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Review Article

Antimicrobial peptides (AMPs) of plant origin and their applications

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Abstract

Plant Antimicrobial peptides (AMPs) are small, naturally occurring polypeptides, synthesized by the plants, as a fundamental component of their innate immune defense systems against a wide range of pathogenic microorganisms. In plants, AMPs are constitutively expressed or induced in response to several different biotic and abiotic stress factors. These peptides exhibit broad-spectrum antimicrobial activity against a wide range of pathogens, including Gram-positive and Gram-negative bacteria, viruses, fungi, and parasites. Structurally, plant AMPs are highly diverse and include several well-characterized families such as defensins, thionins, lipid transfer proteins, cyclotides, and hevein-like peptides, many of which are stabilized by disulfide bonds that enhance their stability and resistance to proteolytic degradation. The mechanism of action of AMPs typically involves disruption of microbial cell membranes, inhibition of cell wall synthesis, interference with intracellular targets, or modulation of pathogen signalling pathways, which reduces the likelihood of resistance development compared to conventional antibiotics. Due to their small size, structural diversity, rapid action, and effectiveness against multidrug-resistant pathogens, AMPs have emerged as promising candidates for the development of next-generation antimicrobial therapeutics. Furthermore, advances in peptide engineering, bioinformatics, and synthetic biology have enhanced the stability, specificity, and therapeutic potential of AMPs, highlighting their significance as viable alternatives to traditional antibiotics in addressing the global challenge of antimicrobial resistance.

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Introduction

Antimicrobial peptides (AMPs), also known as host defense peptides (HDPs) are effective against a wide range of microbes and are synthesized as a result of constitutive defense mechanism induced upon infection in a wide variety of plants. AMPs are postulated to play an important role in the innate immune system of plants similar to that observed in animals. These peptides are encoded by nuclear genes and are usually synthesized as precursor proteins consisting of a signal peptide, a pro-domain, and a mature AMP. These peptides can therefore be utilized to synthesize potent, broad-spectrum antibiotics as they execute significant action against Gram (+)ve and Gram (-)ve bacteria, enveloped viruses, fungi and even transformed or cancerous cells. The first plant AMP to be I solated was purothionin from wheat flour (*Triticum aestivum*) in the year 1942, which showed inhibitory activity against the growth of some phytopathogens such as *Pseudomonas solanacearum*, *Xanthomonas campestris* and *Corynebacterium michiganense* (de Caleya 1972; Pellegrini et al. 2011). More than 1000 types of AMPs have been extracted from plants. Owing to their potency, structural stability, low toxicity, and reduced propensity for inducing resistance, plant AMPs have gained significant attention as promising candidates for the development of next-generation antimicrobial agents. Advances in molecular biology, peptide engineering, and bioinformatics have further facilitated the identification, optimization, and large-scale production of plant AMPs, underscoring their

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potential application in agriculture, food preservation, and human health to combat the growing threat of antimicrobial resistance. Unlike conventional antibiotics, plant AMPs often act through multiple targets, which significantly reduces the likelihood of resistance development. Structurally, plant AMPs are highly diverse and are classified into several families such as defensins, thionins, lipid transfer proteins, cyclotides, and hevein-like peptides. Most of these peptides are rich in cysteine residues that form disulfide bonds, conferring remarkable stability against heat, extreme pH, and proteolytic degradation (Lima et al. 2022).

In recent years, plant AMPs have gained increasing attention due to their potential applications beyond plant defense. Their potent antimicrobial activity, low toxicity to host cells, and structural stability make them attractive candidates for the development of novel antimicrobial agents for use in agriculture, food preservation, and human medicine. Furthermore, advances in genomics, proteomics, and peptide engineering have accelerated the discovery and functional characterization of new plant AMPs, enabling the optimization of their efficacy and specificity. As antimicrobial resistance continues to pose a global threat, plant-derived antimicrobial peptides represent a promising and sustainable source of next-generation antimicrobial compounds (Su et al. 2025).

