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Investigating the Antimicrobial Potential of Plant-Based Protein Against Human Pathogens

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ABSTRACT

The growing incidence of antibiotic-resistant pathogens requires the investigation of alternative antimicrobial compounds, especially plant-based proteins (PBP). This review explores the antimicrobial capability of PBPs against human pathogens, emphasizing their effectiveness against multidrug-resistant organisms. Several studies indicate that plant-derived compounds with important oils and proteins display antibacterial and antifungal properties. Key instructions of PBPs, including lectins, defensins, and protease inhibitors, disrupt microbial membranes and inhibit vital cell features, lowering pathogen viability. The mechanisms of movement of these proteins are numerous, which might also decrease the likelihood of resistance development compared to artificial antibiotics. The potential of plant-derived antimicrobial peptides (AMPs) to successfully kill bacteria at low doses with little resistance makes them interesting. This overview highlights the efficacy of positive plant extracts, particularly those from *Moringa oleifera* and *Myrtus communis*, against infections such as *Staphylococcus aureus* and *Listeria monocytogenes*. PBPs can be used in food safety and to treat continual infection. This study emphasizes the significance of using natural assets to address antibiotic resistance by refining extraction techniques and examining bioactive substances. To improve public fitness strategies against resistant infections and examine their functional roles in current medication, further research is required on the mechanisms and implementation of PBPs.

Keywords: Antimicrobial resistance, Plant-based proteins, Essential oils, Antimicrobial peptides, Phytochemicals

Introduction

Antimicrobial Properties of Plant-Based Proteins (PBPs)

The growing prevalence of antibiotic-resistant bacteria threatens global health and emphasizes the need for alternative antimicrobial techniques.¹ In this context, PBPs have emerged as promising candidates, with developing proof of their exceptional antimicrobial potency against many human pathogens.¹⁻³

Recent research has confirmed that essential oils and other phytochemicals derived from various plant species show antibacterial properties. These compounds from herbs can prevent food spoilage, inhibit the proliferation of foodborne microorganisms, and deal with the problems caused by antibiotic resistance.² Plant-derived antimicrobials have received significant attention due to their safety, rendering them attractive alternatives to synthetic antibiotics.¹

Several PBPs, including those found in Myrtaceae species, were investigated for antimicrobial efficacy.

These critical oils have shown efficacy against various bacterial and fungal pathogens, such as those resistant to standard antibiotics.² Moreover, plant-based compounds have been explored for synergistic consequences while mixed with traditional antibiotics, potentially improving the overall antimicrobial properties and helping to mitigate the issue of antibiotic resistance.¹ Exploring plant-based antimicrobials is a promising approach, as they provide a diverse range of bioactive compounds harnessed to fight the emerging challenge of antibiotic-resistant infections.

The increasing incidence of multidrug-resistant ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) has driven to explore novel antimicrobial agents from herbal sources, which includes flora. Plant-based proteins have been recognized as a promising class of antimicrobial compounds, exhibiting potent properties against various pathogenic bacteria, fungi, and viruses. The antimicrobial results of PBPs are attributed to their capacity to disrupt plasma membranes, inhibit crucial enzymes, and intervene with protein synthesis, thereby compromising the viability and growth of microbial cells.⁴

Numerous studies have investigated the antimicrobial activities of diverse PBPs, such as lectins, thionins, defensins, and protease inhibitors. These proteins have extensive-spectrum antimicrobial properties, which can target each antibiotic-inclined and antibiotic-resistant line of bacteria.^{1,3} The mechanisms of antimicrobial effort of PBPs contain comprehensive goals and pathways, making it much less probable for microbes to increase resistance compared to synthetic antibiotics.^{1,4}

Methodology

A comprehensive literature search was performed from databases such as PubMed, Google Scholar, and Scopus, focusing on studies from the last two decades regarding the antibacterial properties of plant-primarily based proteins. The experimental designs and results of the chosen articles have been evaluated rigorously, and data summarizing the antibacterial effectiveness of different plant-derived proteins against specific diseases have been extracted. This review is based on diverse research indicating that plant proteins possess broad-spectrum antimicrobial properties against numerous pathogens. Research has demonstrated that proteins can compromise microbial cellular membranes and obstruct critical cellular processes. Plant-derived antimicrobial peptides (AMPs) have demonstrated efficacy against antibiotic-resistant strains. Certain

proteins, which include lectins and defensins, control microbial cells through significant mechanisms. Furthermore, researchers indicated that when natural antimicrobials are combined with traditional antibiotics, a synergistic impact occurs, highlighting their capability as options to fight antibiotic resistance. Those findings emphasize the significance of plant proteins in addressing global health-demanding situations associated with antibiotic resistance.

