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"Unveiling The Mechanisms of Actinobacteria In Biocontrol Against Fungal Phytopathogens: Exploring Potential Biocontrol

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Abstract:
Fungal phytopathogens pose significant threats to global agricultural productivity, necessitating sustainable and eco-friendly solutions for their control. Actinobacteria have emerged as promising biocontrol agents due to their versatile metabolic capabilities and antagonistic properties against fungal pathogens. This review aims to elucidate the mechanisms underlying the biocontrol activity of Actinobacteria against fungal phytopathogens, as well as to explore their potential in developing effective biocontrol strategies.

We begin by highlighting the diverse mechanisms through which Actinobacteria exert biocontrol, including competition for nutrients, production of antimicrobial compounds, induction of systemic resistance, and modulation of plant growth-promoting traits. Understanding these mechanisms is crucial for harnessing the full biocontrol potential of Actinobacteria in agricultural settings. Furthermore, we delve into recent advancements in omics technologies, such as genomics, transcriptomics, proteomics, and metabolomics, which have provided invaluable insights into the molecular basis of biocontrol activity exhibited by Actinobacteria.

In addition to elucidating mechanisms, we discuss the factors influencing the efficacy of Actinobacteria-based biocontrol, including environmental conditions, microbial interactions, and formulation strategies. We also explore innovative approaches, such as the use of microbial consortia and nanotechnology, to enhance the biocontrol efficacy and stability of Actinobacteria-based formulations. Moreover, this review underscores the importance of considering ecological factors and promoting sustainable agricultural practices in the development and deployment of Actinobacteria-based biocontrol agents. We discuss challenges and future directions in harnessing the biocontrol potential of Actinobacteria, including the need for standardized testing protocols, optimization of formulation techniques, and integration with other management practices.

In conclusion, Actinobacteria represent promising biocontrol agents against fungal phytopathogens, offering sustainable and environmentally friendly alternatives to conventional chemical pesticides. By unraveling their mechanisms of action and exploring innovative biocontrol strategies, Actinobacteria have the potential to revolutionize pest management practices and contribute to the development of resilient and sustainable agricultural systems.

Keywords: *Actinobacteria, Biocontrol Fungal phytopathogens, Mechanisms, Antagonism, Omics technologies, Microbial interactions, and Formulation strategies*

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I. Introduction:

Fungal phytopathogens pose a significant threat to global agriculture due to their ability to cause devastating diseases in various crops, leading to significant yield losses and economic repercussions (Fisher *et al.*, 2012; Savary *et al.*, 2012). These pathogens infect a wide range of plant species, including staple food crops such as wheat, rice, maize, and fruits and vegetables, thereby jeopardizing food security and livelihoods worldwide (Strange and Scott, 2005; Oerke, 2006).

The impact of fungal phytopathogens is exacerbated by factors such as climate change, globalization, monoculture farming practices, and the continuous evolution of pathogen strains, which contribute to the emergence of new diseases and the spread of existing ones (Garrett *et al.,* 2006; Fisher *et al.,* 2012). Conventional methods for controlling fungal diseases often rely heavily on synthetic chemical pesticides, which raise concerns regarding environmental pollution, human health risks, and the development of pesticide resistance in pathogens (Köhl *et al.,* 2011; Pretty *et al.,* 2018). Therefore, there is an urgent need for sustainable and environmentally friendly alternatives to combat fungal phytopathogens and mitigate their impact on agriculture. Biological control, particularly the use of microbial antagonists, has gained attention as a promising approach for managing fungal diseases in crops (Hirsch *et al.,* 2013; Zhang *et al.,* 2017). Among microbial agents, Actinobacteria have emerged as potent biocontrol agents due to their diverse metabolic capabilities and antagonistic activities against fungal pathogens (Palaniyandi*et al.,* 2013; Rajendran *et al.*, 2016).

By harnessing the biocontrol potential of Actinobacteria, it is possible to develop effective and sustainable strategies for managing fungal diseases in agriculture, thereby enhancing crop productivity and food security (El-Tarabily*et al.*, 2010; Palaniyandi*et al.,* 2013). However, to fully exploit the biocontrol efficacy of Actinobacteria, it is essential to understand the underlying mechanisms of their antagonistic activity against fungal phytopathogens and optimize their application in agricultural systems (Hirsch *et al.,* 2013; Palaniyandi*et al.,* 2013).

Fungal diseases affecting crops have escalated in severity and scope since the mid-20th century, now representing a significant menace to global food security (Fisher *et al.,* 2012; Savary *et al.,* 2019). Despite interventions, approximately 10–23% of crops succumb to diseases before harvest, with an additional 10–20% lost post-harvest (Fisher *et al.,* 2012). These pathogens not only devastate essential calorie crops like rice, wheat, maize, and soybean but also wreak havoc on commodity crops such as bananas, coffee, and barley. The economic stability of numerous nations relies heavily on export revenues generated by trading these commodity crops, which are then used to purchase food from other regions (Fones *et al.,* 2020).

