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Research and Development Progress and Application Challenges of Bacterial Biocontrol Agents

Yi Hu[1]*, Ye Chen[1], Zhenxing Xie[1], Kaijun Song[2]

[1] Hubei Key Laboratory of Economic Forest Germplasm Improvement and Resources Comprehensive Utilization, Huanggang Normal University, Huanggang 438000, China;

[2] Huanggang City Huangzhou District Agriculture and Rural Affairs Bureau, Hubei Huanggang 438000, China;

* Corresponding Author 18164053837@163.com

Abstract

In recent years, there has been a notable increase in global interest in bacterial biocontrol agents as a pivotal approach to the management and control of agricultural pests and diseases. This paper reviews the progress in research and development of bacterial biocontrol agents, including the screening and identification of efficient biocontrol strains, the study of biocontrol bacterial metabolites, and the application of genetic engineering and synthetic biology. The challenges faced in its practical application are analysed, including environmental stability, production cost, regulatory approval, farmers' awareness and resistance management. Finally, the future development direction of bacterial biocontrol agents is discussed, with the aim of providing a reference for research and application in this field.

Keywords

Bacterial biocontrol agents; biocontrol strains; metabolites.

1. Introduction

Agricultural pests and diseases have profound consequences for global food security and ecological stability, representing a significant challenge to the field of agriculture. For an extended period, chemical pesticides have been extensively utilised due to their expeditious effectiveness and ease of application. However, these pesticides have also resulted in ecological degradation, environmental contamination, biodiversity loss, and the emergence of drug resistance.[1] Consequently, the development of safe, effective and environmentally friendly means of pest control has emerged as a major international research focus in the domain of plant protection[2]. Bacterial biocontrol agents, a significant category of biopesticides, are employed to prevent and control agricultural pests and diseases through various mechanisms, including antagonism, inducing plant resistance and promoting plant growth. These agents offer numerous advantages, including environmental safety, harmless residues and a low risk of resistance. In recent years, with the promotion of a green agriculture development strategy and the need for sustainable development of global agriculture, there has been rapid progress in the research and development and application of bacterial biopesticides. In addition, countries have formulated relevant policies to support their application and promotion.For instance, China's Ministry of Agriculture and Rural Affairs promulgated the Action Program for Chemical Pesticide Reduction, which explicitly stipulates that the utilisation of chemical pesticides in China must be substantially curtailed by 2030. Moreover, the program proactively fosters the promotion and implementation of biopesticides, encompassing bacterial biocontrol agents. According to data from the China Pesticide Information Network, as of the end of 2021, more than 540 microbial pesticide products had been registered in China, with the majority of these being bacterial formulations. The existence of policy support and favourable market trends indicates that the bacterial biopesticide industry is currently experiencing a significant period of rapid development. Despite the strides made in earlier research, numerous challenges persist in practical applications, including product instability and inconsistent efficacy in

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field settings. In light of these challenges, the present study aims to provide a comprehensive overview of the recent advancements in the field of bacterial biocontrol agents. A systematic analysis of the prevailing challenges in their practical application will be conducted, and a series of rational recommendations for future research and development will be put forward. These recommendations are intended to provide both theoretical support and practical guidance for the advancement of research and applications in the domain of bacterial biocontrol agents.

2. Progress in research and development

2.1 Screening and identification of biocontrol strains

The primary starting point for the development of bacterial biocontrol agents is the screening and characterisation of efficient biocontrol strains. Natural environments are characterised by a proliferation of microbial resources, with soil, inter-root, and plant endophytes serving as significant reservoirs of biocontrol bacteria. The conventional approach entails the isolation of numerous bacterial strains from these environments, followed by the screening of candidate strains that demonstrate antagonistic effects on target pathogens or pests through plate standoff tests. In recent years, however, the advent of high-throughput screening techniques and miniaturized bioassays has enabled the concurrent evaluation of the antagonistic activity of a greater number of bacterial strains, thereby enhancing the efficiency of the screening process[3].

For instance, researchers isolated and screened a bacterial strain from tobacco inter-root soil that exhibited high antagonistic activity against Fusarium root rot of tobacco, and conducted in-depth studies on its biocontrol properties. Furthermore, a strain of Fusarium graminearum was isolated from the soil of a larch dieback area, exhibiting a substantial inhibitory effect on the pathogen, thereby providing a novel biocontrol resource for the management of this disease. These studies suggest that biocontrol strains with application potential can be obtained through screening strategies targeting specific pathogens[4].

