Application of Housefly Antimicrobial Peptides in Plant Disease Control

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12th March

UNIVERSITY of TASMANIA | WICKING Dementia Research & Education Centre

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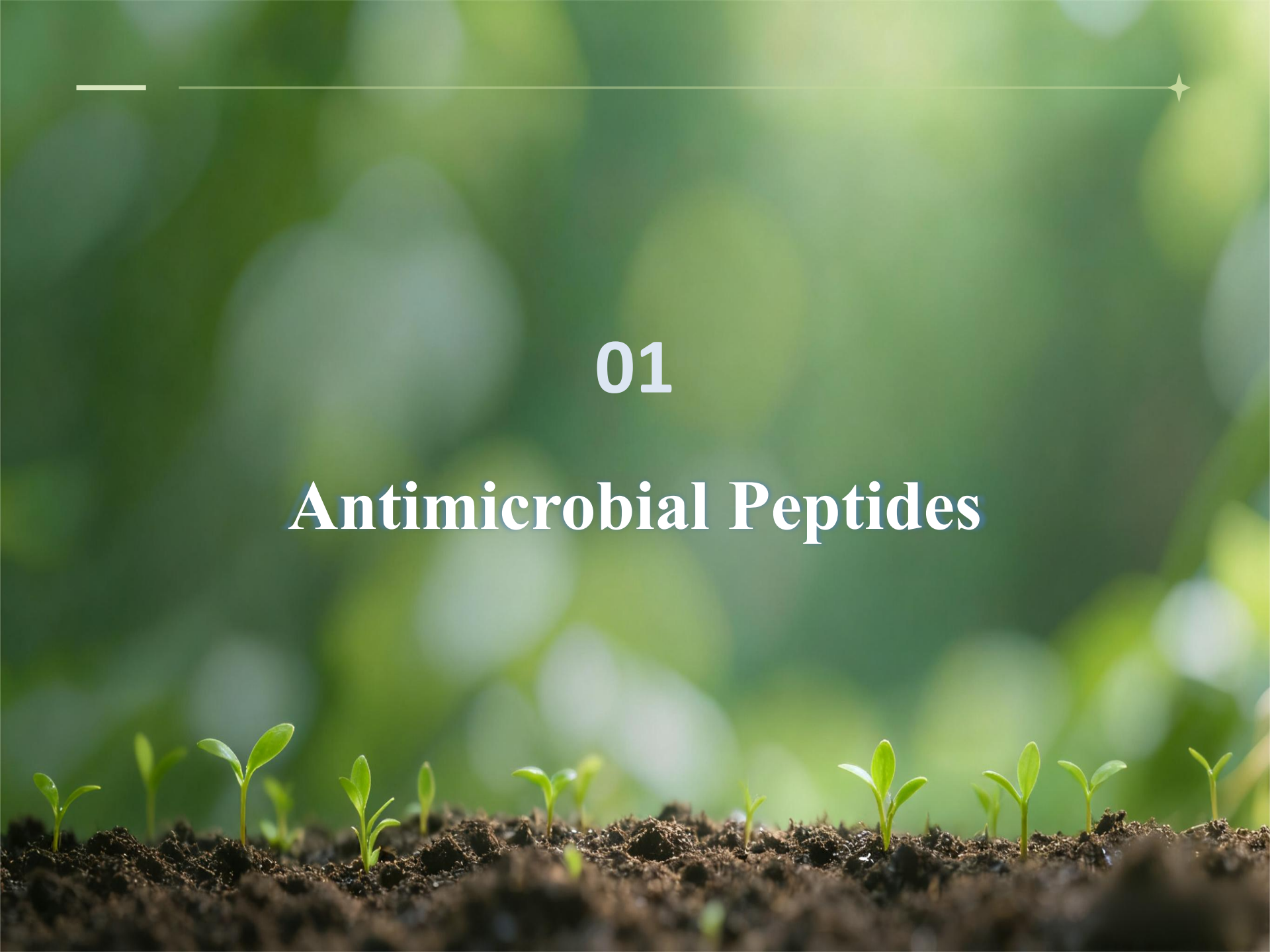

