial membrane disruption, interference with pathogen metabolism, and destroying the cytoplasm contents. Antimicrobial peptides

exhibit membrane activity in various ways, including the Carpet, Toroidal, Barrel-stave, and Disordered Toroidal Pore modes [11].

AMPs exhibit a variety of antibacterial, antifungal, and antiviral properties. They exhibit promising potential in therapeutic and prophylactic uses [2, 12]. These peptides can kill many pathogenic microorganisms by physically breaking microbial cellular membranes. As a result, AMPs are typically thought to be more effective against the microbial membrane [13,14]. Additionally, these peptides make excellent candidates for therapies that combine them with traditional antibiotics due to their exceptional membrane disrupting action [15]. AMPs can make it easier for more antibiotic molecules to penetrate the cytoplasm of the microbe, where they can engage with their intended target (Figure 1).

AMPs kill bacteria in several ways, including membrane rupture, bacterial metabolism disruption, and cytoplasmic components targeting [16]. The target bacterium and the AMP make their initial contact by an electrostatic or hydrophobic interaction, which is highly dependent on the lipid structure of the bacterial membrane [17]. The permeability of the cell membrane can be changed by interactions between AMPs and the surface of the membrane [14]. Osmotic pressure is impacted by the transmembrane potential that forms after AMPs interact with the cell membrane. In other words, the antibacterial activity of the AMPs is directly correlated with how the AMPs interact with the membrane. At the moment, the terms barrel-stave, carpet, toroidal-pore, and disordered toroidal-pore are frequently used to describe the membrane activity of AMPs [16]. A threshold concentration is needed to conduct each of these modalities. Currently, the membrane activity of AMPs is typically described by at least four different modes of action: barrel-stave, carpet, toroidal pore, and disordered toroidal pore [14]. The antibacterial effect must be conducted for each of these mechanisms at a threshold concentration [14]. When AMPs translocate into the pathogens, they can also damage intracellular enzymes and DNA [12]. Some concerns need to be taken into account concerning AMPs' membrane action. For instance, whether a specific membrane receptor exists and whether other elements cooperate in this situation. Additional study is required because the mechanisms of action of various AMPs may vary.

Peptides with antimicrobial properties also exhibit anticancer properties. Many anticancer peptides (ACP) have significant therapeutic efficacy, a minimal likelihood of target cell resistance developing, and little to no damage to mammalian erythrocytes, macrophages, or fibroblasts. Moreover, because they are biocompatible, anticancer peptides are simple to make and manipulate. Anticancer peptides' active motifs are simple to create, adapt, and change. They also effectively penetrate tumors and are biocompatible. The short active motifs of some anticancer peptides exhibit intrinsic anticancer activity and increase the potency of common medications. In the antimicrobial peptide database (APD) (https://aps.unmc.edu/database/anti), there are about 265 entries that describe peptides with anticancer activity. Most anticancer peptides cause cell membrane disruption through lytic activity or trigger apoptosis in cancer cells through mitochondrial damage, frequently causing little harm to healthy mammalian cells. More antibiotic molecules may enter the microorganism's cytoplasm through antibacterial peptides, where they can interact with their intended target [9]. As an illustration, the

cecropin B from Hylophora cecropia prolonged the longevity of mice carrying ascetic murine colon adenocarcinoma cells [2].

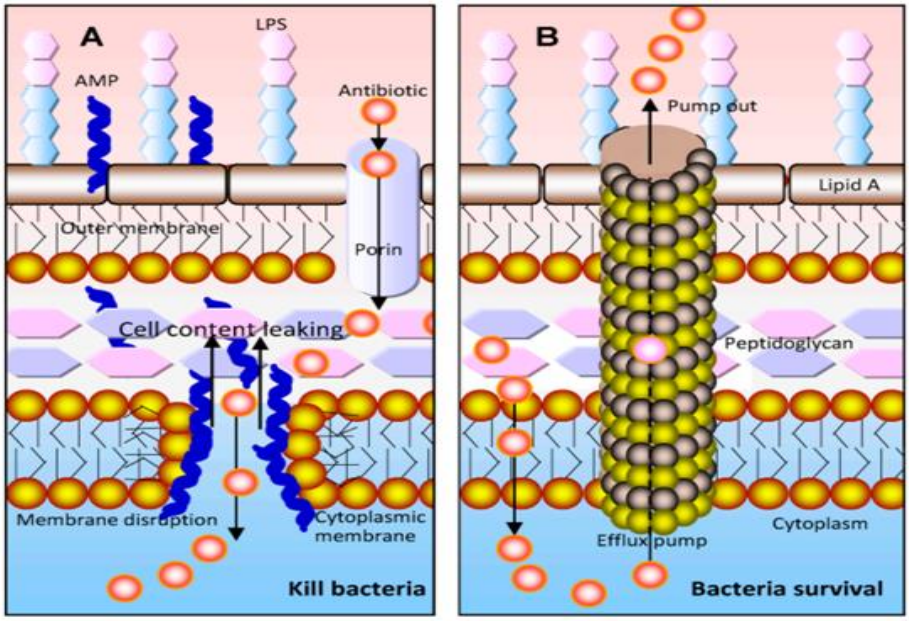
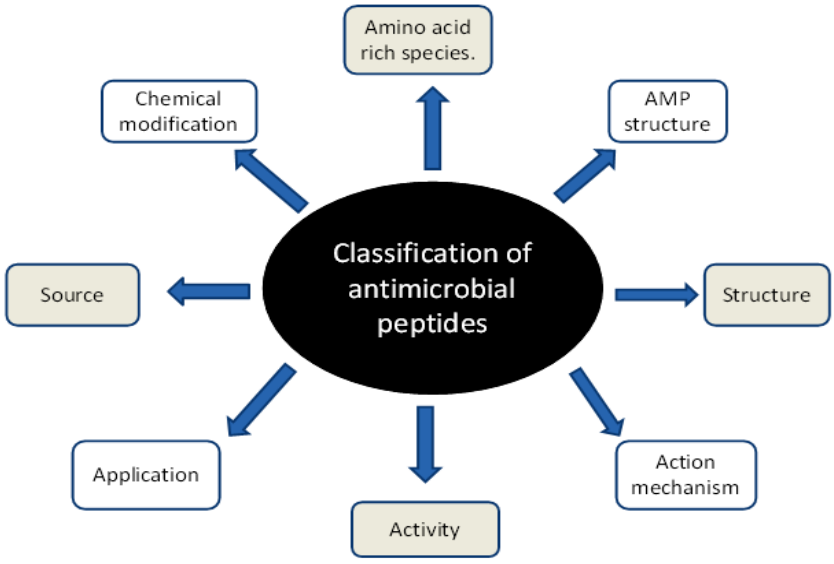


Figure 1: A) Antimicrobial peptides and antibiotic effects on bacteria. This shows the interaction of the peptide with the cytoplasm and the breakdown of the bacterial cell wall by antimicrobial peptides; B) Represents the inhibition or resistance to antibiotics by bacteria through efflux pumps [15].