Structure and classes of AMPs

Plant-derived AMPs show great variation according to their sources, structures, physical and chemical properties, mechanism of action, and pharmacological effects. AMPs act mainly against bacteria and fungi at low concentrations and have been usually discovered from the peripheral layers of seed and vegetative tissues. Based on amino acid sequence homology and the number / position of cysteine residues, AMPs are classified mostly as defensins, lipid transfer peptides, thionins, cyclotides, Ib-AMP4, knottin-like peptides, shepherins, snakins, hevein-like peptides, and non-cysteine rich peptides (Pellegrini et al. 2022). According to Plant PepDB database, plant-derived AMPs can be grouped as per the peptide type as follows- Thaumatin-like proteins (about 60.5%), cyclotides (about 22.5%), thionins (about 9.6%), defensins (about 6.7%), and others (<1%) (Figure 2). In most of the cases, cysteine is present and intramolecular disulphide bond is formed between the cysteine residues, which contribute to the antimicrobial activity to some extent. AMPs are mostly reported to be discovered from the members of families like Amaranthaceae, Poaceae, Brassicaceae, Solanaceae, Rubiaceae, Apocynaceae, Euphorbiaceae and Violaceae along with some gymnosperms (Marciano et al. 2025) (**Figure 2**).

The length of AMPs usually ranges from about 5 to 100 amino acids and molecular weight ranges from 2 to 10 kDa (Pellegrini et al. 2022). However, there are few exceptions. Few AMPs alongwith their source and activity are briefly described in **Table 1**. These small polypeptides are generally amphipathic molecules, containing cationic and hydrophobic residues in high proportion, thus capable of non-specific interactions with the membrane lipids in the cell membranes. AMPs can be again divided in to three groups on the basis of their tertiary structure and composition: α-helical AMPs (eg. cecropins), β-sheet AMPs (eg. defensins) and AMPs rich in Histidine, Arginine, Proline and Tryptophan (eg. Indolicidin) (Gaspar et al. 2013). α-helical AMPs are rich in Glycine residues which provides flexibility and whereas β-sheet AMPs are rich in Cysteine residues and thus can readily form disulphide bonds. It was observed in many studies that α-helix usually favors membrane ruptures, whereas β-sheets and cyclical structures are often involved in peptide internalization. However, these characters cannot be strictly correlated to the antibacterial activity of the AMPS, instead it has been confirmed that the charged residues seem to have an essential role in activity towards pathogenic bacteria. There are other important parameters that influence the antimicrobial activity of the peptides viz. hydrophobicity, amino acid sequence, pH, and salt concentration (Marciano et al. 2025).

Mechanism of action

The mechanism of action of AMPs involves the capacity to cause membrane collapse by interacting with lipid molecules in cell membrane by two major types of action: pore formation (barrel-stave and toroidal pore) and non-pore mechanisms (carpet model and detergent-like action). In barrel-stave mechanism, AMPs form pores by assembling peptides, creating a central channel for leakage, with hydrophobic sides facing the lipid core and hydrophilic sides facing inwards. Whereas in Toroidal pore model, peptides interact with the polar head groups of membrane lipids to form pores, resulting a continuous curvature of the lipid bilayer stable channels that allow the passage of ions and other molecules (Branco et al. 2022). High concentration of AMPs accumulates in a carpet-like manner on the membrane surface that cause subsequent breakage of the membrane

Table 1. List of few plant-derived AMPs and their probable action

Sl. No.	Name of AMP	Origin	Length (amino acid residues)	Molecular Mass (kDa)	Properties
1.	Circulin A	*Chassalia parviflora*	30	3.17	Antibacterial activity against Gram +ve and –ve bacteria, anti-HIV.
2.	Circulin B	*Chassalia parviflora*	31	3.31	Antibacterial and antifungal activity.
3.	Fabatin 1	*Vicia faba*	47	5.23	Antibacterial activity against Gram +ve and –ve bacteria. High activity against *P. aeruginosa.*
4.	Fabatin 2	*Vicia faba*	47	5.21	Antibacterial activity against Gram +ve and –ve bacteria.
5.	Lunatusin	*Phaseolus lunatus*	20	2.18	Antibacterial activity, antifungal activity, inhibit proliferation in the breast cancer cell line and anti-HIV activity.
6.	Kalata B2	*Oldenlandia affinis*	29	2.97	Inhibitory effect on the growth and development of larvae from *Helicoverpa punctigera*. Also has hemolytic activity.
7.	Dendrocin	*Dendrocalamus latiflora*	35	3.86	Antifungal activity against *Fusarium*, *Botrytis* etc.
8.	Ginkbilobin	*Ginkgo biloba*	40	4.21	Antibacterial activity, antifungal activity, and anti-HIV activity by suppressing reverse transcriptases.
9.	Pseudothionin-St1	*Solanum tuberosum*	19	2.21	Antifungal and antiinsecticidal activity.
10.	Cp-DefensinII	*Vigna unguiculata*	46	5.24	Antibacterial activity against Gram +ve and –ve bacteria.
11.	Pg-AMP1 (non-cystine)	*Psidium guajava*	55	6.01	Antibacterial activity against Gram +ve and –ve bacteria.
12.	Mc-AMP1	*Mesembryanthemum crystallinum*	38	4.31	Antibacterial activity against Gram +ve bacteria and antifungal activity.