Conventional methods of identifying biocontrol strains primarily rely on morphological, physiological and biochemical characterisation. However, with the advent of molecular biology techniques, such as 16S rRNA gene sequencing, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), and other techniques, the identification of bacteria has become more accurate and rapid. For instance, MALDI-TOF MS can be used to rapidly identify the species of bioprophylaxis strains, providing a basis for subsequent applied research[19].

2.2 Metabolites and their mechanisms of action

The inhibition of the growth or pathogenicity of pathogenic bacteria is achieved by biocontrol bacteria through the production of a variety of metabolites. These include antibiotics, enzymes and organic acids. For instance, Pseudomonas fluorescens is capable of producing phenazine antibiotics, hydrogen cyanide, and other substances that inhibit the growth of a variety of plant pathogenic fungi[5]. Furthermore, antimicrobial peptides produced by Bacillus subtilis have been shown to have inhibitory effects on a variety of plant pathogenic bacteria. In recent years, significant advancements have been made in the study of the mechanism of action of these metabolites. For instance, it has been determined that certain antibiotics produced by bioprophilic bacteria can interfere with the cell membrane structure of pathogenic bacteria, ultimately resulting in their demise. Furthermore, the capacity of biocontrol bacteria to impede the infestation of pathogens by competing for nutrients and space, in addition to inducing plant resistance, has been demonstrated. A more profound comprehension of these mechanisms is therefore pivotal for the development of enhanced biocontrol agents[6,16].

2.3 Applications of genetic engineering and synthetic biology

Genetic engineering and synthetic biology have emerged as novel methodologies for the development of bacterial biocontrol agents. Through the utilisation of gene editing technology, the genomes of biocontrol strains can be modified in a targeted manner to enhance their antimicrobial activity,

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environmental adaptability and stability. For instance, the antimicrobial peptide synthesis gene cluster of Bacillus subtilis was modified using the CRISPR-Cas system, resulting in enhanced yield and activity of antimicrobial peptides. Furthermore, synthetic biology has been employed to engineer new metabolic pathways, enabling biocontrol strains to synthesize antimicrobial substances that are not naturally produced, thus broadening their applications. For instance, the introduction of exogenous genes into engineered Streptomyces has been shown to facilitate the efficient synthesis of polyketide compounds that possess antimicrobial activity, thereby creating the potential for the development of novel biopesticides. Nevertheless, challenges remain with regard to the practical implementation of these genetic engineering and synthetic biology approaches, including biosafety assessment of GMOs, public acceptance, and limitations of relevant regulations. Consequently, while promoting the advancement of these technologies, it is imperative to thoroughly evaluate the potential risks they may pose and to formulate suitable regulatory and assessment mechanisms[2,7,17].

2.4 Current status of application of bacterial biocontrol agents

The utilisation of bacterial biocontrol agents in agricultural production has been limited, albeit with some notable exceptions. These agents have been employed, primarily, in the management of various plant diseases and pests. For instance, Bacillus subtilis preparations have been employed for the management of rice blight, Pseudomonas fluorescens for the control of wheat blast, and Bacillus cereus for the management of wheat leaf blight[20]. The employment of these biocontrol agents has yielded several notable benefits, including a reduction in the reliance on chemical pesticides, a decline in pesticide residues in agricultural products, and the protection of the ecological environment[3]. However, there are some problems and challenges in the application of bacterial biocontrol agents. Firstly, the efficacy of biocontrol is significantly influenced by environmental factors, including temperature, humidity, and soil properties, resulting in variable outcomes following field application. Secondly, the activity of biocontrol strains may be compromised during the manufacturing and storage processes, potentially impacting product quality and efficacy[6]. Furthermore, the dissemination and implementation of biocontrol agents are hindered by factors such as farmers' awareness, market acceptance, and policy support. Consequently, there is a necessity to enhance the screening and improvement of bioprophylactic strains to improve their environmental adaptability and stability; optimise the production process to ensure product quality; and concurrently increase the publicity and promotion to improve farmers' awareness and acceptance of bioprophylactics. Government departments should also introduce corresponding policies to encourage and support the research and development and application of biological control agents to promote the green and sustainable development of agriculture[8,18].

3. Application challenges

As a significant component of sustainable agriculture, bacterial biocontrol agents offer distinct advantages, including their environmental friendliness and target-specificity. Nevertheless, they continue to encounter numerous challenges in terms of their promotion and application, primarily in the following domains[4].