2. **Classification of antimicrobial peptides:** The antimicrobial peptides are categorized based on several factors like source, activity, structure, amino acid-rich species, action mechanism, chemical modification, and application (Figure 2A and B).



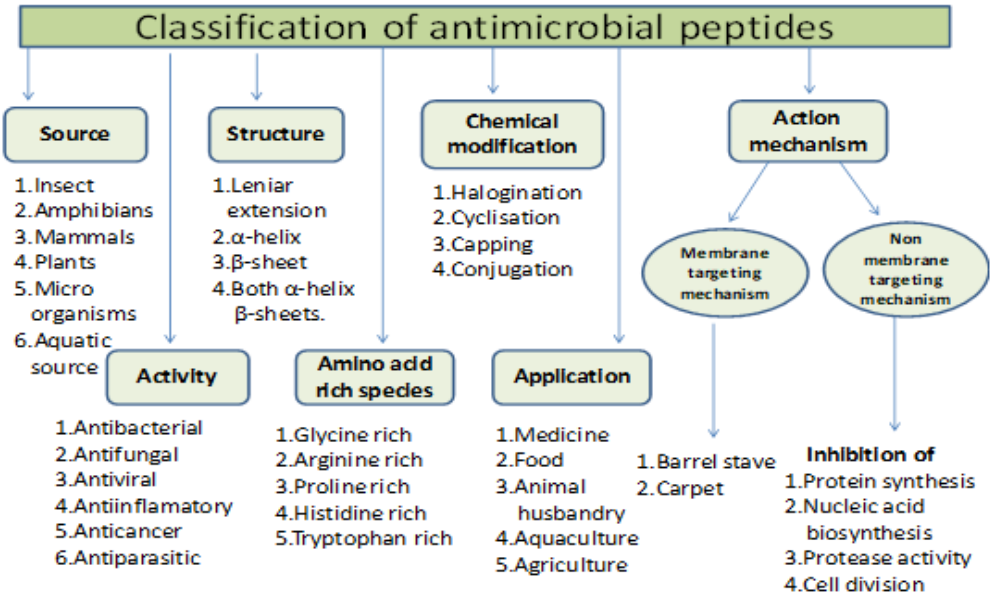


Figure 2: (A) Classification of antimicrobial peptides; (B) Representation of classification in a descriptive manner.

IV. ANTIMICROBIAL PEPTIDES FROM INSECTS

1. **Cecropins:** The term "cecropin" derives from the fact that cecropins were first discovered in the hemolymph of the giant silk moth Hyalophora cecropia (cecropia moth). These are the tiny, cystine-free proteins (around 35 amino acid residues). Other names for insect cecropin include bactericidin, lepidopteran, sarcotoxin, etc. These peptides are mainly composed of numerous antibacterial and poisonous peptides identified from various lepidopteran and dipteran species. These peptides are an important component of insects' cell-free immunity [9]. This was the one that was initially discovered around 40 years ago, and it was investigated for both its physiological role in insect immunity and prospective replacements for traditional antibiotics in the treatment of infectious disorders. Table 1 also provided examples of the structurally related cecropin peptides.

Table 1: The Structurally Related Cecropin Peptides

Sl. no	Cecropin	Accession number
1.	Cecropin A	AAP93872.1
2.	Cecropin B	AAA29184.1
3.	Cecropin B1	1703262B
4.	Cecropin C	AAF57028.1
5.	Cecropin D	AAA29186.1
6.	Cecropin D2	NP_001036924.2

The AMP Cecropin A has a stable α-helical structure [18]. The cell membrane serves as its target site, and Cecropin A induces apoptosis and is controlled by an ion imbalance [19]. Cecropin A (cec A), from the greater wax moth Galleria mellonella, was

discovered to be effective at eradicating biofilms created by uropathogenic Escherichia coli in several of the case studies that tested those insect AMPs for anti-biofilm activity (UPEC) [20]. A naturally occurring linear cationic peptide of 35 amino acids is called cecropin B. This has the highest level of antibacterial action [21]. Low levels of cecropin C are found in H. cecropia's hemolymph [22]. The homology between Cecropin D and Cecropin A and B is evident. Both gram-positive and gram-negative bacteria are susceptible to its action, which is expressed in Pichia pastoris [23]. Ascaris suum, a parasitic worm found in the intestine of pigs, is the source of cecropin P1. When combined with the C-terminal area of the lipopolysaccharide of gram-negative bacteria's outer membrane, cecropin P1 can create an α-helical structure. With a low inhibitory concentration (MIC), it also successfully prevents the growth of enterotoxigenic E. coli. A 36-residue cecropin known as lucilin was found in Lucilia sericata maggots as a partial genomic sequence [9].

The majority of insect cecropins contain peptide residues rather than cystiene. These have the ability to block proline uptake, lyse bacterial cell membranes, and create leaky membranes. Cecropin A can cause oxidative stress by creating reactive oxygen species by dramatically lowering NADPH and glutathione levels (ROS). Cecropin peptides are first organized as antiparallel dimmers with adjacent monomers' conserved residues in contact. The NH2-terminal helices of the dimers may bind to the membrane while being buried within the head group layer [24]. Cecropin B dramatically lowers plasma endotoxin levels and the lethality of the E. coli load in a rat model of septic shock [25]. Additionally, it exhibits antifungal properties against Candida albicans. Due to active phosphorylation, Cecropin D's C-terminal lysine residue may have increased antibacterial action [26]. Additionally, it prevents the infection and in vitro multiplication of the swine reproductive and respiratory syndrome virus [27]. According to Tellez and Castao-Osorio [28], the fusion protein exhibits potential action against the multidrug-resistant (MRD) strain of the E. coli bacterium.

It was discovered through phylogenetic analysis and single genome sequencing that gene evolution's birth and death paradigm was used to create the insect cer and cecropin-like peptides. The presence of transposable elements in the 5" and 3" flanking areas and frequent gene duplication within species provide evidence that gene duplication events have occurred. According to a phylogenetic study, the lepidopteran cec’s comprise a monophyletic group and independently developed in this order of insects [29]. Following experimental and computational research, cec and cec-like peptides share structural similarities. They are distinguished by an N-terminal base, amphipathic domains connected to a more hydrophobic C-terminal segment, and a flexible proline and glycine-rich hinge region (Figure 3A) [1]. It is widely accepted that Cec peptides initially bind with the bacterial membrane along the axis of the α-helical domains parallel to the lipid bilayer surface rather than engage with particular receptors. According to Sato and Feix [30], at this level, the polar residues of the peptide engage with the lipid phosphates while the non-polar side chains slither into the hydrophobic center of the membrane (Figure 3).