01
Antimicrobial Peptides

Pathogen infection

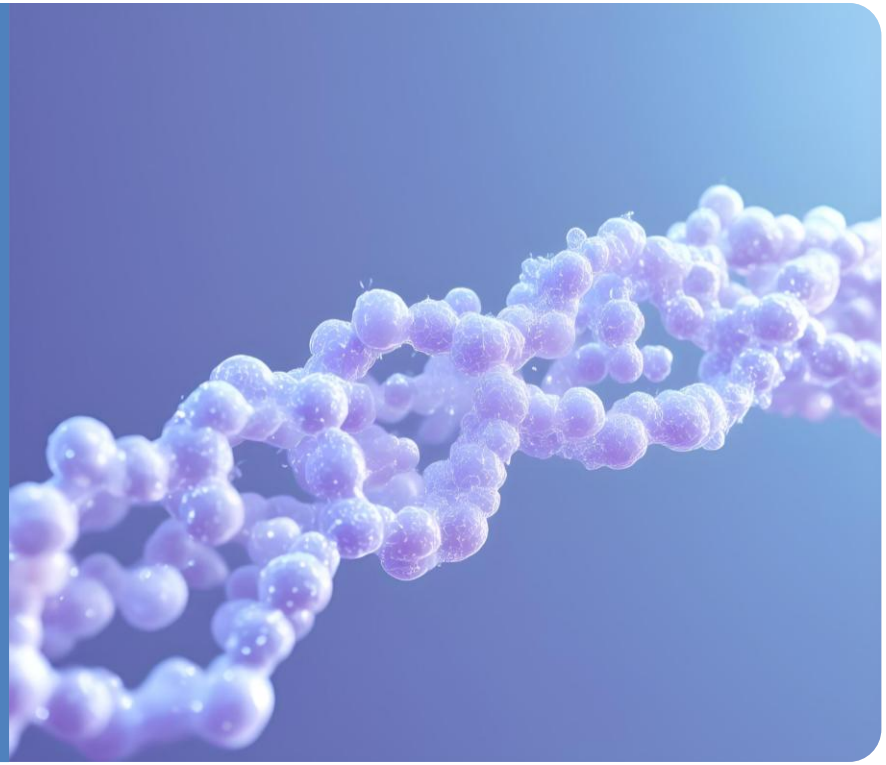
Pathogen infection is one of the major causes of plant disease and yields loss in the crop field.

The rapid increase of antimicrobial resistance in plant pathogens has led to an urgent need for the development of management strategies for plant disease.

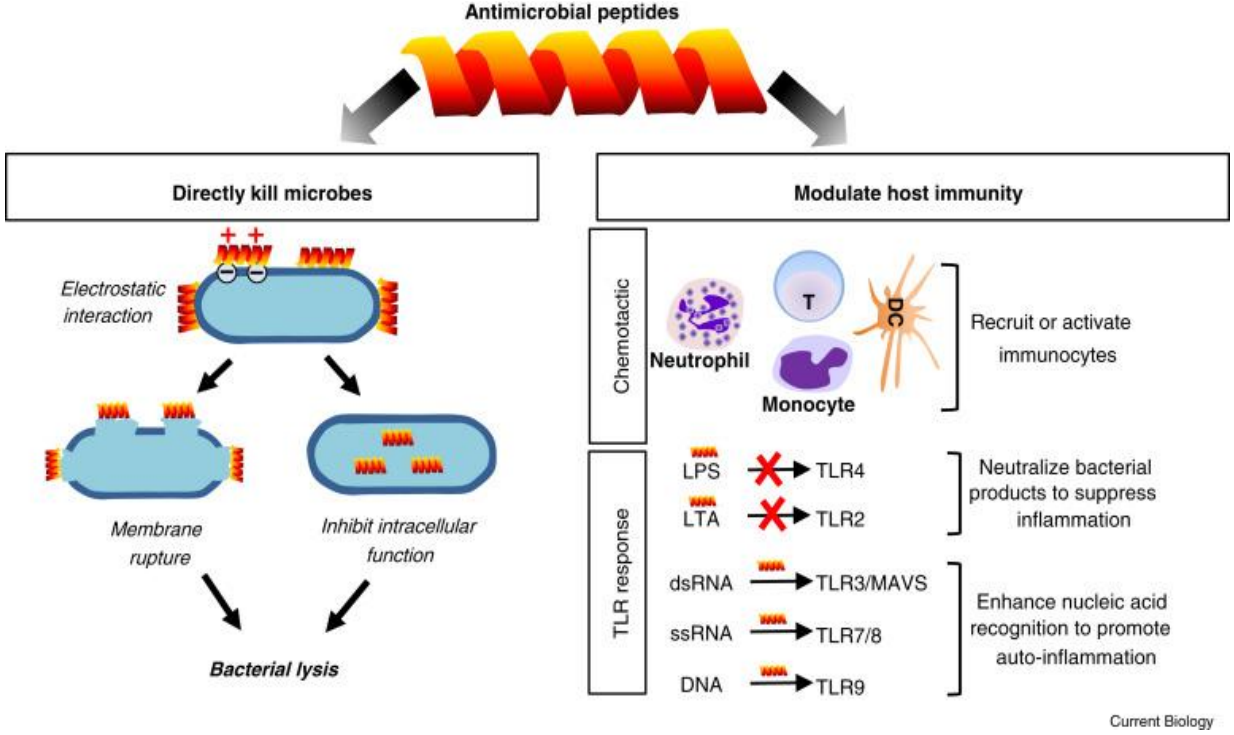
Antimicrobial Peptides (AMPs)