The intensification of modern agriculture exacerbates the fungal disease challenge. Monoculture practices, featuring genetically uniform crops protected by limited resistance genes and single-target antifungals, accelerate the emergence of virulent and fungicide-resistant strains (Fisher *et al.,* 2018). Such monoculture settings provide ideal environments for rapid fungal variant emergence due to their abundant spore production and genetically mutable genomes, susceptible to mutations, gene acquisitions, and hybridizations. Consequently, these pathogens exploit human interventions to realize their evolutionary potential, creating a skewed competition where the struggle is no longer solely between plant and pathogen but between pathogen and humanity (Fones *et al.,* 2020).

Climate change exacerbates the situation, altering disease patterns as pathogens migrate toward the poles in response to global warming (Bebber *et al.,* 2013). Additionally, trade and transportation of plants and plant products facilitate the spread of pathogens to new hosts in previously unaffected regions (Fones *et al.*, 2020). For instance, the livelihoods of tens of thousands in Asia and South America rely on bananas, a highly consumed and widely traded fruit globally (Ploetz, 2015). The recent incursion of the deadly banana pathogen *Fusarium oxysporum*f.sp. cubense Tropical Race 4 (now *Fusarium odoratissimum*, Maryani *et al.,* 2019) into South America in 2019 poses a severe threat to their prosperity (García-Bastidas *et al.,* 2020).

Fungal phytopathogens are a significant threat to global agriculture.

Fungal phytopathogens represent a formidable threat to global agriculture, posing significant challenges to crop productivity and food security. These pathogens can cause devastating diseases in various crops, leading to substantial yield losses and economic repercussions. The severity of this threat has been increasingly recognized in recent years due to the escalation in both the prevalence and impact of fungal diseases on agricultural systems worldwide.

Numerous studies have documented the detrimental effects of fungal phytopathogens on crop yields and food production. For instance, Fisher et al. (2012) emphasized the emerging fungal threats to animal, plant, and ecosystem health, highlighting the widespread impacts of these pathogens. Similarly, Savary et al. (2019) provided an overview of the global burden of pathogens and pests on major food crops, underlining the significant economic and agricultural implications of fungal diseases.

The scale of the problem is evident from statistics indicating substantial pre-harvest and post-harvest losses attributed to fungal diseases. Fisher et al. (2012) estimated that 10–23% of crops are lost before harvest, despite disease interventions, with an additional 10–20% lost post-harvest. These losses not only affect essential calorie crops such as rice, wheat, maize, and soybean but also commodity crops like bananas, coffee, and barley.

The intensification of modern agricultural practices has exacerbated the challenge posed by fungal diseases. Monoculture farming, characterized by the cultivation of vast areas with genetically uniform crops, coupled with the use of single-target antifungals, has facilitated the emergence of virulent and fungicide-resistant strains (Fisher *et al.*, 2018). This monoculture cropping system provides an ideal environment for the rapid evolution of fungal variants, leading to increased disease pressure on crops.

Climate change further exacerbates the situation by altering disease dynamics and expanding the geographic range of pathogens. Bebber et al. (2013) highlighted the global spread of crop pests and pathogens in response to climate change, indicating shifts in disease demographics as pathogens migrate toward the poles in a warming world. Additionally, globalization and trade have facilitated the dissemination of plant pathogens to new regions, further exacerbating the spread of fungal diseases (Fones *et al.,* 2020). The fungal phytopathogens pose a significant and multifaceted threat to global agriculture, impacting crop yields, food security, and economic stability. Addressing this challenge requires concerted efforts to develop sustainable disease management strategies, enhance crop resilience, and promote biodiversity in agricultural systems.

Fungi pose a significant threat to global food security, impacting food supply chains through various avenues. Their destructive potential manifests in multiple ways, including crop diseases, spoilage, and the production of mycotoxins, thereby jeopardizing both crop yields and food safety. Addressing these challenges is imperative to safeguarding food security, particularly in the face of escalating pressures from human population growth and climate change. To effectively combat fungal threats, it is essential to invest in innovative research aimed at developing sustainable strategies for fungal control, fostered through international collaboration and interdisciplinary approaches.

Fungal infections and diseases significantly contribute to crop losses, with estimates suggesting that fungi destroy up to 30% of crop products worldwide through disease and spoilage processes (Fisher *et al.*, 2012; Savary *et al.*, 2019). These losses not only diminish overall food production but also exacerbate food shortages and drive-up prices, particularly in regions heavily reliant on agriculture for sustenance. Moreover, fungi pose a grave threat to food safety by producing mycotoxins, toxic compounds that contaminate food and feed supplies. Mycotoxin-producing fungi, such as Aspergillus and Fusarium species, can contaminate crops both pre- and post-harvest, leading to serious health risks when consumed by humans or animals (Bennett & Klich, 2003). Exposure to mycotoxins has been linked to various health issues, including liver damage, cancer, and neurological disorders, underscoring the importance of mitigating fungal contamination in the food chain.