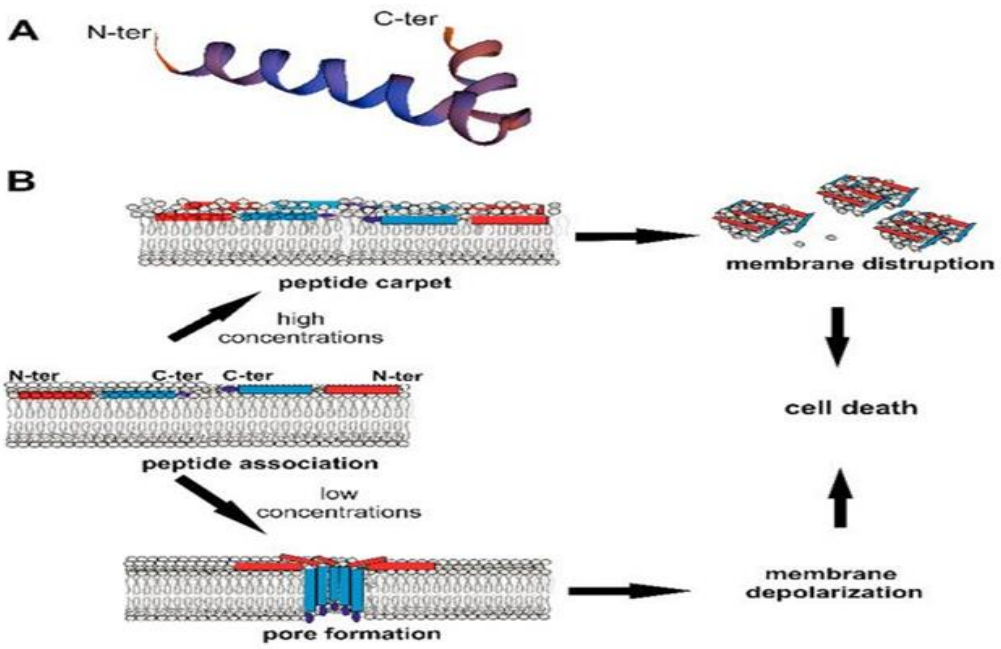


Figure 3: (A) Cecropin B, a natural variation identified from the bacterium B. mori, displays N and C terminal α-helices joined by a flexible hinge region.; (B) Mechanism of antibacterial activity. When cecropin interacts with the bacterial membrane, its non-polar residues are buried in the hydrophobic core while its polar residues react with the lipid bilayer. Cell death is eventually brought on by cecropin, which interacts in a carpet-like manner and disrupts membranes [1].

Insects belonging to the cecropin family exhibit antibacterial activity against gram-positive bacteria. Additionally, it exhibits promising action against fungi, including Candida albicans ECT and Beauveria bassiana. Cecropin/melittin (CAME) hybrid peptides are well-known AMP analogues, as is well known. It demonstrates novel antibacterial properties on the pathway that triggers apoptosis [31]. Bacillus bombyseptis, Bacillus subtilis, Bacillus thurengenesis, Escherichia coli, Pseudomonas aeruginosa, Serratia marcescens, and Rulstonia solaanacenum are all susceptible to its bactericidal effects [32]. Given their new mechanism of action against pathogenic cells, which lowers the possibility of resistance arising in comparison to the usage of antibiotics, these are promising options for eradicating biofilms [20].

2. **Defensins:** The word "defensins," which means to "repel," is derived from the Latin word defend. There are numerous antimicrobial peptides called defensins that belong to a large family. They promote the small intestine's mucosal host defense, the skin's epithelial host defense, and the granulocytes' antimicrobial function [33]. Neutrophils and macrophages produce a group of powerful antibiotics in the body. These arginine-rich cationic peptides are tiny family members. More than 300 defensins have been discovered so far, and they are not just exclusive to insects. Ancient natural antibiotics known as defensin peptides have potent antibacterial activity against various pathogens [33].

They have between 18 and 45 amino acids and 6 to 8 conserved cysteine residues. Classical α-defensins are composed of insect defensins and 29–35 amino acids. 29–34 amino acids are present in defensins [34]. An α-hairpin is the primary structural component of the defensin molecule, typically stabilized by three disulfide bonds. Defensins from insect orders such Diptera, Hymenoptera, Co. Leopteran, Trichoptera, Hemiptera, and Odonata are separated. Except for insect defensins, all AMP kinds have been found in lepidopteran insects. Royalisin was extracted from Apis mellifera royal jelly. It is an amphipathic protein with a total of 51 amino acids. Charged amino acids are abundant in its C-terminal [35].

Figure 4: Insect defensins have a distinctive structure with a conspicuous α-helical segment connected to the C-terminal β-sheet by two disulfide links [33].

Arginine-rich cationic peptides make up the majority of the known insect defensins. The binding of defensins to the cell membrane or the formation of pore-like membrane defects allow for the outflow of vital ions and nutrients. Defending against invasive microorganisms is crucial [36]. Alternatively, it is known as a human neutrophil peptide (HNP). Multidrug-resistant Pseudomonas aeruginosa strains are affected by the Defensins from rabbit neutrophils [37]. The amphipathic property of royalisin. capable of eradicating Paenibacillus larvae, a bee pathogen. According to Blikova et al. [38], it results in American foulbrood. Inducible antibacterial peptides known as insect defensins are active against gram-positive and gram-negative bacteria. They easily defeat staphylococcus aureus and other gram-positive bacteria. These peptides work less well against gram-negative bacteria, however. Bacteria and fungi are inhibited by royalisin [38]. Numerous bacteria, such as Micrococcus luteus, Aerococcus viridians, Bacillus megaterium, Bacillus turengenesis, etc. are susceptible to these peptides' activity [32].

3. **Attacins:** The first attacins were found in Hylophora cecropia. Glycine-rich proteins from the AMP group are what these are [39]. They are categorized as Attacins A through F, isolated from the hemolymph of vaccinated cecropia moth pupae (Hylophora cecropia). Based on the amino acids they contain, the attacins A through F can be split into two groups: the basic attacins A through D and the acidic attacins E and F. Each group's shapes are remarkably similar (Figure 5) [9].

Figure 5: A-F Attacins' Amino-Terminal Sequence. The Highlighted (red) Residues Allow Seeing Their Different Sequences [9].

Three of the four basic attacin peptides and two acidic peptides shared an identical N-terminal sequence. In contrast to many other known AMPs, attacin adopts a random coil secondary structure in an aqueous buffer and does not exhibit any shift to helical shape in an anisotropic environment [40]. Prior to antibacterial characterization, attacins must be generated as recombinant proteins due to their size. Bombyx mori, Glossina morsitans (tse-tse fly), Helionthis virescens, Trychoplusia ni, Samia Cynthia ricini (wild silk moth), and Musa domestic (house fly) are a few species from which attacins and attacin-related proteins have been identified [41].