Table 1 summarizes the antimicrobial efficacy and mechanisms of diverse plant-derived proteins toward various pathogenic microorganisms. It highlights significant plant sources and their respective protein, combined with the particular pathogens they defend against and the mechanisms through which they exert their antimicrobial activities. The review highlights the capability of such natural compounds as replacements for synthetic antibiotics, primarily addressing the growing issue of antibiotic resistance. Table 1 highlights the importance of exploring plant-derived proteins to improve antimicrobial techniques by emphasizing various plant sources and their particular capabilities.

Antimicrobial Mechanisms of PBPs

AMPs, a considerable class of plant-derived proteins, display broad-spectrum interest in various pathogens, such as microorganisms and fungi. Those peptides regularly own particular structural functions and disulfide bonds that stabilize their conformation, which is critical for their activity. For example, thionins and

defensins disrupt microbial cell membranes and inhibit important cellular methods like DNA and protein synthesis, ultimately leading to microbial cell death. Those peptides are characterized by their charge capacity and structural range, allowing them to disrupt microbial cell membranes correctly. Their multifunctionality extends beyond antimicrobial properties, as they play roles in plant morphology and disease resistance.⁵⁻⁷ Figure 1 presents the collective efforts of AMPs to protect the plants against pathogens.

Many plant-derived metabolites, including phenolic compounds and terpenes, exhibit membrane-active antimicrobial activity, disrupting their integrity. This disruption can result in leakage of cytoplasmic components and lack of membrane potential, which can be essential for preserving cellular homeostasis. Furthermore, these compounds can intrude with microbial quorum sensing and enzymatic capabilities, enhancing their antimicrobial efficacy. Such interactions effectively inhibit the increase of pathogens and reduce resistance development due to their diverse activities.^{8,9}

Moreover, particular plant proteins have been recognized that possess inherent antimicrobial activities. For instance, storage proteins such as 2S albumins and Kunitz inhibitors have displayed activities against numerous pathogens. Those proteins can be collected in reaction to pathogen attacks and play a critical role in plant protection by performing as nutrient reserves and antimicrobial compounds. The synergistic relationship between these proteins' structural characteristics and their biological activities underscores the capacity of plant-based antimicrobials to address the demanding situations posed by resistant pathogens.

Antimicrobial Activity and Applications of Plant-Derived Protein Compounds

Plant protease inhibitors (PPIs) have emerged as attractive antimicrobial agents because they inhibit the proliferation of harmful bacteria, fungi, and protozoans. Figure 2 depicts that those substances showcase broad-spectrum efficacy against multiple microorganisms by disrupting critical metabolic methods or changing the permeability of microbial membranes. In the face of developing antibiotic resistance, PPIs from families like Solanaceae and Fabaceae have proven promising as modern medicinal marketers by effectively addressing the ramifications of infections.¹⁰

Moreover, contemporary research has tested the chemical ability of numerous plant-derived components. Plant secondary metabolites disrupt DNA/RNA synthesis and enzymatic methods in pathogens and concentration on microbial cell membranes. The effectiveness of contemporary antibiotics against resistant microorganisms can be multiplied through the synergistic action of those metabolites. To address antimicrobial resistance (AMR) and global health threats, innovative techniques need to be developed, necessitating scientific investigation into these natural compounds.^{8,11}

Challenges persist in optimizing extraction methodologies and ensuring the reproducibility of

Table 1 | Summary of antimicrobial efficacy and mechanisms of plant-derived proteins against pathogenic microorganisms