Controlling fungal growth and mitigating the associated risks are paramount for ensuring food security in a rapidly changing world. However, existing measures for fungal control often fall short, and emerging challenges, such as population growth and climate change, further exacerbate the problem. Population growth increases the demand for food, placing additional strain on agricultural systems already grappling with fungal threats. Additionally, climate change alters environmental conditions, creating new niches for fungal pathogens to thrive and facilitating the spread of diseases to previously unaffected regions (Bebber *et al.*, 2013).

Investment and innovation in research are crucial for developing effective strategies to combat fungal threats and enhance food security. This necessitates collaborative efforts that transcend disciplinary and geographical boundaries, drawing upon expertise from diverse fields such as biology, agronomy, genetics, and food science. By fostering international collaboration and sharing knowledge and resources, researchers can leverage collective expertise to tackle the complex challenges posed by fungal pathogens. Finally, fungi represent a multifaceted threat to global food security, with their detrimental effects extending from crop losses to food safety risks. Addressing these challenges requires concerted efforts to develop innovative strategies for fungal control, underpinned by investment in research and facilitated by international collaboration. By harnessing the power of interdisciplinary approaches and global cooperation, we can work towards ensuring a more resilient and sustainable food supply for future generations.

Mention the need for sustainable and eco-friendly solutions for controlling these pathogens.

The need for sustainable and eco-friendly solutions for controlling fungal pathogens in agriculture is increasingly urgent due to the adverse environmental and health impacts associated with conventional chemical pesticides. As concerns about pesticide residues in food, soil, and water continue to grow, there is a pressing need to transition towards safer and more sustainable alternatives.Conventional chemical pesticides not only pose risks to human health and wildlife but also contribute to environmental degradation, soil erosion, and loss of biodiversity (Pretty *et al.*, 2008; Pimentel, 2005). Furthermore, their indiscriminate use can lead to the development of pesticide-resistant strains of fungal pathogens, rendering these chemicals ineffective over time (Rosenberg and Zilber-Rosenberg, 2016).

In this context, sustainable and eco-friendly alternatives offer promising solutions for controlling fungal pathogens while minimizing adverse environmental impacts. Biological control agents, such as microbial antagonists and natural enemies of pests, can effectively suppress fungal diseases in crops without causing harm to the environment or human health (Müller *et al.*, 2016; Palaniyandi*et al.*, 2013). These biocontrol agents work by competing with pathogens for resources, producing antimicrobial compounds, or inducing systemic resistance in plants, thereby providing long-term protection against diseases.

Furthermore, sustainable agricultural practices, such as crop rotation, intercropping, and use of cover crops, can enhance soil health and resilience to fungal diseases (Altieri, 1999; Lynch and Oki, 2016). By promoting natural biological processes and ecosystem services, sustainable agriculture reduces reliance on external inputs and fosters ecological balance within agroecosystems.

In finally, the transition towards sustainable and eco-friendly solutions for controlling fungal pathogens in agriculture is imperative for ensuring long-term food security and environmental sustainability. By embracing biocontrol agents and adopting sustainable agricultural practices, we can effectively manage fungal diseases while safeguarding human health and the environment.

The objective of this review is to elucidate the mechanisms underlying Actinobacteria's biocontrol activity against fungal pathogens and to explore their potential in developing effective biocontrol strategies.

Through a comprehensive analysis of the literature, this review aims to provide insights into how Actinobacteria exert their antagonistic effects against fungal phytopathogens and how these mechanisms can be harnessed to develop sustainable and eco-friendly biocontrol strategies for agricultural applications.

The focus of this study is to investigate sustainable and eco-friendly solutions for controlling fungal pathogens in agriculture, to identify effective strategies that minimize environmental impacts while ensuring long-term food security.

Biological Control

The most effective non-chemical method for managing pests and diseases in organic farming is biological management, also known as biocontrol. This approach is highly specialized, profitable, sustainable, and environmentally safe. Biocontrol methods harness natural biological mechanisms to control pests and diseases, making them ideal for organic farming practices.

One widely utilized biocontrol strategy involves the use of soil bacteria that naturally exist to combat a range of illnesses and pests. These beneficial bacteria can suppress the growth and activity of harmful pathogens through various mechanisms, such as competition for resources, production of antimicrobial compounds, and induction of systemic resistance in plants (Berg *et al.,* 2005; Mendes *et al.,* 2011).

However, the successful implementation of biocontrol strategies requires a thorough understanding of the interactions between plants and pathogens, as well as the local environmental factors influencing these interactions. In situations of widespread disease, such as those encountered in organic farming, it becomes essential to comprehend the complex dynamics at play before applying biocontrol measures (Pieterse *et al.,* 2014).

Biocontrol in plant pathology encompasses the interplay of several environmental elements aimed at reducing the deleterious impacts of harmful species while promoting the establishment of beneficial insects, bacteria, and crops (Compant*et al.,* 2019). This approach relies on the numerous agonistic and antagonistic interactions that occur between microorganisms in the rhizosphere (the soil zone influenced by plant roots) and phyllosphere (the above-ground parts of plants) (Berendsen *et al.,* 2012). By harnessing these interactions, biocontrol strategies can effectively lower disease incidence and control pest populations in agricultural settings.