Most insect attacins include 10–24% or more glycine residues. These attacins prevent the key outer membrane proteins in dividing gram-negative bacteria from synthesizing. Consequently, the cell wall's integrity is compromised, which encourages the growth of lengthy chains of bacteria. The inducible immune protein P5 has an antibacterial function in the form of attacins. Attacins are the third antibacterial protein in the humoral immune system of Hylophora cecropia, after Cecropin and Lysozyme. Against gram-negative bacteria, attacins are quite effective. These glycine-rich peptides have anti-E. coli activity. The intriguing and understudied class of insect AMPs known as attacins merits more research to clarify its potential therapeutic applications [42].

4. **Mellitin:** A peptide toxin called melettin, which is present in bee venom, effectively kills germs. With 26 amino acid residues, this peptide has a linear structure. One of the most well-known membrane-active AMPs is melittin [43]. The most distinctive lytic peptide was discovered in the Apis mellifera honey bee. These α-helical peptides have a net charge of +6, are hydrophobic, and are very positive. Used in membrane research as a control peptide, it shows apparent lipid membrane rupture and produces a α-helical structure with both parallel and perpendicular positions. Melittin is a monomer that can attach to the lipids in erythrocyte membranes [31]. Melittin's gain-of-function version, Mel P5, is a brand-new synthetic peptide [44].

It is a highly effective insect peptide that helps macromolecules move between the bilayers. Melittin forms pores on membrane surfaces when it attaches to them with a negative charge, disrupting the phospholipid bilayer's integrity. This causes atomic ions to flow out, which ultimately causes cell lysis [45]. Proline residues play a crucial role in cytotoxicity and reduce inhibitor concentrations. Melittin is known to cause apoptosis in C. albicans via the ROS-mediated mitochondria and caspase pathway. Additionally, it causes the endoplasmic reticulum to release ca2+, which in turn causes a tremendous accumulation of ca2+ in the mitochondria [46]. Melittin, which causes the release of cytochrome C to activate the caspase. Some apparent morphogenic apoptotic alterations, such as the development of phosphatidyl serine on the outer leaflet of cell membranes,

DNA degradation, and nuclear fragmentation, are seen when a positive control peptide is administered. Still obscure was its intricate mechanics [47].

Borrelia burgdorferi, Listeria monocytogenes, S. aureus, and P. auruginosa are just a few of the bacteria that melittin has a potent antibacterial impact against. Additionally, it exhibits efficacy against the dangerous bacterial disease of rice known as Xanthomonas oryzae pr. oryzae, suggesting that this peptide may have potential use in plant protection. Melittin-related peptide RV-Z3 exhibits significant antibacterial action against S. aureus and E. coli [48]. Melittin and conventional antibiotics have been shown by Akbari et al. [49] to have powerful synergistic effects against MRD strains isolated from Acinetobacter baumannii and P. auriginosa. After combination, the geometric means of the MICs for melittin and doripenem against A. boumannii isolates were decreased to 61.5 and 51.5 fold, respectively. Melittin's antibacterial action successfully combats MRSA strains. It is believed that AMPs are a cutting-edge option to replace traditional antibiotics. Since most current research is in the preclinical stage, there is still much work to be done in the clinical application of melittin [50].

5. **Metchnikowin:** This immune-inducible linear peptide from Drosophila melanogaster, which has 26 residues rich in proline, was notable for its peculiar antimicrobial activity. In honor of E. Metchnikowin, who founded this field of study, this was given the name metchnikowin. In the original drosophila strains, two isoforms of metchnikowin are distinct by a single residue [51].

Scientists in St. Petersburg initiated the study of invertebrate immunity, and their descriptions of the phagocytosis of pathogens by blood cells and of the concurrent inflammatory reactions paved the way for the comprehension of both invertebrate and vertebrate innate immunity [51]. Insect antimicrobial peptides' fundamental makeup makes it easier to interact with cell membranes—analyzing these transcription profiles following immunological challenges using conventional acute phase kinetics [51]. Metchnikowin also targets the succinate-coenzyme Q residues' iron-sulfur subunit (SdhB) (SQR). Up to 52% of the SDH activity of the mitochondrial SQR in Fusarium gramin carum is inhibited by metchnikowin [9]. Against gram-positive and gram bacteria and fungi, this peptide exhibits unique antibacterial action. According to the investigations, this peptide is ineffective against gram-negative bacteria. This AMP specifically targets the fungus' (1, 3)-glucanosyl transferase gel, a key enzyme in forming various fungi's cell walls [52].

6. **Moricin:** It was initially isolated from Bobyx mori and is a new antimicrobial peptide. Staphylococcus aureus is actively suppressed from multiplying by immunized B. mori, which produces antimicrobial peptides in the hemolymph. Cations make up the moricin protein, which several gene families encode. The amphipathic -helix that forms the N-terminal half of the peptide chain, which is around 42 residues long, is charged [32]. When the protein identification resources database searched, no significant peptides or proteins comparable to moricin were found. It is basic, and the more basic something is, its antibacterial effects are usually more substantial. Positively charged peptides are considered to stick to the negatively charged bacterial surface by electrostatic contact because of their basicity [53].

Without post-transcriptional modifications, all genes encoded mature moricin, which has a positively charged C-terminal and an amphipathic -helical N-terminus. Because of the absence of this post-transitional alteration, this moricin can be produced chemically. These cationic peptides readily bind to the bacterial cells' positively charged surfaces, where an amphipathic -helical motif develops [32]. Using the growth inhibition zone assay to analyze B. mori larvae in their fifth instar, it was discovered that its hemolymph was effective against the gram-positive bacterium S. aureus. Insects lack an immune system that relies on antigen-antibody interactions and effective defenses against bacterial infections. Both gram-negative and gram-positive bacteria were resistant to the antibacterial effects of these peptides [53]. Both gram-negative and gram-positive bacteria were resistant to the antibacterial effects of these peptides [53]. Since moricin is produced in response to bacterial infection and has potent antibacterial properties, it has a more decisive action against gram-positive bacteria. It is very effective against bacterial and fungal illnesses. The critical component in increasing membrane permeability and killing bacterial pathogens is the -helical motif of moricin. The B subtype of moricin is still inactive against the tested microorganisms [32]. Moricin is crucial in B. mori's ability to defend itself against bacterial diseases. Currently, some are producing artificial moricin on a large scale to gather enough quantity for further investigation of its precise function in the self-defense mechanism [53].