Plant Source	Protein Type	Pathogen Targeted	Mechanism of Action
<i>Moringa oleifera</i>	Moringin ¹⁴	<i>Listeria monocytogene</i> ¹⁴	Disrupts cell wall integrity ¹⁴ Oxidative stress ¹⁴
<i>Myrtus communis</i>	Essential oils ¹¹	<i>Staphylococcus aureus</i> ¹¹ <i>Escherichia coli</i> ¹⁶	Disrupts microbial membranes ¹¹
<i>Croton lechleri</i>	Extracts ^{16,17}	Various pathogens ^{16,17}	Antibacterial activity ^{16,17}
<i>Citrullus lanatus</i>	Seed protein fractions ²²	Pathogenic bacteria ²²	Varies by amino acid profile ²²
Plant-derived AMPs	Antimicrobial peptides ⁵⁻⁷	Multidrug-resistant bacteria ⁵⁻⁷	Disrupts membranes ⁵⁻⁷ Inhibits DNA/protein synthesis ⁵⁻⁷
Solanaceae & Fabaceae	Plant protease inhibitors ¹⁰	Fungi ¹⁰ Protozoans ¹⁰	Disrupts metabolic processes ¹⁰

Table 2 | Potential applications of plant-derived proteins and peptides as antimicrobials

Application Area	Examples/Specifics	Potential Benefits
Agriculture	Use as biopesticides, crop protection	Reduced reliance on synthetic pesticides. Environmentally friendly
Food Safety	Preservation of food Inhibition of foodborne pathogens	Extended shelf life Reduced risk of foodborne illness
Therapeutics	Treatment of bacterial, fungal, and viral infections, Immunomodulation, treatment of diabetes and cancer	Alternative to synthetic antibiotics Potential for synergistic effects Broad-spectrum activity Prevent chronic diseases
Biotechnology	High-yield production of AMPs	Large-scale production of novel therapeutics
Wound Healing	<i>Croton lechleri</i> extract	Used in ethnomedicine for wound healing May have antibacterial properties contributing to healing