These characteristics make it potential weapons to counteract the antibiotic resistance

- A class of positively charged small molecule peptides
- Usually <100 amino acid residue
- Broad-spectrum activity, low target resistance and low immunogenicity
- Non-toxic or low toxicity to normal eukaryotic cells, and almost no drug resistance



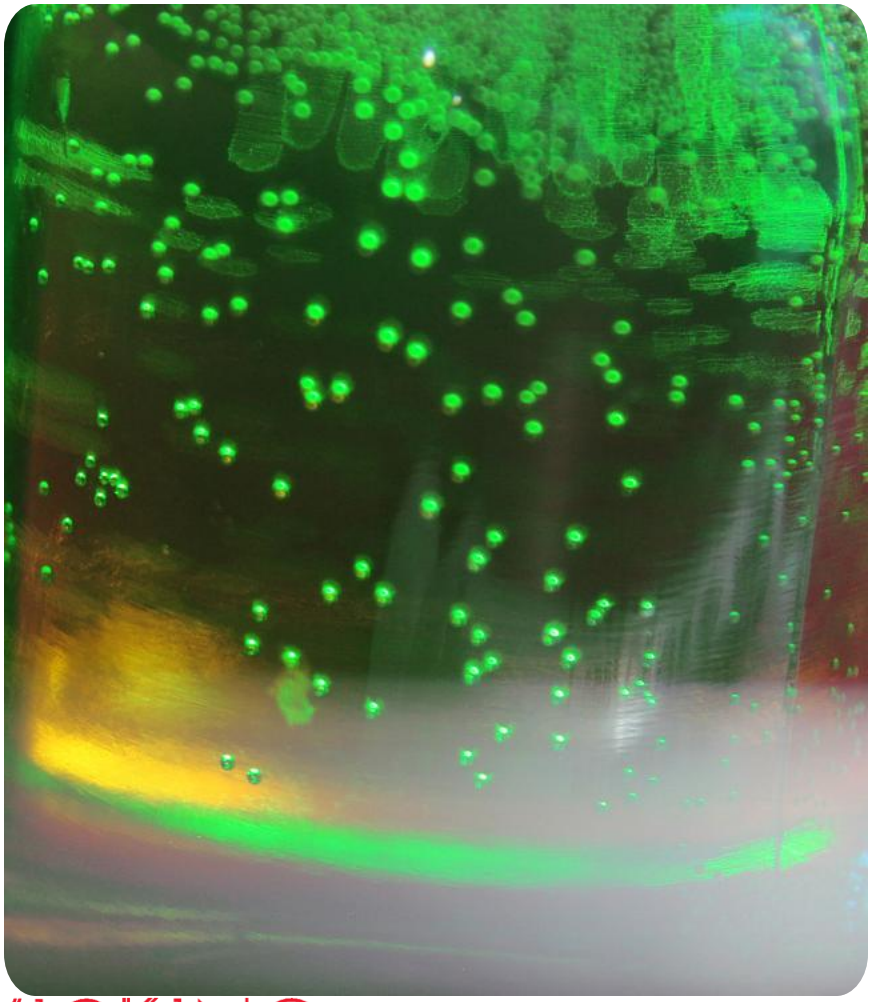
Mechanism of action for antimicrobial activity



- Direct killing
  - membrane-targeted mechanisms
  - non-membrane-targeted mechanisms
- Immunomodulation

(Zhang and Gallo, 2016)

Enhancing AMP Bioavailability



Delivery Systems

Optimizing delivery systems can significantly improve the bioavailability of AMP products by ensuring efficient absorption and targeted release within the body.