Rhizosphere organisms play a crucial role in biocontrol. These microorganisms can be obtained from the surrounding environment through a "black box" approach, where their natural dynamics and interactions are leveraged for pest and disease management (Berg *et al.,* 2005). Alternatively, beneficial microorganisms can be introduced into the field from outside sources, representing a "silver bullet opportunity" to enhance biocontrol efficacy (Pieterse *et al.,* 2014).In final, biological management or biocontrol stands out as the most effective non-chemical method for managing pests and diseases in organic farming. By understanding the intricate interactions between plants, pathogens, and beneficial microorganisms, organic farmers can harness the power of biocontrol to promote sustainable agriculture while minimizing environmental impacts.

II. Review Of Literature:

Fungal pathogens pose a significant threat to global agriculture, impacting crop yields and food security. Traditional methods of pest and disease management, such as chemical pesticides, have raised concerns about environmental and health risks. In response, organic farming practices have increasingly turned to biological management or biocontrol as a sustainable and eco-friendly alternative. This review aims to explore the effectiveness of biocontrol strategies in managing fungal pathogens in organic farming systems.

Biological Management in Organic Farming

Biological management, or biocontrol, involves the use of natural enemies, such as beneficial microorganisms, predators, and parasites, to suppress pests and diseases. This approach aligns with the principles of organic farming, which emphasize sustainable practices that minimize environmental impact (Berg *et al.,* 2005).

Mechanisms of Biocontrol

Biocontrol mechanisms can vary widely, including competition for resources, production of antimicrobial compounds, induction of plant systemic resistance, and predation on pest organisms (Mendes *et al.,* 2011; Pieterse *et al.,* 2014). Beneficial microorganisms, such as certain species of bacteria and fungi, play a crucial role in biocontrol by outcompeting and inhibiting the growth of pathogenic fungi in the rhizosphere and phyllosphere (Berendsen *et al.,* 2012).

Effectiveness of Biocontrol

Studies have demonstrated the efficacy of biocontrol agents in managing fungal pathogens in various crops. For example, Berg et al. (2005) found that certain rhizosphere-associated fungi could suppress the growth of Verticillium dahliae, a common fungal pathogen, in tomato plants. Similarly, Mendes et al. (2011) identified disease-suppressive bacteria in the rhizosphere microbiome that could protect plants against soil-borne pathogens.

Challenges and Opportunities

Despite the promise of biocontrol, challenges remain in its implementation in organic farming systems. Factors such as variability in environmental conditions, specificity of biocontrol agents, and regulatory constraints may limit the effectiveness of biocontrol strategies (Compant*et al.,* 2019). However, ongoing research and technological advancements offer opportunities to overcome these challenges and enhance the sustainability of biocontrol practices in agriculture.

In final, biological management or biocontrol represents a promising approach to managing fungal pathogens in organic farming. By harnessing the natural antagonistic interactions between microorganisms and pathogens, biocontrol offers a sustainable and eco-friendly alternative to chemical pesticides. Continued research and collaboration are essential to optimize biocontrol strategies and promote their widespread adoption in organic agriculture.

Biological control approaches for managing plant diseases involve reducing the number or impact of pathogens through the induction of biological mechanisms or the action of naturally occurring or introduced antagonists (Stirling and Stirling, 1997). Microbial biocontrol agents (BCAs), typically bacteria or fungi isolated from the rhizosphere, endosphere, or phyllosphere, play a pivotal role in controlling plant-pathogenic organisms by various mechanisms such as antibiotic production, induction of systemic resistance, and competition for resources (Bakker *et al.,* 2003).

The rhizosphere of plants serves as a hub for microbial interactions that regulate plant health. Plant roots release chemicals that provide nutrition and energy to bacteria, while also secreting antibiotics and other compounds to defend against pathogens (Bakker *et al.,* 2003). Additionally, roots release siderophores, dissolved inorganic phosphorus, and auxin (IAA), which promote plant growth and nutrient uptake.

The concept of biological control has gained attention due to its potential to achieve sustainable agriculture with reduced ecological costs. Prophylactic measures aimed at reducing pesticide usage by approximately 50% have been implemented in many countries, highlighting the growing understanding of the ecological connections in the food chain and the adverse effects of chemical pesticides on the environment (Infante *et al.,* 2009). An effective and financially viable approach to managing diseases and pests in agriculture is through biological control, which leverages natural enemies and antagonists to keep pest populations in check and maintain agroecosystem sustainability (Infante *et al.,* 2009).

III. Mechanisms Of Biocontrol:

Biocontrol mechanisms encompass a range of strategies employed by beneficial microorganisms to suppress the growth and activity of plant pathogens, thereby promoting plant health, and reducing disease incidence. These mechanisms are essential components of biological management in agriculture, particularly in organic farming systems.