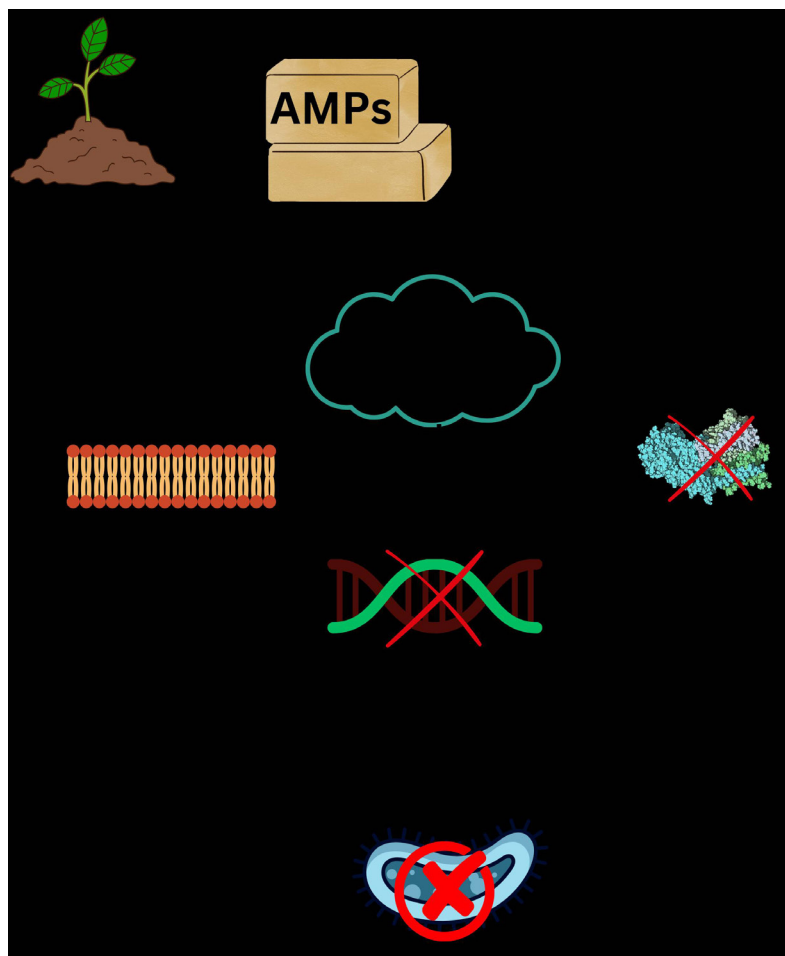


Fig 1 | Collective efforts of AMPs to protect the plants against pathogens

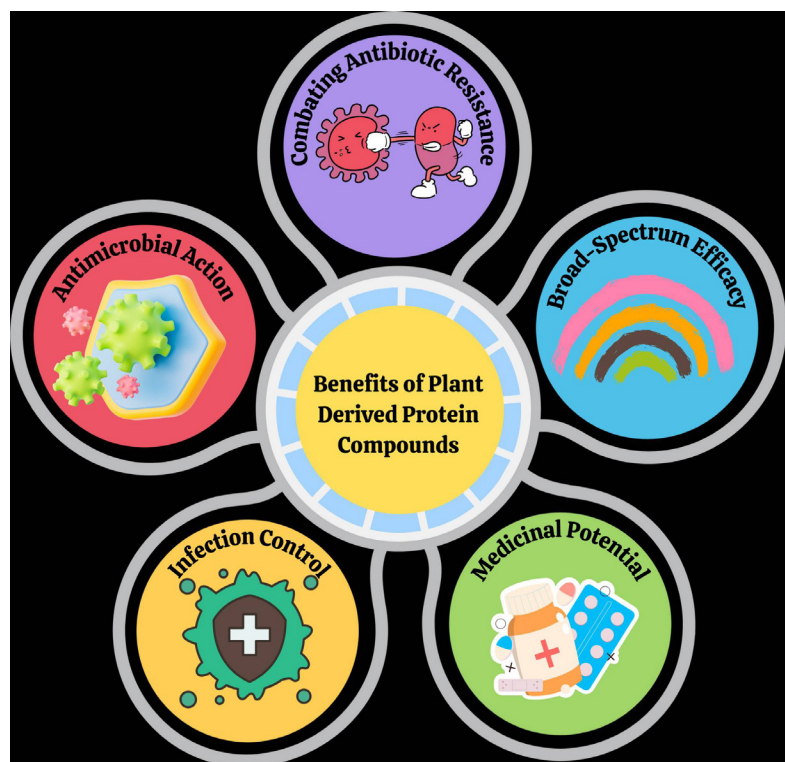


Fig 2 | PBPs showcase broad-spectrum efficacy against multiple microorganisms by disrupting critical metabolic methods or changing the permeability of microbial membranes

antimicrobial efficacy throughout different plant species. However, ongoing research centers on finding particular bioactive compounds among medicinal crops that could serve as powerful antimicrobial agents. This includes reading the mechanisms by which these compounds exert their consequences and addressing the complexities associated with their use in scientific settings.^{11,12}

The potential packages of those plant-derived proteins and peptides encompass agricultural practices, food protection, and remedies, highlighting their versatility and importance in modern-day antimicrobial strategies.¹³

The bioactive moringin extracted from *Moringa oleifera* seeds exhibits a minimum inhibitory concentration (MIC) of 400 μM , demonstrating significant efficacy against *Listeria monocytogenes*. The mechanism of the cellular signaling pathway induces oxidative stress, compromises cell wall and membrane integrity, and disrupts the microorganism’s energy metabolism and DNA replication strategies. This illustrates the potential of isothiocyanates as a unique form of antibacterial capsules, necessitating further research into their mechanisms and consequences to other infections.¹⁴

Figure 4 illustrates that in addition to moringin, different plant extracts exhibit significant antimicrobial efficacy. For instance, *Myrtus communis* and *Verbena officinalis* extracts have sturdy antibacterial properties towards *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella typhi* pathogens. Furthermore, *Myrtus communis* established effectiveness toward *Pseudomonas aeruginosa*, a common and difficult pathogen in medical settings. Furthermore, important oils like the ones from carrot seeds (*Daucus carota*) and tea tree (*Melaleuca alternifolia*) have been powerful against *Helicobacter pylori* and *Mycoplasma pneumoniae*, respectively. These findings underscore the diverse antimicrobial potential of plant-derived compounds.¹¹