7. **Gloverin:** A new insect antibacterial peptide was discovered in the giant silk moth's (Hylophora cecropia) hemolymph for the first time. It is a glycine-rich protein without cystein C [54]. The four genes encode Bmgl 1, 2, 3, and 4 are only found in lepidopteran insects, such as B. mori and silkworms [55]. These peptides overexpress in B. mori's fat body following E. coli induction. The Bmgl gene's NF-Kb motif serves as a binding site in the area upstream of the gene. Bmglov 1 is the oldest, and the rest have evolved by duplication during the embryonic stage, showing that derived genes have acquired embryonic expression and unique function [56].

   This peptide permeabilizes bacterial cell membranes to destroy them without harming mammalian cells. Bmglv is thus a possible replacement for traditional antibiotics. Despite their co-evolution over millions of years, antimicrobial peptides are among these intriguing therapeutic agents that target membranes and maintain action against multidrug-resistant (MRD) bacteria [57]. Gloverin is inactive against E. coli mutant strains with smooth LPS on their cell surfaces but actively inhibits those strains with lipopolysaccharides (LPS) on their cell surfaces (Islam et al. 2016). Gloverin exhibits antibacterial activity against B. thuringenesis, B. thuringenesis galleriae, E. coli, S. marcescene, P. aeurginosa, and R. solanacearum, except for S. aureus and B. subtilis [55].

8. **Diptericins:** It is now widely known that lepidopteran and dipteran insects produce peptides with antibacterial activity in response to a bacterial challenge and injury [58]. Diptericins are a group of closely similar, glycine-rich antibacterial peptides (approximately 8KD) derived from the 82 amino acid depteran hemolyph protein [59]. From dipteran Phormia terranovae vaccinated larvae, diptericins A–C have been identified [60]. It is occasionally expressed in D. melanogaster, Sarcophaga peregrine, and Mayetiola destructor [61]. The new AMP prolixicin sis is a member of the diptericin family. It is distinct from Rhodnius prolixus, a hemipteran bug. It has 21 amino acids and

two potential phosphorylation sites, but no sites for glycosylation have been found. Following the bacterial infection of the hemolyph, midgut tissue can create this AMP [62].

Evidence indicating the presence of several heat-stable, basic antibacterial proteins in the hemolymph of vaccinated larvae was discovered during research on the cellular and humoral defence response of the dipteran Phormia terranovae, a species closely related to Calliphora erythrocephala. These are stable basic protein molecules [63]. Only a few gram-negative bacteria, including E. coli K12, Erwinia hericola T, and Erwiria carotovora 113, are susceptible to this peptide's activity. Growing bacteria's cytoplasmic membrane is mainly affected by AMP [9].

9. **Coprisin:** A defensin-like 43-mer peptide with three disulfide linkages called coprsin was discovered in the dung beetle Copris tripartitus [31]. This insect spends most of its time in dung, a haven for infections. Some of the bacteria in dung balls are what its pupae eat. In order to defend themselves, they use antimicrobial substances to invade microorganisms [64]. Dot blot hybridization was used to find the clones of the coprisin cDNA. There was a Northern blot analysis. Full-length cDNA libraries from C-tripartitus d that had been exposed to bacteria were evaluated, and up-regulated clones were then chosen utilizing differential screening and dot hybridization analysis. Therefore, several tests validated the minimal inhibitory concentration and conducted combination experiments to examine the effects of coprisin and antibiotics [65].

   When used against different fungal infections like Aspergillus and Candida species, this coprisin demonstrates a wide range of antifungal activity. unable to cause cytotoxicity to human erythrocytes [31]. Additionally, it has antibacterial qualities and works in concert or a complementary manner with antibiotics. Combined with vanconycin, coprisin is highly efficient against gram-negative bacteria [65]. Cop A3 is a subtype that has been studied for its antibacterial properties and ability to prevent the proliferation of cancer cells. It displays a broad line of lung, breast, lymph, and melanoma cancers.

10. **Papiliocin:** A novel antibacterial peptide called papiliocin was discovered in the swallowtail butterfly Papilio xunthus [31]. It is a 37-mer peptide with a helix-hinge-helix structure that is effective against gram-negative bacteria with medication resistance and less harmful to mammalian cells [66]. Papiliocin acts differently from traditional antibiotic compounds in that it causes the bacterial cell membrane to become permeable [66]. It exhibits notable antibacterial properties against Candida albicans and gram-positive and gram-negative bacterial strains. Confocal Laser Scanning Microscopy analysis of the intracellular distribution of papiliocin in C. albicans (CLSM). It implies that the main parts of the cell surface, the cell wall or membrane, could be the papiliocin's target site. The exploration of DPH (molecular probes) as a membrane probe allowed researchers to look at changes in membrane dynamics. Consequently, papiliocin possesses a mechanism for disrupting membranes [67].

    Without harming human erythrocytes, papaliocin demonstrates strong antibacterial activity against gram-positive and gram-negative bacteria and fungi. The C. albicans fungus's fungal plasma membrane is substantially disrupted by this. Specifically

in fungal infections, papiliocin peptides demonstrated a dual mechanism of membrane-active activity and apoptosis induction, in contrast to coprisin [31]. Four standard gram-negative bacteria (E. coli, Pseudomonas auregunosa, Accaetobacter baumannii, and Salmonella typhirium) and three gram-positive bacteria were used to assess the antibacterial properties of Pap12 peptides (Staphylococcus aureus, Bacillus subtilis and staphylococcus epidermis).

11. **Abaecin:** Abaecin is a peptide of 34mer residues identified from honeybees (Apis mellifera). It has 10 prolines (29%), no acidic residues, and no cysteins. At positions 12, 13, 27, and 29, there has been a net change of 4+. There is no chance that the peptide will adopt a -helical structure because the pralines are evenly distributed along the entire length. Pralines also have an internal alignment of repetitive motifs. Significant similarities between the abaecin and diptericin sequences have also been found. It has typical pro-arg-pro or pro-his-pro motifs, which are absent from the O-glycosylated threonine residues, and contains up to 33% of proline residues [68]. Honeybees are frequently exposed to and susceptible to infection by bacteria linked with plants (Apis mellifera). By injecting live bacteria into bees, they could replicate this process, and by comparing liquid chromatographic mapping of the heamolymph, they could isolate five induced bacterial compounds. Three antibiotics come from a special group of tiny peptides called abecins [69].

    By degrading the peptide and its fragments, Edman determined the entire sequence. The amino terminal quarter of the much longer fly diptericins shares proline motifs with the amino-terminal half of the related but distinct apidaecin. The hymenoptera order includes bees as well as ants and wasps. Field bees are exposed to and likely to contract plant-associated microorganisms while collecting pollen and nectar. When bacteria were exposed to abaecin in low-ionic strength media, the highest activity was achieved [69]. The abaecin peptides differ from the abaecin in that they have a broader spectrum of action, less concentrated specificity against gram-negative plant diseases, and the ability to stop bacterial growth at moderate ionic strength. It is also resistant to several Xanthomonas strains. They primarily work against gram-negative organisms [69].