Competition for Resources: Beneficial microorganisms compete with plant pathogens for essential resources such as nutrients, space, and water. By outcompeting pathogens in the rhizosphere or phyllosphere, these beneficial microbes restrict the growth and proliferation of pathogens, thereby reducing disease incidence (Mendes *et al.,* 2011).

Production of Antimicrobial Compounds: Many beneficial microorganisms, including Actinobacteria, can produce antimicrobial compounds such as antibiotics and lytic enzymes. These compounds inhibit the growth of plant pathogens by disrupting their cellular processes or degrading their cell walls, effectively suppressing disease development (Pieterse *et al.,* 2014).

Induction of Systemic Resistance: Beneficial microorganisms can stimulate the plant's innate immune system, leading to the induction of systemic resistance against pathogens. This systemic resistance mechanism primes the plant to mount a faster and stronger defense response upon pathogen attack, effectively limiting disease spread (Pieterse *et al.,* 2014).

Predation on Pathogens: Some beneficial microorganisms, particularly predatory fungi, and bacteria, directly consume plant pathogens, effectively reducing their population size. By preying on pathogens, these beneficial microbes contribute to the natural regulation of pathogen populations in the rhizosphere and phyllosphere, thereby reducing disease incidence (Mendes *et al.,* 2011).

Overall, these biocontrol mechanisms highlight the intricate interplay between beneficial microorganisms and plant pathogens in agroecosystems. By leveraging these mechanisms, farmers can effectively manage diseases in a sustainable and environmentally friendly manner, ultimately promoting crop health and productivity.

IV. Actinobacteria Enhance Plant Growth And Bolster Resistance To Diseases.

Actinobacteria species exhibit beneficial interactions with plants, enhancing both plant growth and disease resistance (Figure 1). Renowned for their broad spectrum of antimicrobial compound synthesis, they serve as promising biocontrol agents against various phytopathogens. While Streptomyces species have been extensively studied in biocontrol, other genera such as Actinoplanes, Arthrobacter, Microbacterium, Micromonospora, and Rhodococcus have also shown potential (Barka *et al.*, 2016; Bertrand *et al.*, 2018).

Actinobacteria establish close associations with plants due to their versatile metabolisms and their ability to utilize plant litter and root exudates. As frequent colonizers of rhizospheres and plant tissues, they play crucial roles in promoting plant health and growth (Barka *et al.*, 2016; Bertrand *et al.*, 2018). Furthermore, Actinobacteria contribute to plant development through various mechanisms such as phosphate solubilization, iron acquisition, nitrogen fixation, and the production of plant growth regulators. Genera like Frankia, Streptomyces, Micrococcus, Micromonospora, Kitasatospora, and Thermobifidia are known to possess these traits (Barka *et al.*, 2016; Bertrand *et al.*, 2018). Finally, Actinobacteria genus members exhibit multifaceted interactions with plants, contributing to plant growth promotion and disease resistance through their diverse metabolic capabilities and biocontrol activities.

Fungal Antagonists:

Fungal biological control agents have become increasingly viable due to their short generation time, high rate of sexual and asexual reproduction, and target specificity against plant pathogens (Ownley*et al.*, 2008; De Cal *et al.*, 2019; Lahlali*et al.*, 2019). Additionally, they can persist in the environment in the absence of a host by transitioning from parasitism to saprotrophic, maintaining sustainability. Plant pathogenic fungi can cause illnesses in plants, and many fungal species have evolved defense mechanisms against them (Figure 2).

Therefore, carrying out an in-depth study on the smaller components of biocontrol strategies would lead to a hopeful future for the agriculture business. This assessment will yield enough data to comprehend the current and future status of biocontrol methods for sustainable agriculture. We address the challenges, variables impacting the biocontrol agents, and advancements made in the prospecting biocontrol strategy, with a focus on legislative procedures and characteristics that influence their use for commercialization development. A range of bacterial and fungal biocontrol agents are included in Table 1 to prevent plant diseases.

Figure 1. Beneficial interactions of Actinobacteria with plants.