Another example investigated the inhibitory effects of various plant-derived bioactive compounds, such as quercetin and curcumin, on antibiotic-resistant canine pores and skin germs. The results showed that those capsules should efficaciously combat multidrug-resistant microorganisms, with MIC values ranging from 0.04–16 mg/ml. These substances are believed to disrupt the integrity and functionality of the cytoplasmic membrane, which is crucial for bacterial survival.¹⁵

Furthermore, traditional medicinal herbs are a precious aid for developing novel antibacterial drugs. Several plant species utilized in ethnomedicine were shown to have innate antibacterial characteristics that can be employed for modern therapeutic functions. For example, extracts from *Croton lechleri*, which has long been used in the US to treat diseases, have encouraging antibacterial activity. This emphasizes the necessity to investigate understudied plant species that allow you to find new bioactive substances capable of assisting with the escalating hassle of antibiotic resistance.^{16,17}

Antimicrobial Screening of Plant-Based Protein Extracts
 Researchers explored the antimicrobial activities of diverse plant-based protein extracts, revealing

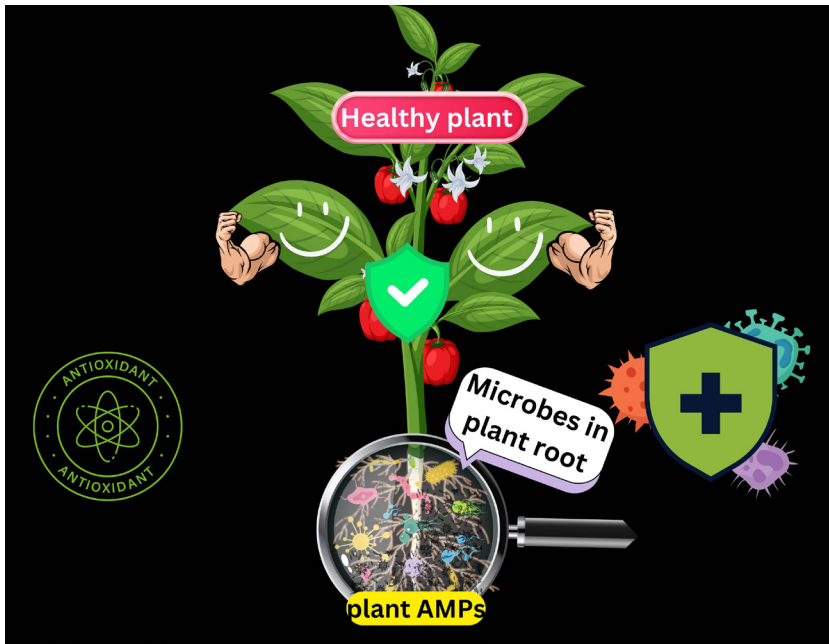


Fig 3 | Finding particular bioactive compounds among medicinal crops that could serve as powerful antimicrobial agents

considerable potential for many herbal substances in fighting microbial infections. Variations in extraction techniques could lead to different results in antimicrobial susceptibility checks. This underscores the need for standardized methods to appropriately evaluate the antimicrobial ability of plant extracts. It was pointed out that many plant compounds represent mechanisms of movement distinct from conventional antibiotics, providing a new therapeutic approach against resistant varieties.^{8,11}

In a comparative study of five herbal vegetation, consisting of *Psidium guajava* and *Salvia officinalis*, researchers assessed the antimicrobial outcomes of ethanolic extracts at various dilutions. The results verified antibacterial properties throughout all tested concentrations, with zones of inhibition measured towards preferred commercial antibiotics. This observation also confirmed that plant extracts could function as effective alternatives or adjuncts to conventional antimicrobial compounds.¹⁸

One excellent research focused on the venom of *Naja ashei*, wherein specific protein fractions exhibited antibacterial properties against *Staphylococcus epidermidis*. Their research recognized key additives, along with 3-finger toxins and L-amino acid oxidases, as individuals to the antimicrobial impact. Notably, the F2 fraction demonstrated a higher concentration of functional proteins than F1, suggesting that the composition and concentration of those proteins are important for their efficacy, as represented in Figure 5. Damage to bacterial cell walls becomes the movement mechanism, causing cytosolic material to leak; however, extra research is needed to discover the appropriate additives inflicting this effect.¹⁹