Formulation Strategies

Advanced formulation techniques, such as nanoparticle encapsulation, enhance stability and uptake, offering superior performance for AMP-based therapies in clinical applications.

Future Innovations

Emerging technologies in drug delivery hold promise for further advancements, enabling customizable solutions tailored to specific therapeutic needs and patient profiles.

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Application of AMPs in agriculture

- It can be used in fruit and vegetable cultivation to improve soil and enhance crop disease resistance.
- Given the wide application of peptide drugs in the pharmaceutical field, many scholars have begun to explore the possibilities of peptide applications in agriculture.

Antibacterial and antifungal activities of AMP

AMPs have long been proposed as a potential anti-bacteria and anti-fungi reagents in plant disease control (Van der Biezen, 2001; Montesinos, 2007; Marcos et al., 2008; Montesinos and Bardajı,2008; Wang et al., 2018; Lobo and Boto, 2022)

AMP

Plant disease control

Effectively inhibit a variety of plant pathogens, such as bacteria, fungi, and viruses, thereby reducing the occurrence of crop diseases and improving yield and quality.

Improve crop stress resistance

Enhance crops' resistance to abiotic stresses, such as drought and salinity, thereby improving their survival ability under adverse conditions.

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Challenges

The application of AMP in crop cultivation is currently mainly in the laboratory research stage and has not yet achieved large-scale commercialization.

High Cost

The cost of large-scale extraction or synthesis of antimicrobial peptides is far higher than that of traditional pesticides.

Safety Verification

As a novel biological agent, its effects on non-target organisms (such as beneficial insects and soil microorganisms) still require long-term evaluation.

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AMPs from Housefly

AMPs from housefly

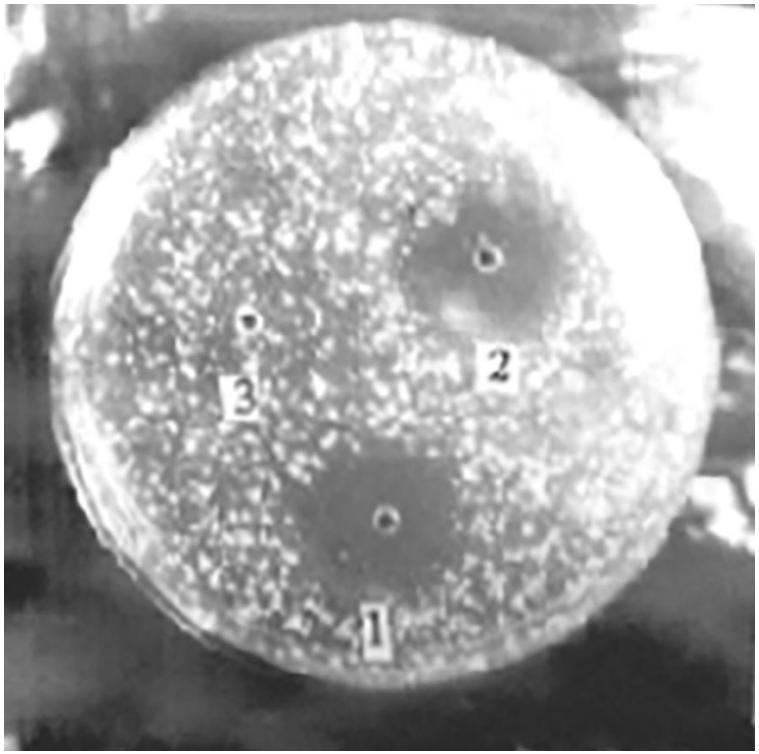
- Until now, more than 3100 AMPs have been discovered and isolated from bacteria, fungi, amphibians, insects, higher plants, mammals and even humans (Lazzaro et al., 2022).
- Insects represent a significant source of AMPs.
- Houseflies have a unique immune defence mechanism, which is more effective than that of other insects in resisting infection by pathogens.

A natural AMP in the housefly

- An antimicrobial peptide was isolated and purified from the hemolymph of adult houseflies.
  - Small natural peptide: molecular weight is 10Kda.
  - Strong thermal stability: strong ability to withstand high temperatures, 100 ℃ treatment for 10 minutes is still active
  - Broad-spectrum antimicrobial activity: it is resistant to Gram-positive (e.g. Staphylococcus aureus) and negative bacteria (e.g. Escherichia coli), as well as to fungi(e.g.Aspergillus niger) , with the strongest inhibitory activity against pathogenic Staphylococcus aureus.
  - Its antibacterial activity has been shown to be stronger than that of penicillin and cecropin in controlled tests.