13.	Ib-AMP4	*Impatiens balsamina*	20	22.52	Antimicrobial effect against various pathogens, including MRSA and resistant *E. coli*, often synergizing with other antimicrobials.
14.	Cn-AMP1 (non-cystine)	*Cocos nucifera*	<10	0.876	Strong antibacterial and immunomodulatory activity.
15.	MOp3	*Moringa oleifera*	7	20.19	Antimicrobial activity against *Staphylococcus aureus* by membrane damage and inducing apoptosis
16.	RsAFP1 & RsAFP2	*Raphanus sativus*	51	5.8	Antifungal activity against *Candida albicans*
17.	Kalata B1	*Oldenlandia affinis*	29	2.9	Antimicrobial activity against both *S. aureus* and *E. coli*
18.	NaD1	*Nicotiana alata*	47	5.2	Antifungal activity against *Candida albicans*
19.	Purothionin	*Triticum aestivum, T. monococcum*	45-47	4.9–5.2	Antifungal activity against *S. cerevisiae*, *C. albicans*, *R. solani*, Gram-negative & Gram-positive bacteria
20.	Lc-Def	*Lens culinaris*	47	5.4	Antifungal activity against *Candida* spp.

(Carpet model). Other AMPs exert detergent-like effect by solubilizing membrane lipids and thus causing dissipation of the electrochemical gradient (Chen et al. 2023). The positively charged amino acid residues in AMPs interact with the negatively charged molecules such as anionic phospholipids, lipopolysaccharides in Gram negative bacteia and teichoic acid in Gram positive bacteia which are located asymmetrically in the membrane architecture. The positively charged residues can also interact with membrane lipids through specific receptors on the cell surface. Ultimately, peptide binding to the membrane activates several pathways leading to cell death. AMPs initially accumulate on the membrane surface and a threshold number of molecules are required in order to complete cell lyses (Lee and Park 2014) **(Figure 1)**. Intrinsic and extrinsic parameters also influence the peptide concentration and therefore affect the antimicrobial activity of the AMPs. Intrinsic factors include the ability of the peptides to form clusters on the bacterial surface, whereas extrinsic factors include bacterial membrane composition, fluidity and head group size. Also, AMP activity has been linked to the environment of the host niche where the pathogenesis is initiated. This includes factors like pH, temperature, nutrient concentration etc. At the site of disease, the function of AMP is often multifactorial and successful eradication of pathogens is induced by influencing the dynamics of host-pathogen interaction through modulation of bacterial gene expression for virulence factors and their responses to environmental factors (Heimlich et al. 2014).

Generally, an AMP is highly specific against microorganisms; however, there are exceptions and some broad-spectrum AMPs are also known, that have different modes of action against different types of microorganisms.