(1). Environmental stability and field effect fluctuation The field effect of bacterial biocontrol agents is susceptible to environmental factors such as temperature, humidity, UV irradiation and rainfall. These factors may lead to a decrease in the activity of the biocontrol bacteria, thus affecting the control effect. For instance, the inactivation of microbial insecticides by ultraviolet light from sunlight has been observed, and heavy rainfall has also been shown to affect their effectiveness in the field. Consequently, the development of strains that exhibit strong environmental adaptability, in conjunction with the enhancement of formulation to improve their tolerance, is identified as a pivotal strategy to enhance the effectiveness of field application.

(2). Production cost and scale-up constraints Cultivation, fermentation and formulation processing of biocontrol bacteria are complicated, and the production cost is relatively high. In addition, the production process requires strict quality control to ensure the activity and stability of the product.

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These factors are a significant hindrance to the large-scale production and popularisation of bacterial biocontrol agents. The optimisation of the production process, the reduction of production costs and the improvement of product quality are identified as the key factors in achieving large-scale production.

(3). Regulatory approval and market access The registration and approval process for biocontrol agents is often complicated and time-consuming, and can require significant investment. The existence of differing regulatory requirements across various geographical regions has the potential to act as a barrier to market access for products. The harmonisation and simplification of legal frameworks, for instance to enhance the efficiency of evaluating biocontrol products, could facilitate their wider use. Consequently, the establishment of a unified and scientific regulatory system, coupled with the simplification of the approval process, is imperative to facilitate the marketisation of biological control agents[1].

(4). Farmers' Awareness and Acceptance It is evident that some farmers lack sufficient knowledge regarding bacterial biological control agents, which can lead to reservations concerning their efficacy and application. Furthermore, the long-standing practice of relying on conventional chemical pesticides may hinder the adoption of biocontrol agents among farmers. Consequently, there is an imperative for enhanced training and information dissemination to farmers to augment their knowledge and confidence in biological control agents, thereby promoting their adoption in agricultural production.

(5). Resistance risk and management It is important to note that the long-term use of a particular biocontrol bacterium may lead to the development of resistance in the target pathogen or pest, thereby reducing the effectiveness of control. A pertinent example of this phenomenon is the pervasive issue of bacterial resistance to antibiotics, which has garnered significant global attention. Consequently, there is an imperative for the formulation of scientific resistance management strategies, such as the rotation of biocontrol agents with differing mechanisms or the combination of biocontrol agents with alternative means of control, to forestall the emergence of resistance.

(6). Product stability and storage conditions The activity of bacterial biocontrol agents is significantly influenced by storage conditions, including temperature, humidity and light. Inadequate storage conditions may result in a decline in the activity of the bacterial strains, thereby impacting the product's efficacy in controlling the desired outcome. Consequently, the development of more stable formulations, in conjunction with the establishment of reasonable storage and transport specifications, is imperative to ensure the quality of the product.

(7). The compatibility of biological control agents with chemical pesticides is also a crucial consideration in practical applications, as the combination of these agents is often essential to enhance the efficacy of control. However, the interaction between these agents can potentially impact the activity of biocontrol bacteria, thereby diminishing the overall efficacy of the integrated pest management strategy. Consequently, there is a necessity to study the compatibility of biocontrol agents with chemical pesticides and to develop reasonable mixing and rotation strategies for achieving integrated pest management.

(8). Target specificity and the necessity for broad-spectrum control It is evident that a significant proportion of bacterial biocontrol agents demonstrate a high degree of target specificity, being effective only against specific pathogens or pests. This limitation, particularly in scenarios necessitating broad-spectrum control, restricts the scope of application. Consequently, there is a need to develop bacterial biocontrol strains with broad-spectrum activity, or to expand the range of control by compounding multiple biocontrol agents.

In conclusion, the challenges associated with the application of bacterial biocontrol agents necessitate a collaborative effort among research institutes, production enterprises, government departments, and farmers to promote their widespread utilisation in agricultural production through technological innovation, policy support, publicity, and promotion.

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4. Future directions

The mounting international demand for sustainable agriculture and eco-friendly pest management strategies is set to catalyse novel prospects for the advancement and implementation of bacterial biocontrol agents[6]. The future direction of this field can be conceptualised through the following aspects:

(1). Selection and breeding of efficient bacterial strains and function optimisation The utilisation of modern biotechnology, encompassing genomics, transcriptomics and proteomics, facilitates the comprehensive exploration of the abundant microbial resources in the environment, enabling the identification and enhancement of strains with superior biocontrol properties. Through synthetic biology or gene editing technology, the resistance, colonisation ability and antimicrobial activity of target strains can be enhanced to meet the needs of different crops and pest control. For instance, researchers have modified biocontrol strains through genetic engineering to enhance their inhibitory effect on specific pathogens[7].