A natural AMP in the housefly

- Its antibacterial activity has been shown to be similar to penicillin in controlled tests.

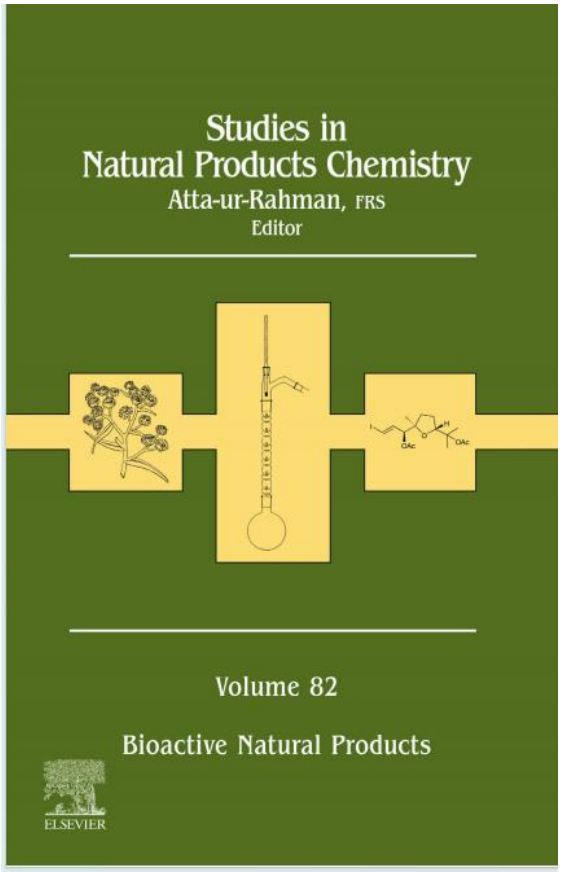


1. AMP
2. Positive control (penicillin)
3. Negative control (1M ammonium acetate)

Synthetic small molecule peptides

- The developed small molecules have the functions of bacteriostatic cell growth, and at the same time, it is non-toxic to normal human cells.
- Several linear small peptides with 9-12 amino acids , which are not only convenient for artificial chemical synthesis, but also genetically engineered to produce linear peptide without folding the three-dimensional structure, which can maintain the original antibacterial activities.

I was invited to published a book chapter on housefly AMP



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Antimicrobial peptides from the housefly

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Introduction

Since the discovery of penicillin, antibiotics have been widely used around the world. However, the misuse of antibiotics has led to an acceleration in the evolution of pathogenic bacteria, resulting in the proliferation of drug-resistant and multidrug-resistant bacteria [1]. The emergence and evolution of drug-resistant and multidrug-resistant bacteria and the gaps in antibiotic development have led to an urgent need for the development of new antimicrobial drugs [2]. In recent years, researchers have conducted a lot of research on additives such as oligosaccharides, probiotics, plant extracts, and antibacterial peptides in an attempt to determine the feasibility of their role in the development of new antibiotics [3].

Natural compounds exhibit great chemical diversity, making them an important and reliable source of novel drugs. AMPs are one such class of natural products that are commonly found in living organisms and have a variety of biological functions [4]. Natural AMPs have gradually become popular research targets with the progression of research [5,6]. A large number of AMPs have been found in bacteria, archaea, protozoa, fungi, plants, and