Protein fractions derived from *Cornu aspersum* mucus highlighted their promising antibacterial capability during experimental studies. The research observed that fractions with a molecular weight beneath 20 kDa exhibited substantial antimicrobial properties against pathogenic bacteria. The antimicrobial effects corresponded to vancomycin at higher concentrations, indicating that those protein fractions need to be characteristics that are effective options or complements to standard antibiotics. The observed peptides from this mucus have an abundance of amino acids associated with antimicrobial effect, suggesting a significant group of AMPs.²⁰

Moreover, a complete evaluation of plant-derived peptides mentioned their various bioactivities, along with antimicrobial outcomes. It emphasized the importance of various extraction and manufacturing techniques, including microbial fermentation and enzymatic hydrolysis, in improving the bioavailability and stability of those peptides. The evaluation also mentioned the useful activities of plant-derived peptides and their programs in food structures and nutraceuticals, underscoring their function in sustainable food manufacturing.²¹

Studies on seed protein fractions further confirmed varying antimicrobial properties amongst isolated proteins. This review provided insights into the amino acid profiles associated with these activities, reinforcing

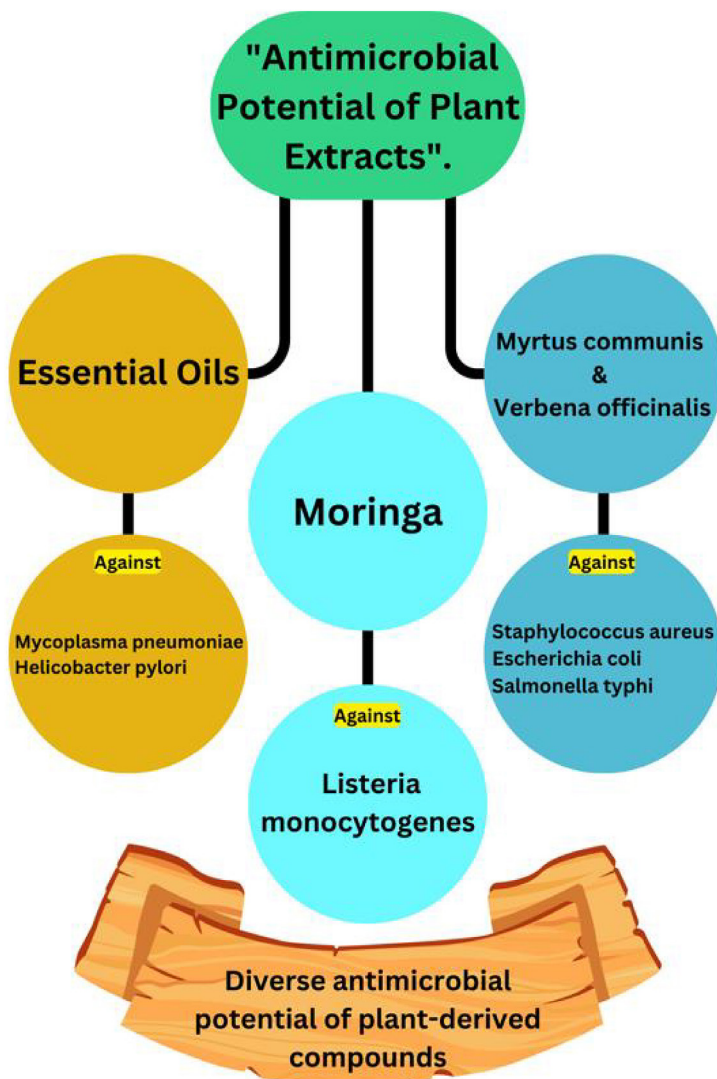


Fig 4 | Diverse antimicrobial potential of plant-derived compound

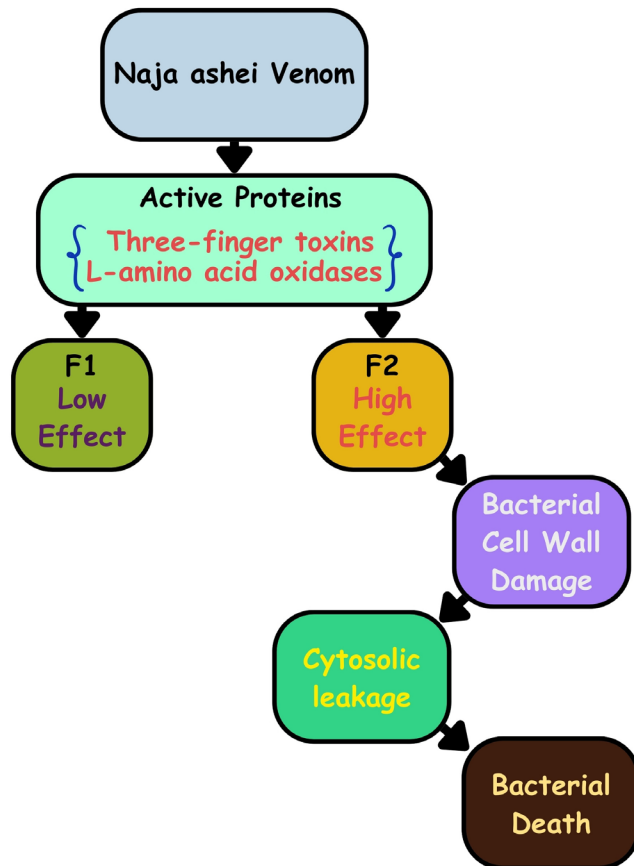


Fig 5 | Antibacterial potential of *Naja ashei* venom: mechanism and key components

that unique compositions can extensively affect the effectiveness of plant-derived proteins against microbial proliferation.²²

Potential Uses in Treating Infections in Human

Plant-derived AMPs have been found to possess immunomodulatory activities, strengthening the host's defenses against infections. Plant AMPs are useful therapeutic components in managing infectious issues due to their dual motion, which combines direct antibacterial activities with immune responses.^{21,23}

Research has also emphasized using enzymatic hydrolysis methods to show plant proteins in bioactive peptides, increasing the number of antimicrobial compounds used in scientific settings.²³