12. **Drosocin:** Drosophila melanogaster produces the peptide known as drosogon. It has 19 amino acids. The action of drosocin is eliminated by removing the first five N-terminal residues [9]. Drosocin and apidaecin are two insect antimicrobial peptides with a common mechanism of action that contains stereoselective components but is free of any pore-forming activity. They exhibit high sequence homology and share similar properties [68].

    Out of 19 amino acid residues, approximately a third are pralines in the first antibacterial peptide known as drosovin, which also has three distinctive pro-arg-pro patterns. Drosocin has either a monosaccharide or a disaccharide glycosylated on Thr. The most active form of drosocinin contained disaccharides, while the activity of unglycosylated drosocinin was much lower than that of glycosylated peptides. Recently, it was discovered in some studies that glycosylated drosocin was completely inactive when administered intravenously to mice infected with a lethal dose of E. coli. To enhance this finding and make drosocin more suitable for dng development, a structural activity relationship study was carried out [68]. High effectiveness of rosogin against

gram-positive bacteria (M. leutius). Grass-negative bacteria are the main enemies of this. Drosocin that has been glycosylated has antifungal and E. coli activity [70].

13. **Lebocins:** Lebocins are 32 amino acid-long antimicrobial peptides found in the hemolymph of silkworms (Bombyx mori) [71, 72]. The fact that lebocin is O-glycosylated at Thr is crucial to its antibacterial activity. From silk worm larvae inoculated with E. coli, four lebocins, numbered 1-4, were recovered. Lebocins 1 and 2 are known as lebocin 1/2 because they share the same amino acid sequence. Lipopolysaccharides (LPS) may produce lebocins 3 and 4. In physiological conditions, lebosin 1-3 showed less antibacterial action against gram-negative bacteria than cecropin B. Their sugar moiety is the only difference between lebocins 1 and 2's main sequence [73].

    One of the significant economic insects spinning cocoons is the silkworm (Bombyx mori). The devastating white muscardine disease that affects silkworms is brought on by the pathogenic fungus Beauveria bassiana, which is also a persistent problem in sericulture. Directly penetrating the insect cuticle, B. bassiana colonizes, then engages the host's innate immune system, which mainly consists of cellular and humoral mechanisms, in combat. A collection of antimicrobial peptides created by the humeral immune system to defend the host against invasive microbes. Transcriptional analysis was used to examine the expression of a novel elevated homologous sequence gene of lebocine in normal and B. bassiana-infected silkworm larvae [74]. Against gram-negative bacteria, lebocins are incredibly effective [9]. Some of the genes' increased expression throughout the entire silkworm larvae, in the fat body, and in the hemolymph suggests that it may be crucial for the silkworm's immunological response to protect against B. bassiana [74].

14. **Pyrrhocoricin:** An antimicrobial peptide with a high proline content was found in the hemolymph of the sap-sucking insect Pyrrhocoris apterus. Healthy animals can be protected against bacterial challenges and are not hazardous to them. Pyrhocoricin's structural antibacterial activity investigation on E. coli and Agrobacterium tumificience revealed that the N-terminal half, residues 2–10 area, is what prevents ATPase activity [75].

    The heat shock protein DnaK interacts with these pyrrhocoricin peptides, which is associated with antibacterial activity. This binds to encourage the molecular chaperones DnaK's ATPase activity. Pyrrhocoricin might serve as a delivery method for peptides that must cross the parasite Cryptosporidium parvum's cell membrane. Target validation is facilitated by successful transduction. Additionally, it will aid in the delivery of peptide-based medications to this crucial region for the native peptides' antibacterial activity [9]. The N-terminus was identified by Ala and Try scans as the region containing crucial residues for the antibacterial action, and the C-terminus as a necessary but replaceable domain [76]. On DnaK, L-pyrrhocoricin mainly binds to a "non-conventional binding site." L-pyrrhocoricin does not prevent ATP hydrolysis mediated by DnaK [77]. Antimicrobial polycationic peptides are what it is. Proline-rich peptides can help fight against bacteria that have developed an immunity to antibiotics. Since high doses of pyrrhocoricin are hazardous to animals with impaired immune systems, pyrrhocoricin

analogues with reduced virotoxicity have been produced. Due to their inventive action, these peptides can eliminate resistant bacteria [75].

15. **Jelleines:** A class of peptides known as jellines was discovered in royal jelly from the Aphis mellifera plant [78]. These hydrophobic peptides differ significantly from other honeybee-derived antimicrobial peptides in their sequence. They have one histidine and one proline residue each [78]. They contain 8 to 9 amino acids and have a +2 charge at their C-terminus. Jelleine 1, Jelleine 2, Jelleine 3, and Jelleine 4 are around 4 antimicrobial peptides extracted from honey bee royal jelly [79]. Jelleines are the smallest cationic antimicrobial peptides that lyse model membranes.

    Because they still have histidine and proline residue. Histidine's protonation state, which can affect the peptide's activity, depends on the pH of the surrounding environment. Since many organs and disease states have or acquire an acidic environment, pH-dependent activity plays a significant role. The acidic environment created by solid tumors protonates the histidine residues, which explicitly activates the peptides' lytic activity [78]. In terms of their effectiveness as antimicrobials, jellies are active against both gram-positive and gram-negative bacteria, typically in that order. Both Pseudomonas aeruginosa and Staphylococcus aureus are susceptible to these. The proline-rich antimicrobial peptides have limited hemolytic activity and a preference for bacteria in their mode of action [80]. The characterization phase of jelleine molecules is ongoing.

16. **Ponericins:** It is a peptide that was isolated from the venom of the predatory ant Pachycondyla goeldii, a member of the ponerinae subfamily, and it has antibacterial, insecticidal, and hemolytic effects [69]. Orivel and colleagues isolated, recognized, and described these proteins' amino acid sequences. Ponericins are divided into three families according to how similar their main structures are- G, W, and L Ponericins. These share many sequence similarities with known peptides; for example, ponericin G is equivalent to peptides resembling cecropin. Ponericin L and Ponericin W are identical to dermaseptin peptides and mellitin, respectively [81].

    In the battle against skin cancer, Ponericin G1 offers a wide range of possible applications. Excellent mechanical characteristics, hydrophobicity, and antibacterial activity are features of the PLGA poly (lactic-co-glycolic acid) nanofiber scaffold produced by modifying polydopamides. It was loaded with bFGF (basic fibroblast growth factor) and ponericin G1. In skin restoration, the scaffold is coated with bFGF (basic fibroblast growth factor) and ponericin G1 [82].