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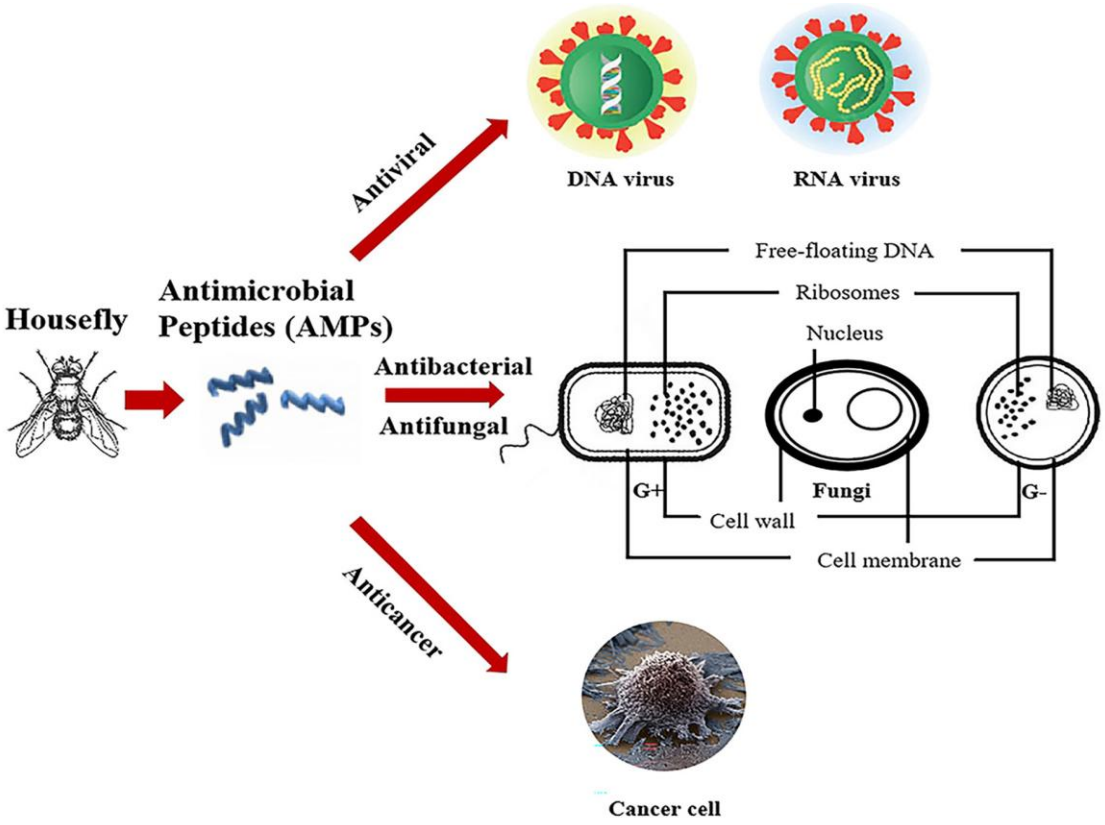
Plant Disease Control

AMPs from housefuly

TABLE 1.7 Summary of the applications of AMP from housefly.

Application	Example	Function	References
Antibacterial	CM-III	G^+ and G^-	[141]
	House fly maggot extracts	MRSA (Methicillin-resistant *Staphylococcus aureus*) and VRE (Vancomycin-resistant enterococci)	[155]
	Musca domestica cecropin	G^+ and G^-	[156]
Antiviral	A protein-enriched fraction (PE) from the larvae of the housefly	Strong antiviral activity against influenza virus	[157]
		Inhibited DNA replication of HBV and suppress HBV core protein expression	[158]
Antifungal	AMP-17	Strong antifungal activity	[159,160]
Anticancer	*Musca domestica* cecropin	Inhibit the proliferation, invasion, and migration of BEL-7402 cells of human liver cancer	[165]
	AMP from the housefly	The proliferation of human K562 and MCF-7 cells could be inhibited	[166]
	AMPs of the housefly larvae	Inhibit the proliferation of leukemia cells K562	[167]
	AMP from the housefly	Inhibit the proliferation of leukemia cells FBL-3	[168]
	A small antitumor peptide derived from Musca domestica cecropin (M1-8)	Promote cell apoptosis of liver cancer cells	[171]



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Unique Advantages of AMPs from housefly

Rapid killing bacterials	Unlike antibiotics, which take several hours to take effect, high concentrations of antimicrobial peptides can kill pathogens within 30 seconds to several minutes.
Broad-spectrum activity	It also has an inhibitory effect on Gram-positive bacteria, Gram-negative bacteria, fungi, viruses, and even some nematodes (such as pine wood nematode).
Environmentally friendly	Antimicrobial peptides eventually degrade into ordinary amino acids, leaving no toxic residues in soil and plant tissues.
High stability	Antimicrobial peptides derived from houseflies typically exhibit good thermal stability and water solubility, making them suitable for application in agricultural field environments.

The mechanism of housefly AMP in Plant Disease Control

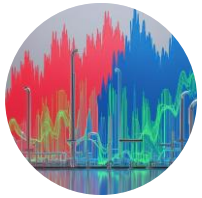
Direct suppression and killing: Highly effective in killing multiple types of pathogens

It has a significant killing effect on various pathogenic fungi and bacteria of crops, such as rice blast fungus and gray mold fungus, and causes leakage of cell contents by changing cell membrane permeability.