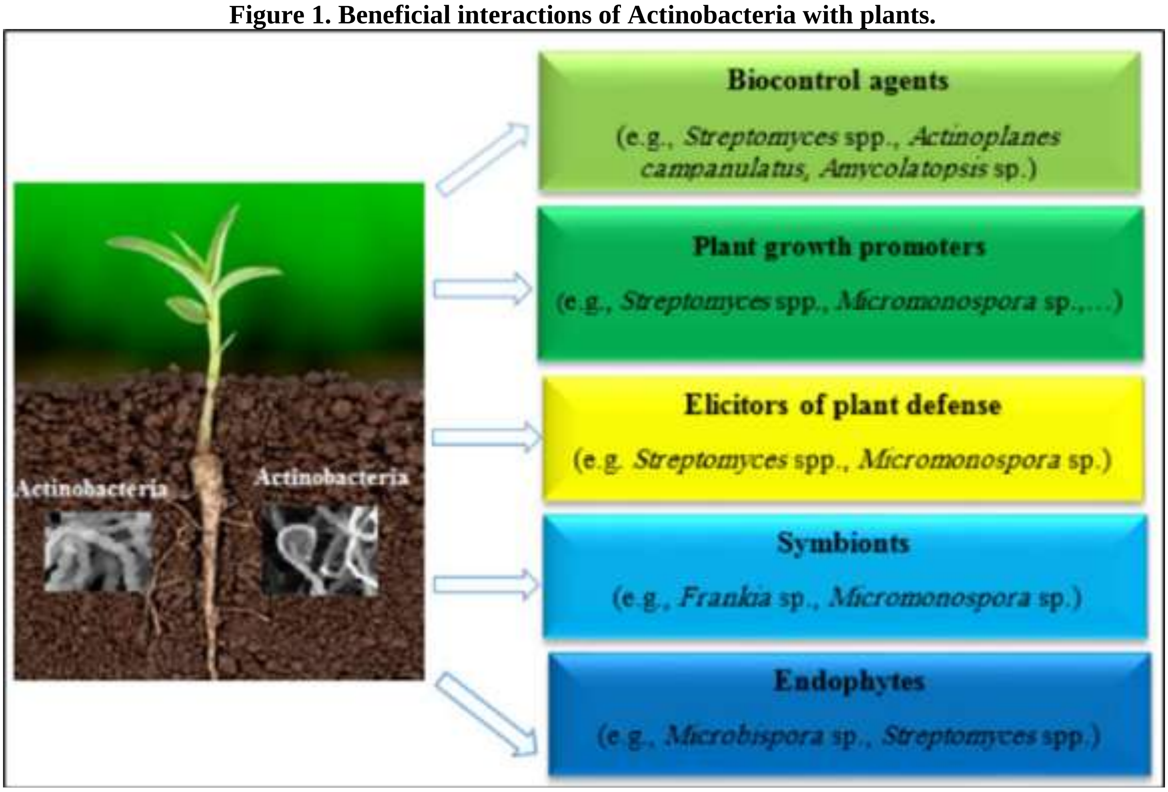

Figure 2: Key mechanisms of action involved in biological control of plant fungal diseases by fungal antagonists.

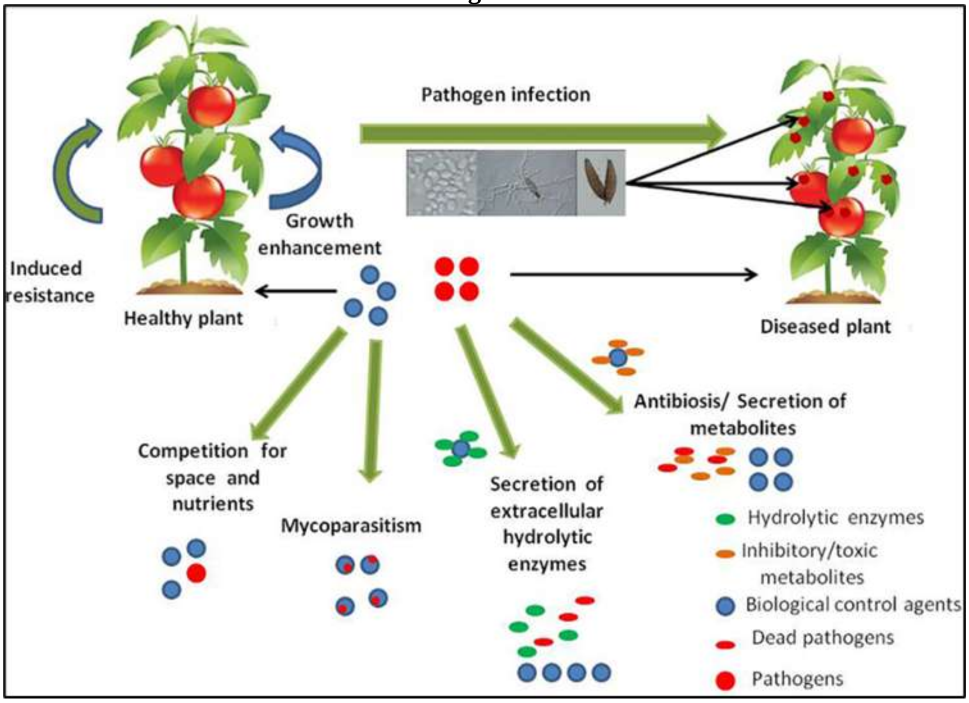

Table 1. Various bacterial and fungal biocontrol agents against plant pathogens.