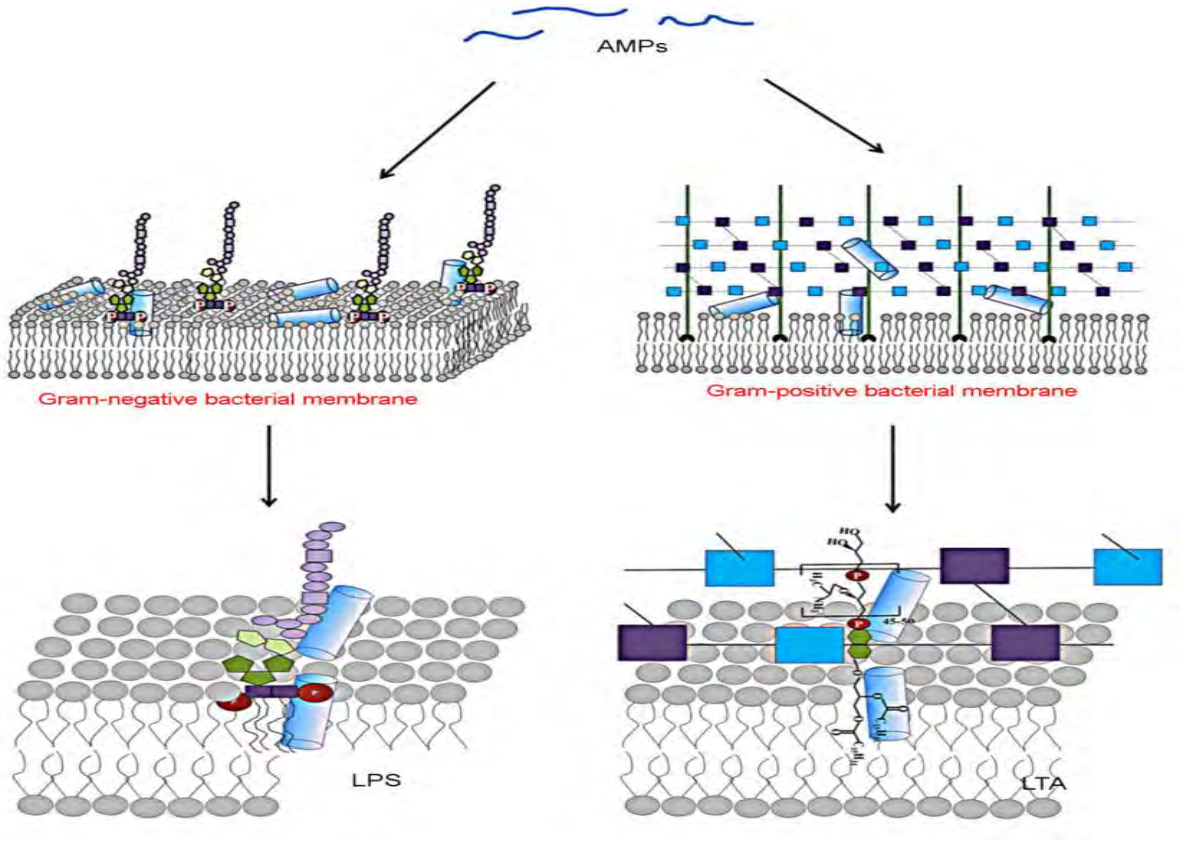

Figure 1. Illustration of the action of AMP on the lipopolysaccharides and lipoteichoic acid in bacterial membrane

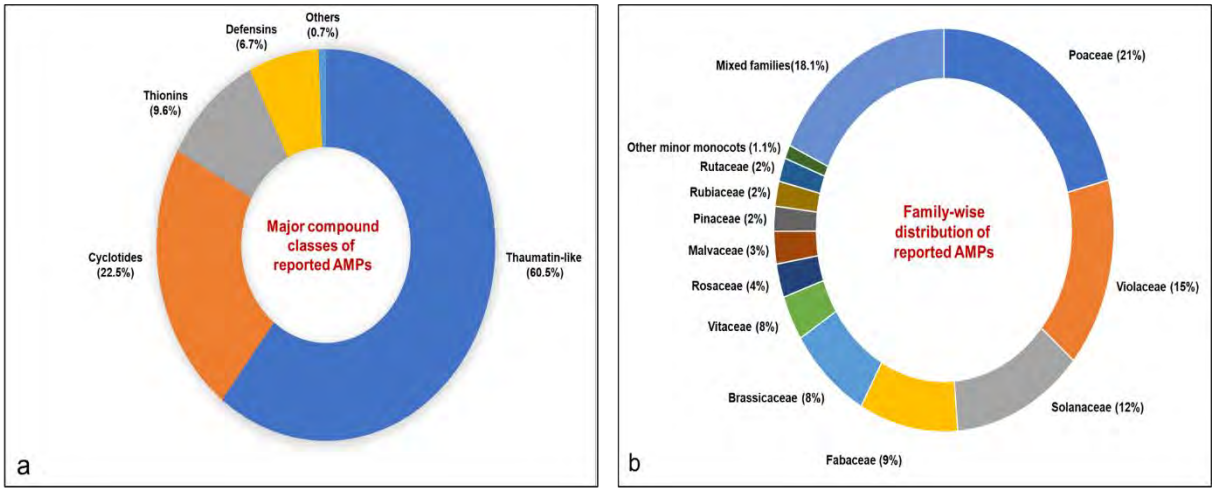

Figure 2. Pie chart showing (a) Different classes of reported AMPs and (b) Distribution pattern of AMPs within plant families