Immune activation: Stimulating the plant's systemic defense capabilities

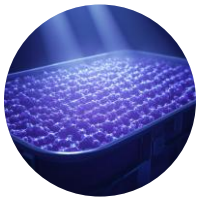
As a signaling molecule, it activates systemic acquired resistance (SAR) in plants, induces the synthesis of plant protectants, and enhances the activity of defense enzymes such as peroxidase (POD) and polyphenol oxidase (PPO).

Biosynthetic technologies



The biosynthetic preparation methods of peptide pesticides deserve further in-depth research.

Heterologous expression systems used for peptide production include bacteria (such as Escherichia coli and Bacillus subtilis), fungi (such as Pichia pastoris and Saccharomyces cerevisiae), and plants (cell and tissue cultures).



Traditional chemical synthesis methods (liquid-phase/solid-phase synthesis) are costly and difficult to scale up, while biosynthetic technologies such as enzyme catalysis, fermentation, and genetic engineering are low-cost

Application Forms

Leaf protection technology solutions

The extracted or synthesized antimicrobial peptides are made into biological pesticides and sprayed directly onto crop leaves or soil to inhibit pathogen growth.

Genetic Engineering

Transferring housefly antimicrobial peptide genes into crops to cultivate transgenic crops with natural disease resistance. This is currently a hot research topic, aiming to enable crops to "produce antibodies" themselves.

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Conclusion

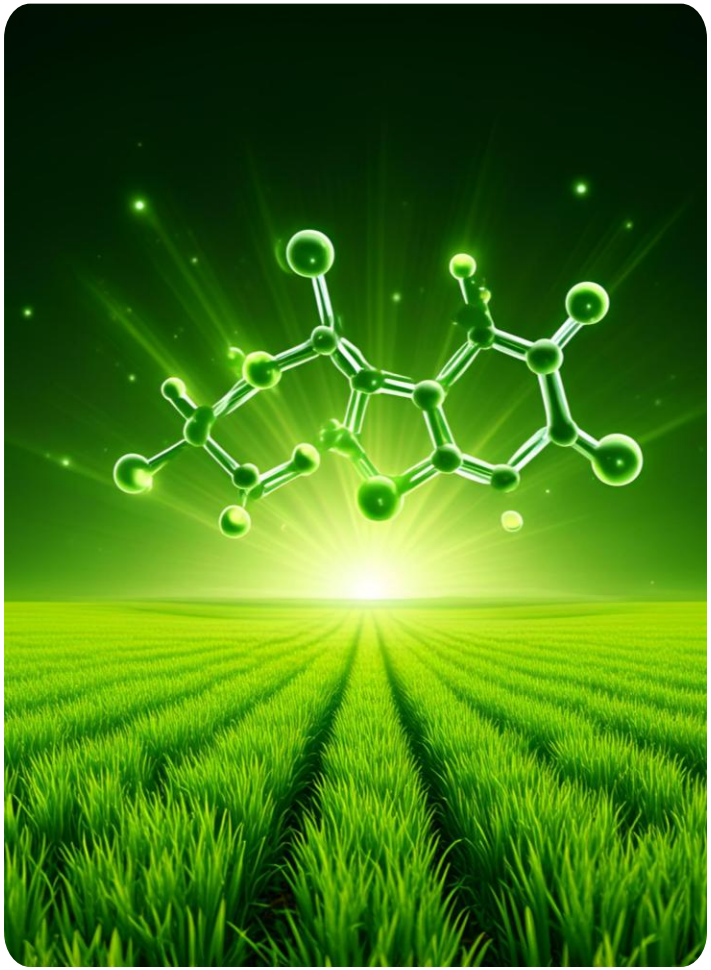
Conclusion

Promising Application Value

- A promising area in plant disease control, representing the future direction of green agriculture development
- Good environmental compatibility, thus promoting sustainable agricultural development.

Challenges and solutions

- Low systemic stability: the stability and delivery system of peptides
- High cost of production: Biosynthetic technologies

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Future study

Cooperation with Prof. Meixue Zhou at UTAS

- Detecting the bactericidal activity of housefy AMPs against a wider range of bacteria and fungi that cause plant diseases.

- Improve the stability and delivery system of peptides to enhance their field performance.


Thank you!
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