    Ponericins were studied for their antibacterial effects on gram-positive and gram-negative bacterial strains and their insecticidal and hemolytic effects on cricket larvae. Bacillus stearothermophilus, B. subtilis, B. megaterium, and Lactococcus lactis were the gram-positive bacteria strains that were the most susceptible. Gram-negative bacteria were particularly vulnerable to Pseudomonas aeruginosa [69].

17. **Apisimin:** A protein peptide called apisimin, found in the royal jelly of Apis mellifera produced by honeybees, has an unknown function. It is produced by the hypopharyngeal and mandibular glands of nursing and foraging honeybees and has been identified as

apisimin in honey. It has been shown to interact with the protein Apa1 in royal jelly to create a complex. It is a peptide with high levels of valine and serine and only one aromatic amino acid, phenylalanine [4].

This particular protein stimulates the development of human monocytes. Apisimin has been found in nurses' heads and foraging honeybees, exhibiting significant levels of tiny mRNA expression. In honeybee colonies, they play a physiological purpose. Since honey also promotes the production of anti-inflammatory substances from monocytes or macrophages, its immune-stimulatory activities are ostensibly more complex [4].

The apisimin gene has a high level of transcription. At the nucleotide level, the apisimin gene shared 100% and 95% of homologies with A. mellifera and A. cerena indica. In order to combine with GST and create a recombinant vector, the coding area of the matured peptide was sub-cloned into the prokaryotic expression vector. For fusion expression, this recombinant was next transformed into E. coli. The expressed gene GST-apisimin fusion protein was around 31 kDa, 22.1% in proportion, and 50% solubility, according to the results of the SDS-PAGE and thin layer scanning [83].

18. **Persulcatusin:** Ixodus persulcatus' midgut has been found to contain persulcatusin [84]. A common tick species, Ixodus persulcatus, transmits various animal infections, including Borrelia garinii, which causes Lyme disease [85]. Three S-S bonds, which are energetically significant for the stability and development of the α-helix and β-sheet structure, keep the persulcatus' structural integrity. Methicillin-sensitive S. aureus (MSSA) and methicillin-resistant S. aureus (MRSA) can both be prevented from growing by this peptide [86]. This antimicrobial peptide from persulcatusin is effective against gram-positive bacteria like S. aureus. Most insect and arthropod antimicrobial peptides retain a distinctive motif of cysteins, which create three disulfide linkages [85].

V. APPLICATIONS OF AMPS

1. **Medicine:** The misuse and abuse of antibiotics result in antibiotic resistance, a serious health problem. Through the development of AMPs-based therapeutics, AMPs with broad-spectrum antibacterial activity are anticipated to replace antibiotics in medical practice. AMPs are increasingly being used in ophthalmology, dental, surgical infection, and other fields of medicine. However, only three AMPs—gramicidin, daptomycin, and colistin—have received FDA approval [6]. Antimicrobial peptides play a role in the immunological regulation of human skin, respiratory infections, and inflammatory illnesses by regulating pro-inflammatory reactions, recruiting cells, stimulating cell proliferation, promoting wound healing, and altering gene expression [87]. Human oral diseases include periodontal disease, dental caries, endodontic infections, candidiasis, and dental infections. Dental caries is a common dental condition, and Streptococcus sp. is one of the main microorganisms linked to caries [88].

Several AMPs have also demonstrated their promising activity against diseases acquired from surgical infections and wound healing, such as burns, unintentional injuries, skin diseases, and chronic wound infections that pose a major threat to human life [89]. AMPs like Lactoferricin B and Protegrin-1 showed antibacterial action against pathogenic bacteria like S. aureus, Streptococcus pneumonia, P. aeruginosa, Aspergillus

spp., and C. albicans. However, their use in the field of ophthalmology is still largely theoretical. Antimicrobial peptides have shown promising application prospects in ophthalmology, given the prevalence of contact lenses and the rise in infections of the eyes associated with them [90]. The use of AMPs as medications in medicine requires the application of additional techniques. The main methods involve (1) developing precursors to lessen cytotoxicity and enhance protease stability; (2) utilizing AMPs in conjunction with currently available antibacterial agents; (3) inducing the proper expression of AMPs with suitable drugs; and (4) engineering probiotics as vectors to express AMPs. For instance, many formulation techniques have been devised to efficiently transport AMPs to the wound in the field of wound repair, including dosing AMPs in nanoparticles, hydrogels, creams, gels, ointments, or glutinous rice paper capsules.

2. **Biomedical device manufacturing:** With an emphasis on the potential for personalization, several unique technologies are emerging to produce implants. We will briefly discuss electrospinning and additive manufacturing regarding the methods of incorporating antimicrobial agents and the possibilities for AMPs. A significant development in the fabrication of medical devices is additive manufacturing, or 3D printing, which permits the production of implants with specialized size, shape, and possibly high porosity, increasing the surface area. These features make this method appealing for individualized implants. The 3D-printed implants are prone to infection, much like regular implants. As a result, many methods are currently being investigated to create 3D-printed medical devices with antibacterial capabilities. For instance, the surface of the 3D-printed implants might be modified to add antimicrobials utilizing plasma electrolytic oxidation, sometimes referred to as micro-arc oxidation [91].

There are numerous opportunities for producing medical devices using fundamentally distinct electrospinning technology. As an illustration, consider the electrospun prosthetic heart valve, which is currently undergoing advanced preclinical testing [92]. By electrospinning, biocompatible nanofibers with a sizable surface area resembling the body's extracellular matrix can be created. However, bacterial colonization may be possible due to the matrices' porosity. Antimicrobial agents have been added to the polymers used in the electrospinning process to lower the possibility of contamination of electrospun products.

Functional groups are necessary for both AMPs and polymers for covalent conjugation methods between AMPs and polymers, such as amide bond production and click chemistry. However, other techniques, such as Michael addition/Schiff, base reaction, photo cross-linking, and oxidation reaction, can also be used to immobilize AMPs onto the polymers [93]. Surface confinement is less significant thanks to the flexible linker that the structure of a polymer brush creates between the substrate and the AMPs. In several experiments, polymer brushes were used to load AMPs onto titanium (Ti) implant surfaces [94]. The covalently attached peptide prevents adhesion and the development of biofilms, while the electrostatically released peptide inhibits bacterial growth in solution. Working together when an engineered surface meets tissue can prevent bacterial colonization while preserving cell development. The peptides have potent antimicrobial action against clinical isolates of Staphylococcus aureus, Staphylococcus epidermidis, and Pseudomonas aeruginosa. They can be modified to interface with a surface while maintaining good efficacy against various microorganisms

(the bacteria most commonly found in joint infections). The dAMP coating provides short-term tissue sterilization followed by long-term sustained antibacterial activity of the surface by integrating numerous fragments with diverse features (surface binding and antimicrobial activity) without impairing the unique functions [95].