For example, ginkbilobin derived from *Ginkgo biloba* seeds can kill wide range of bacteria, fungi and even viruses. It exhibits antifungal activities by directly damaging the cell membrane; antibacterial activities by penetrating into the cells and inhibiting DNA synthesis and antiviral activities by inhibiting reverse transcriptase enzyme (Yeamn and Yount 2003). Majority of the AMPs on the other hand have similar mode of action against different microrganisms. However, AMP resistance is also quite evident in bacteria. There are mainly two different types of resistance mechanisms in bacteria: constitutive and inducible. The inducible resistance mechanisms include substitution, modification and acylation of the membrane lipids, activation of some proteolytic enzymes and efflux pumps; whereas the constitutive resistance mechanisms include electrostatic shielding, changes in membrane potential during different stages of cell growth and biofilm formation (Bahar and Ren 2013).

Defensins are the major class of AMPs that were isolated from the peripheral regions of almost all the plant organs which showed both antifungal and antibacterial activity, but majority of them have been found to possess antifungal activity. Antifungal defensins binds specifically to the sphingolipids rich regions of the cell membrane resulting in increased membrane permeability and ultimately growth cessation (Hegedus and Marx 2013). Thionins possess both antifungal and antibacterial activities which is initiated by its ability to bind with the phospholipids present in cell membrane (Stec et al. 2004). Hevein-like AMPs isolated from rubber trees are known to possess antifungal activity mainly due to the presence of chitin binding domains in their structure (Broekaert et al. 1992). Similarly, knottins also possess chitin-binding domains, therefore are mainly antifungal in nature with limited activity against Gram positive bacteria also (Yokoyama et al. 2009). Cyclotide group of AMPs are non-cationic and possess a wide range of biological properties like anti-HIV, cytotoxic, insecticidal activity in addition to antimicrobial activity. The charged residues of cyclotide induce hydrophobic interactions with the membrane of target microorganisms leading to membrane disruption (Ireland et al. 2010). Snakins on the other hand possess both antifungal and antibacterial activity. These AMPs do not directly affect the lipid membranes, rather they act by promoting the aggregation of liposomes (Caaveiro et al. 1997).

Application of AMPs

Functional analyses of the AMPs from plant sources have revealed major antifungal, antibacterial and antiviral activities and thus may be useful in isolating and characterizing novel plant AMPs with higher potency against pathogens or with broad antimicrobial spectra. Because AMPs can directly target bacterial cells, they have huge prospect in controlling antibiotic resistant bacterial cells by inhibiting biofilm formation. Plant-derived AMPs may also function by scavenging ROS and modulate MAPK signaling to elicit a defense response against pathogen or pests (Bakare et al. 2022). AMPs can also be utilized as immunomodulatory agents or bacterial toxin neutralizers. Many of them have been shown to be active against tumour cells and lower toxicity towards normal eukaryotic cells, so their use as anticancer drugs has also been valued. The negative charge on the membranes of the tumour cells due to the abundance of anionic phosphatidylserines are the driving factor for the action of highly positively charged AMPs. However, very few plant AMPs or synthetic derivatives of these have achieved their due credit in clinical trials. Presently, there are no AMP drugs approved for human use by the Food and Drug Administration (FDA) (Nawrot et al. 2014). Also, the rate of AMP discovery from plant kingdom is highly limited in comparison to other sources. In the year 2014, only 5% of the AMPs discovered were from plant sources. Out of which, EcAMP3 from *Echinochloa crusgalli* was the first disulfide bond stabilized hairpin-like helical peptide to be discovered that had both antifungal and antibacterial activity (Wang et al. 2015). In the context of plant biotechnology, transgenic plants resistant to diseases and pests have been developed through the introduction of AMP producing genes from other plant species and even human defensins to confer better resistance of the transgenic plants towards the harmful pathogens. For instance, Rs-AFP2, radish defensin AMP was expressed in tobacco and tomato conferred protection against *Alternaria longipes* and Mj-AMP1 jalapa defensin expressed in tomato against *Alternaria solani* (Nawrot et al. 2014). Moreover, through biotechnological approaches, plant defensins and thionins have been expressed in mammalian cells, which showed activity against bacteria, fungi and tumour cells (Lopez-Meza and A. Ochoa-Zarzosa 2011). Cyclotides AMPs like Kalata B1 has proved to be invaluable in the development of novel antibiotics and bioinsecticides (Lopez-Meza and Ochoa-Zarzosa 2011). Most recently, it has been found that AMPs tagged to nanoparticles impart a site-specific targeting and delivery of drug molecules which can be used in treating a variety of diseases, including cancer (Laverty et al. 2014). The role of AMPs in the prevention of multidrug-resistant (MDR) bacteria has been highly valued due to its small size, rapid action on cell membrane and the inability of bacterial cells to develop resistance. Moreover, the synergistic role of AMPs and clinically used antibiotics has facilitated the decrease in development of antibiotic resistance in bacteria and increase in the effectivity of the antibiotics at low doses. For instance, the combined application of AMPs like magainin and cercopins with rifampicin increased the activity of the antibiotic against MDR *Pseudomonas aeruginosa* which was mainly attributed to the activity of membrane disrupting AMPs to facilitate the entry of the drug molecules (Cirioni et al. 2008). Although bacteria have inherent mechanisms for resistance to AMPs, it is enticing to notice that the lipid bilayer structure of bacterial cell membranes makes it difficult for a bacterial cell to develop complete resistance against AMPs. However, the cases of resistance against AMPs are comparatively lesser than the antibiotics.