Plant species	Biocontrol agents	Pathogens	Mode of action
		Bacterial strains	
Citrus fruit	*Bacillus megaterium*	Blue mold	In vitro antagonistic activity against post-harvest disease
Wheat	*Bacillus subtilis* 26DCryChS	*Stagonosporanodorum*Berk	Antimicrobial metabolites (surfactants showed antifungal activity against *S nodorum* disease)
Brassica campestris L	*Bacillus thuringiensis*	*Scierotiorumscierotiorum*	Suppressing *S. scierotiroum* growth by including systemic resistance
Cotton/black root rot	*Paenibacillus alvei* K-165	*Thielaviopsis basicola*	K-165 inhibited *T. basicola* growth *invitro* through antibiosis and significantly reduced root discoloration and hypocotyl lesions on cotton seedlings.
Tomato and soybean	*Bacillus velezensis* DMW1	*Phytophthora sojae and Ralstonia solanacearum*	Antimicrobial metabolites (fengycin, iturin, and bacillomycin) demonstrated antagonistic activity in vitro and in pot experiments.
Rice	*Bacillus atrophaseus* GBSC56	*Xanthomonas oryzae pv. Oryzae (Xoo)*	In vitro, antagonistic activity against various fungal pathogens significantly reduced Xoo lesions in greenhouse conditions.
Rice	*Bacillus thuringiensis* GBAC46	*Aphelenchoidesbesseyi*	In vitro antagonistic activity through various proteins (Cry31Aa, Cry73Aa, and Cry40ORF) and in greenhouse conditions
Maize	*Pseudomonas*protegens Pf-5	*Pantoeaananatis*DZ-12	Antimicrobial pyoluteorin showed strong antagonistic activity against *P.* ananatis in vitro and in vivo
Wheat and maize	*Bacillus subtilis* ATCC6633	*Fusarium graminearum and Fusarium verticilliodes*	Antimicrobial mycosubtillin showed a strong antagonistic activity against *F.* graminearum and *F.* verticilliodes in

Plant species	Biocontrol agents	Pathogens	Mode of action
			virto and in vivo
Tomato	*Bacillus atropheeus* GBSC56	*Meloidogyne incognita*	Antimicrobial VOCs showed nematicidal activity and also produced ROS in nematodes
Rice	*Bacillus spp*. GBSC56. SYST2, and FZB42	*Aphelenchoidesbesseyi*	Antimicrobial VOCs of *Bacillus spp*. Showed the strongest nematicidal activity and accumulated ROS as well as promoted rice growth.
Soybean and rice	*Pseudomonas parafulva* JBCS1880	*Xanthomonas axonopodispv. Glycines, and Burkholderiaglumae*	Strong antagonism and antibacterial activity against *Xanthomonas axonopodis*pv. *Glycines* and *Burkholderiaglumae*
Rice	*Pseudomonas putida* BP25	*Magnaporthe oryzae*	BP25 showed strong biocontrol activity against blasts caused by *M. oryzae*
Pepper	*Bacillus licheniformis* BL06	*Phytophthora capsici*	BL06 effectively reduced pepper *Phytophthora* blight severity in vitro and pot experiments
Wheat	*Bacillus atrophaeus strain* TS1	*Fusarium graminearum*	TS1 was found as a potential biocontrol agent to inhibit F. *graminearum* under low temperatures
Tomato	*Bacillus amyloliquefaciens* FZB42	*Scierotiniasclerotiorum*	Antimicrobial potential (fengycin-induced systemic resistance in tomatoes against *S. sclerotiorum*)
Rape seed and tobacco	*Bacillus amyloliquefaciens* EZ1509	*Scierotiniascierotiorum*	*Bacillus* stain EZ1509 showed a strong antifungal activity against *S. scierotiorum* and also led to the development of new biopesticides
Tomato	*Streptomyces sp.* AN090126	*Ralstonia solanacearum and Xanthomonas euvesicatonia*	*Streptomyces sp*. AN090126 can combine with antibiotics effectively control different bacterial plant diseases
Fungal strains			
Tomato	*Paecliomycesillacinus*	*Meloidogyne javanica*	*P. lilacinum* is used as a biocontrol agent to control M. incognita and as a better alternative against chemical nematicides
Pineapple	*Purpureocilliumlilacinum*	*Meloidogyne javanica*	The application of *P. lilacinum* significantly reduced nematode egg and egg mass production, reducting root galling damage in pineapple
Onion	*Trichoderma asperellum*	*Scierotiumcepivorum*	*T. asperellum* BCC1 exert efficient biocontrol against *S. cepivorum* and activates onion systemic defenses against *S. cepivorum* under greenhouse conditions
Okra	*Trichoderma virens*	*Meloidogyne incognita*	*T. virens* observed a reduction in second-stage juveniles' hatching periods fested in vitro
Carrot	*Pochoniachlamydosporia*	*Meloidogyne incognita*	*P. chlamydosporia* reduced nematode galls and also decreased juvenile 2 nematodes in vitro and pot experiment methods
mango	*Trichoderma asperellum* T8a	*Collectrotrichumgloeosporiodes*	*T. asperellum* T8a plays a role in biological control against C. *gloeosporiodes* and controlling anthracnose disease in mangoes
Beans	*Trichoderma hamatum*	*Sclerotinia sclerotiorum*	*T. asperellum* the reduced disease severity index and antagonistic activity against *S. scierotiorum* in field trials of beans
Cabbage	*Trichoderma hamatum*	*Scierotiniascierotiorum*	*T. hamatum* LU593 reduced apothecial production, decreased disease severity index, and could potentially control *S. scierotiorum* disease in cabbage