Plant AMPs are also being tested for their role in preventing and therapeutic interventions for non-communicable diseases. Figure 3 shows that their antioxidant activities endorse the ability to cope with continual diseases such as diabetes and cancer. For example, many peptides derived from plant proteins have verified efficacy in reducing oxidative strain and improving the cellular environment, which is important in the prevention of chronic and dangerous diseases.^{7,21}

Fermented plant-extracted proteins are focused on their antimicrobial activities. These fermented products incorporate bioactive peptides which could inhibit the proliferation of pathogenic microorganisms, amplify the storage life of commercial products, and prevent lipid peroxidation.²⁴

The fermentation procedure complements the bioavailability and functionality of plant proteins, making them powerful in improving intestinal conditions and combating harmful microorganisms.²⁵

Current advancements in biotechnology have enabled the excessive-yield, plant-based manufacturing of AMPs with better balance and efficacy.²⁶ This approach is promising for the large-scale, economical production of various therapeutics, including novel antimicrobial compounds.

Development of Novel Therapeutics from PAMPs

The research showed that expertise in the chronological launch of PAMPs/DAMPs could help identify subsets of septic sufferers, which might also be an advantage of centered treatments. A relevant study conducted on PAMP validated the importance of continuous PAMP expression for the most appropriate anti-pathogen immunity.²⁷

Researchers observed that transgenic expression of bacterial PAMPs on *Trypanosoma cruzi* led to improved pathogen resistance and improved adaptive immune responses. This innovation highlights the capacity of PAMP-based treatments to sustain strong adaptive immunity after the early phases of contamination. Concentrated on innate immune pathways has been proven to protect against most cancers in recent years. Researchers have located approaches to rewire tumor-related macrophages to exhibit anti-tumor traits, such as inhibiting CD47 on tumor cells.²⁸

These approaches exhibit the capability of harnessing innate immune pathways for healing development in oncology. In AMR, novel therapeutic techniques for multidrug-resistant *Pseudomonas aeruginosa* are being explored.²⁹ These encompass the improvement of inhibitors concentrated on important proteins in lipopolysaccharide transportation, consisting of MsbA and LptD.