(2). R&D and application of composite fungicides The biocontrol effect of a single strain may be limited, and the compounding of a variety of strain preparations with complementary functions can play a synergistic role and improve the control effect. By optimising strain combinations, composite fungicides with broad-spectrum pest and disease resistance can be developed to meet the control needs of different crops and regions. However, it is imperative to exercise caution and meticulously consider the interactions between these diverse strains to avert the potential occurrence of antagonistic effects.

(3), Advancements in formulation technology and enhancement of product stability The development of novel formulation technologies, including microencapsulation and nanocarriers, has led to significant progress in safeguarding biocontrol bacteria against detrimental environmental factors. These innovations have also contributed to enhancing the stability and persistence of these bacteria during storage and field applications. In addition, the optimisation of the production process is aimed at reducing production costs and enhancing the market competitiveness of the products[15].

(4). Research on compatibility with chemical pesticidesIn actual agricultural production, biological control agents often need to be used in combination with chemical pesticides. Consequently, it is imperative to investigate the compatibility of bacterial biocontrol agents with prevalent chemical pesticides, formulate a rational mixing and rotation strategy to achieve integrated pest management, and reduce the utilisation of chemical pesticides and environmental pollution[9].

(5). Policy support and market promotionThe government should formulate relevant policies to encourage the R&D and application of biological control agents. Such policies might include the provision of financial support for R&D and the simplification of the approval process. Concurrently, efforts should be made to enhance the training and awareness programmes for farmers and agricultural practitioners. These initiatives are designed to augment their knowledge and acceptance of biological control agents, thereby fostering the market application of these products. For instance, China's '14th Five-Year Plan for the Development of Bio-economy' aims to expedite the development of bio-economy and promote the application of biotechnology in agriculture.

(6). International cooperation and standardisation

Strengthen international cooperation and exchanges, learn from advanced experiences, and jointly address the challenges of global agricultural pest control. Concurrently, the formulation and enhancement of international standards and norms for bacterial biological control agents is imperative, along with the promotion of trade and application of products, and the assurance of product quality and safety.

In summary, the application of bacterial biological control agents is expected to be broad in the future sustainable development of agriculture. Through the efforts of science and technology innovation, policy guidance and market promotion, it is expected to realise their wide application in agricultural

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production and make positive contributions to global food security and ecological environment protection.

5. Conclusion and Outlook

Bacterial biocontrol agents are playing an increasingly important role in the sustainable development of global agriculture by virtue of their advantages such as environmental friendliness and low risk of drug resistance[1]. This paper reviews the progress in research and development of bacterial biocontrol agents, including the screening and identification of efficient biocontrol strains, the study of metabolites, the application of genetic engineering and synthetic biology, as well as the current status of their application in agricultural production. Concurrently, the prevailing challenges, including environmental stability, production costs, regulatory approvals, farmer awareness and resistance management, are analysed[10,11,12,13,14].

In the following sections, we propose a series of recommendations to guide future research and development in this field.

Selection and breeding of efficient strains and function optimisation: the utilisation of contemporary biotechnology to unearth and enhance strains that boast superior biocontrol properties, whilst concomitantly augmenting their resistance and colonisation capabilities, thereby ensuring their capacity to adapt to the evolving field environment.

Research and development of composite fungicides: combining multiple strains with complementary functions to develop composite fungicides with broad-spectrum resistance to pests and diseases, thus meeting the control needs of different crops and regions.

Improvement of preparation technology and product stability: the development of new preparation technology to improve the stability and efficacy of biocontrol bacteria in storage and field application to ensure stable control effects.

Research on compatibility with chemical pesticides: The development of reasonable mixing and rotation strategies to achieve synergistic effects between biocontrol agents and chemical pesticides is also recommended, with the aim of promoting integrated pest management.

The provision of policy support and market promotion is also recommended. The government should introduce relevant policies to encourage the R&D and application of biological control agents, strengthen the training and publicity for farmers and agricultural practitioners to enhance their awareness and acceptance, and promote the market application of the products.

International cooperation and standardisation: International cooperation and exchanges should be strengthened, international standards and norms for bacterial biological control agents should be formulated and improved, and the trade and application of products should be promoted, ensuring product quality and safety.

It is anticipated that the implementation of these measures will enable bacterial biocontrol agents to assume a more significant role in the pursuit of sustainable agricultural development, thereby contributing positively to global food security and ecological environmental protection.

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