Application of micelles containing plant-derived AMPs can offer their controlled release to increase target selection and efficiency in therapeutic action. These micelles are relatively easy to design, by regulating their sizes and charges by adjusting hydrophilic and hydrophobic balance, as well as in terms of biocompatibility and biodegradability, hence proved to be useful to control foodborne pathogens. In this regard, The Food and Drug Administration (FDA) has authorized PEG-PLA micelles (Prencipe et al. 2021).

Challenges and opportunities

The identification and application of novel antimicrobial peptides (AMPs) from plant sources have expanded substantially with advances in next-generation extraction and purification technologies, particularly through the integration of omics approaches and bioinformatics tools. Despite this progress, significant discrepancies persist in the computational design and chemical synthesis of AMPs, necessitating extensive experimental screening and validation. Similarly, outcomes observed *in vitro* often fail to translate effectively into clinical applications. Sun (2025) highlighted several key challenges associated with AMP development and application:

i) The relatively short shelf life of AMPs poses a major limitation to their widespread use, as they are highly susceptible to environmental and wound-specific degradation.
ii) Antimicrobial efficacy may be weak or inconsistent due to variations in tissue microenvironmental factors such as pH, temperature, and ionic strength.
iii) Limited understanding of the structure-activity relationships of many novel AMPs restricts accurate determination of optimal dosage and therapeutic efficacy.
iv) Potential cytotoxicity and undesirable side effects raise concerns regarding safety.
v) High research and development costs hinder large-scale production and commercialization of plant-derived AMPs.

Despite these challenges, the future of plant-derived AMPs remains promising. Biotechnological interventions aimed at enhancing AMP production, target-specific nanodelivery systems, and the application of computational tools and artificial intelligence have led to significant advancements in the extraction, purification, characterization, and evaluation of pharmacokinetics and pharmacodynamics of novel AMPs. These innovations hold considerable potential across agricultural, food, and pharmaceutical sectors (Biswaro et al., 2018).

Epilogue

The importance of antimicrobial peptides (AMPs) is increasing steadily due to the urgent need to discover novel antimicrobials capable of combating potentially uncontrollable pathogens that are rapidly developing resistance to existing antibiotics. Beyond their antimicrobial activity, AMPs exhibit diverse applications, including the induction of disease resistance in plants, development of biofertilizers, and potential use in cancer therapy. In recent years, the role of AMPs in the treatment of several human diseases associated with microbial homeostasis—such as disorders of the nasopharynx, pulmonary infections, oral cavity diseases, gastric mucosal conditions, intestinal disorders, and urinary tract infections—has been extensively investigated (Heimlich et al. 2014).

Despite their promising potential, the commercialization of AMP-based therapeutics remains at a nascent stage and is hindered by several challenges, including limited specificity, high manufacturing costs, potential cytotoxicity to animal cells, and the absence of robust guidelines for rational peptide design. Therefore, the substantial promise offered by AMPs must be realized by overcoming these constraints with careful consideration for human safety and therapeutic efficacy. Importantly, there exists considerable scope and feasibility for the discovery of novel AMPs from plants with unique properties, as only approximately 10% of currently known AMPs have been derived from the plant kingdom.

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