Table 2 lists the numerous properties of plant-primarily based antimicrobials in food preservation, medicine, and agriculture. These characteristics demonstrate their adaptability in reducing dependency on synthetic chemical substances, extending food's shelf lifestyles, and offering techniques for curing sicknesses and infections.

Challenges in PAMP Production, Stability, and Bioavailability

The manufacturing and yield of PAMPs face numerous challenges. Although effective for peptide generation, recombinant techniques often result in low production yields and may not alleviate existing toxicity from the source. Furthermore, the inability to incorporate non-organic additives presents significant limitations. To address the issues, researchers have explored the fusion of peptides with thioredoxin, chloroplast expression structures, and different cell vectors that can prevent cellular breakdown and assist in forming disulfide bonds. Moreover, the stability and bioavailability of PAMPs are major issues. Those peptides are at risk of proteolysis, which could appreciably lessen their effectiveness in vivo. The layout and technology of PAMPs is a sensitive procedure that needs careful dealing with

components including toxic effects, haemolytic properties, and susceptibility to enzymatic degradation. Modifications to reduce cytotoxicity and improve protection are necessary. However, these changes need to be made without compromising the antimicrobial characteristics and potency of the outcome.²³

Another major difficulty in PAMP research and application is the temporary nature of their interactions with target cells. Those short-lived interactions can result in instability in physiological environments and terrible manipulation of the density and orientation of the molecules.³⁰

This instability can substantially affect the efficacy of PAMP-primarily based treatment plans or vaccines, particularly in keeping a sustained immune reaction. Moreover, the complex interaction between PAMPs and the host immune device offers demanding situations in predicting and controlling the immune reaction, which is crucial for developing powerful and safe treatments.³¹

Future Directions

More research investigating the antimicrobial capability of plant-primarily based proteins against human pathogens must emphasize leveraging genetic engineering techniques to improve manufacturing and exploring synergistic effects with other compounds. Researchers could employ CRISPR-Cas9 generation to regulate plant genomes, grow the expression of antimicrobial proteins, or optimize their shape for enhanced efficacy. Moreover, studies should be performed to explore the aggregate of plant-primarily based antimicrobial proteins with conventional antibiotics or other AMPs to attain synergistic outcomes. This method should enhance treatment efficacy, lessen toxicity, and protect the improvement of resistance.

Furthermore, exploring the interaction between plant-derived antimicrobial proteins and metallic nanoparticles, such as nickel oxide, should lead to innovative approaches for addressing bacterial antibiotic resistance. Ultimately, researchers must perform comprehensive *in vivo* studies to assess the efficacy and safety of these mixtures, emphasizing their capacity to modulate immune responses, reduce irritation, and enhance tissue regeneration alongside their direct antimicrobial properties.

Conclusion

Exploring PBPs as antimicrobial compounds provides a promising road to prevent the development of the danger of antibiotic resistance. This study highlights the sizable capacity of diverse plant-derived proteins, consisting of AMPs, protease inhibitors, and secondary metabolites, in displaying vast-spectrum antimicrobial activities against a wide range of human pathogens. The mechanisms by which these compounds exert their effects, interfering and disrupting microbial cellular membranes, inhibiting vital enzymatic techniques, and interfering with protein synthesis, underscore their efficacy and the reduced chance of resistance improvement compared to traditional antibiotics.

Moreover, the synergistic outcomes that might be visible when conventional antibiotics and plant-primarily

based antimicrobials are blended provide promising prospects for improving positive effects. This study highlights the need for standardized extraction strategies to maximize the effectiveness of these herbal materials and guarantee reproducibility throughout several investigations. Ongoing research of disregarded plant species may additionally screen new bioactive compounds that could improve human defenses against resistant microbes. Beyond their medicinal settings, plant-derived antimicrobial proteins can be used in agricultural and food preservation techniques.

Plant-based antimicrobials could be critical in growing sustainable and powerful substitutes for synthetic antibiotics, as antibiotic resistance is causing a growing global health situation. Moreover, studies of these natural products are crucial to convert their beneficial impacts into clinical and practical applications, resulting in improved global health initiatives.

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