3. **Agriculture and control of disease vectors:** Plants have been genetically modified to produce AMPs that give resistance to bacteria and fungi diseases [10]. Potential uses for insect AMPs include disease vector control, agriculture, and medicine. The functional and structural properties of plant and animal AMPs have been studied, along with the use of recombinant AMPs in the paratransgenic control system and the paratransgenic control of vector-borne diseases [10].

   Transgenic rice, banana, tomato, "Egusi" melon, peanut, tobacco, and Arabidopsis all express plant defensins. It also reduces harmful fungi when an insect defensin (G. mellonella gallerimycin) and cecropin (sarcotoxin-IA) are expressed transgenically in tobacco. Cecropin expression can resist bacterial and fungal diseases in transgenic plants, such as rice and tomato. Transgenic barley has been produced with metchnikowin, a proline-rich peptide, to improve resistance. To increase resistance or widen the spectrum of resistance to infections, chimeric peptides created by joining the active areas of two AMPs have also been employed in transgenic plants. However, host gene expression or host plant fitness may be impacted by the production of AMPs in transgenic plants [10]. Some parasites, such as Plasmodium, filarial nematodes, and Trypanosome, are responsive to insect AMPs. Current research on antimalarial and antiparasitic peptides is summarised in two recent reviews. It has been demonstrated that cecropins and defensins are effective against parasites. A novel method for eliminating or preventing the spread of parasites is the expression of AMPs in transgenic vectors like mosquitoes [10].

4. **Animal husbandry and aquaculture:** Numerous AMPs have the potential to be used in the breeding of poultry, swine, and ruminants as well as in aquaculture because they can enhance production performance, immunity, and intestinal health, and some of them have a more substantial inhibiting effect on bacterial inflammation when combined with antibiotics [96]. For instance, broilers under prolonged heat stress showed more remarkable average daily growth and feed efficiency when supplemented with swine gut intestinal antimicrobial peptides (SGAMP) [97]. Fish farming is severely harmed by Nodavirus, Septicaemia hemorrhagic virus, Infectious pancreatic necrosis virus, and Spring viremia carp virus; these viruses are effectively inhibited by frog caerin 1.1, European sea bass dicentracin, and NK-lysine peptides (NKLPs) [98].

5. **Food:** The use of food preservatives could be harmful to a person's health. Therefore, more people are advocating the use of natural preservatives. While many AMPs are resistant to acids, alkalis, and high temperatures, they are rapidly degraded by proteases in the human body. AMPs have a good inhibitory impact on common bacteria and fungus in food. AMPs are a viable replacement for preservatives as a result. The L. lactis subspecies make a bacteriocin called nisin. Many people utilize lactic acid bacteria for food preservation. The US Food and Drug Administration (FDA) has classified nisin as generally recognized as safe (GRAS), and it is employed as a food preservative in other nations [99]. However, the FDA has only currently allowed nisin and polylysine as food additives [100]. Additionally, adding AMPs to packaging creates active packaging, a

unique packaging technique with enormous potential in the food sector. For example, nisin, a highly surface-active chemical from Penicillium expansum, has the potential to be utilized as a dairy preservative due to its sound inhibitory effects on Aspergillus parasiticus (a generator of aflatoxin) when used in conjunction with starch biofilms [101].

VI. FUTURE PROSPECTS

Antimicrobial peptides are a significant area of research around the world. However, numerous pressing design and application problems must be resolved [102]. Insect antimicrobial peptides represent a promising approach to treating medical issues brought on by antibiotic resistance. Insect cecropin has been employed in numerous investigations to fictionalize biomaterials used in biomedicine. Finding substitute medications is difficult. Studies on techniques to strengthen insect peptides against proteolytic susceptibilities, such as D-amino acid substitutions, N-terminus modifications, cyclization, and dimerization, need to be put into practice. The World Health Organization recently amended the list of bacterial infections for which antibiotics must be developed [5]. There are currently no insect-derived antimicrobial peptide products on the biopharmaceuticals market. The clinical use of insect antimicrobial peptides is minimal due to a lack of knowledge regarding bioavailability, instability to proteases, toxicity, and side effects.

Nevertheless, it is possible to use insect antimicrobial peptides as an alternative to conventional antibiotics or as a support to enhance their activity [5]. A significant global public health issue is multi-drug antibiotic resistance. Therefore, there is a critical and urgent need to create new antibiotic classes that do not cause resistance. For the past three decades, antimicrobial peptides have appeared as a promising alternative class of antibiotics. However, there are not many real success stories. We believe that one of the main obstacles to developing novel antimicrobial medications is our inability to fully explain their mode of action in words that can be applied to design and engineering [103]. The origin, structure, and biological properties of antimicrobial peptides have been extensively studied, which has enhanced understanding and use [104]. Several factors need to be considered about antimicrobial peptides' membrane action. Do these situations involve a particular membrane receptor, and if so, are additional components acting in concert with it? There is a need for more research because the mechanisms of action of various antimicrobial peptides may differ. The need for novel antimicrobial medications has become critical in the medical community. It is necessary to conduct more research on the cellular and molecular mechanisms behind antimicrobial peptide actions. Antibacterial peptides are, therefore, intriguing prospects for therapeutic usage given their broad-spectrum antimicrobial activity and will undoubtedly be the subject of additional investigation in the future.

VII. CONCLUSION

Antimicrobial peptides are desirable candidates for creating a new generation of antibiotics due to their wide range of activity against microbial infections as both innate defense molecules and immunomodulators. The diversity of antimicrobial peptides in insects also reflects the species-level diversification of those organisms. At least in part, insects' evolutionary success can be credited to their innate immune system, which exhibits extraordinary adaptability in terms of functional changes, gene diversity, or loss of antimicrobial peptide-encoding genes. Even on chronic and non-healing wounds, insect

secretion has significant therapeutic effects, including cleaning the lesion, eliminating necrotic tissue, and stimulating the healing process. Despite being a cornerstone of our present healthcare system, specialized microbial metabolites have numerous clinical uses for treating various illnesses. Due to the resources and effects needed for their manufacture, many specialized metabolites exhibit little to no activity in clinical testing. However, one can still presume that they have an ecological purpose. Insect-derived natural compounds have been utilized for millennia in traditional medicine and are a vital source of therapeutic agents in underdeveloped nations. Large-scale production would be necessary to create antimicrobial peptides for use as cosmetic components, focusing attention on peptide length and structure. Due to basic residues that have antibacterial properties, most insect antimicrobial peptides are cationic molecules. Chemicals are a means by which insects can communicate with the ecology. The primary immune system effector molecules are therefore antimicrobial peptides produced from insects.

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