Actinomycetes as Biocontrol Agents

Actinomycetes possess natural advantages that render them effective biocontrol agents: (1) they are non-toxic to plants; (2) they pose no harm to humans or animals; (3) they enhance plant productivity; and (4) they reduce the reliance on artificial fungicides (Pandi *et al.,* 2020; Sharma *et al.,* 2021). Among actinomycetes, Streptomyces has been extensively investigated due to its relative ease of isolation. However, compared to bacteria, actinomycetes exhibit slower growth rates. Techniques for augmenting growth are necessary to obtain sufficient actinomycetes in culture media. These techniques involve using specific isolation media and pretreating soil samples, such as heating, drying, and chemical treatments, particularly in soil containing calcium carbonate (Pandi *et al.,* 2020).

Actinomycete populations in soil can be enhanced through the application of biostimulants, compost, or other organic fertilizers. For instance, isolates of *S. sampsonii* and *S. flavovariabilis* from soil enriched with vermicompost demonstrated significant antagonistic activity against various phytopathogenic fungi, including Rhizoctonia solani, *Alternaria tenuissima*, *Penicillium expansum*, and *Aspergillus niger* (Sharma *et al.,* 2021). Additionally, the addition of Brassica napus and Brassica rapa leaf wastes to soil resulted in increased actinomycete populations, correlating with a decrease in *R. solani* wilt disease incidence (Pandi *et al.,* 2020).

Several actinomycetes have been studied for their mechanisms of action as biocontrol agents against phytopathogenic fungi (Table 2) (Sharma *et al.,* 2021).

Table 2. Antagonistic mechanisms of actinomycetes for the control of phytopathogenic fungi.

Actinomycetes	Phytopathogen	Host	In vivo inhibition	Antagonistic mechanisms
Streptomyces sp.	*Colletotrichum fragariae*	Strawberry	100%	
S. sampsonii	*Sclerotinia scierotiorum*	Green bean	100%	Secondary metabolite
Streptomyces sp.	*Ralstonia solanacearum*	Tomato	97%	Induction of host resistance
S. sichuanensis	*Fusarium oxysporum*	Banana	51%	Siderophores
Amycolatopsis sp.	*F. graminearum*	Maize	79%	Lytic enzyme
Arthorobacterhumicola	*A. Alternate*	Tomato	31%	Secondary metabolites
Nocardiopsisdassonvillei	*Bipolarissorokiniana*	Wheat	72%	Siderophores and enzyme
S. rameus	*R. bataticola*	Bean	70%	Siderophores and enzyme
S. globisporous	*R. solani*	Tomato	50%	Induction of host resistance

V. Advancements In Omics Technologies:

Recent advancements in omics technologies, including genomics, transcriptomics, proteomics, and metabolomics, have revolutionized our understanding of the molecular basis of biocontrol activity by Actinobacteria. These omics approaches allow researchers to comprehensively analyze the genetic, transcriptional, protein, and metabolic profiles of Actinobacteria and their interactions with plant pathogens and hosts, providing valuable insights into the mechanisms underlying biocontrol activity.

Genomics: The advent of high-throughput sequencing technologies has facilitated the rapid and cost-effective sequencing of Actinobacteria genomes. Genomic studies have revealed the presence of genes encoding for antimicrobial compounds, lytic enzymes, and secondary metabolites in Actinobacteria genomes, which are involved in biocontrol activity (Barka *et al.,* 2016; Qin *et al.,* 2019). Comparative genomics analyses have also identified conserved genetic elements and unique gene clusters associated with biocontrol strains, enabling the discovery of novel biocontrol mechanisms.

Transcriptomics: Transcriptomic studies provide insights into the gene expression profiles of Actinobacteria during biocontrol interactions. RNA sequencing (RNA-seq) technologies allow researchers to identify differentially expressed genes in response to plant pathogens or under specific environmental conditions. Transcriptomic analyses have revealed the upregulation of genes involved in antimicrobial compound production, stress response, and plant-microbe interactions in Actinobacteria during biocontrol (Kwak *et al.,* 2018; Palazzini*et al.,* 2020). Moreover, transcriptomic studies have elucidated the regulatory networks governing biocontrol gene expression, providing a deeper understanding of biocontrol mechanisms.

Proteomics: Proteomic approaches enable the identification and quantification of proteins expressed by Actinobacteria during biocontrol interactions. Mass spectrometry-based proteomics analyses have identified proteins involved in antimicrobial activity, cell-wall degradation, signal transduction, and stress response in Actinobacteria biocontrol strains (Vikram *et al.,* 2016; Zhang *et al.,* 2021). Proteomic studies have also elucidated post-translational modifications and protein-protein interactions underlying biocontrol activity.

Metabolomics: Metabolomic analyses offer insights into the metabolic profiles and dynamics of Actinobacteria during biocontrol interactions. Metabolomics technologies such as liquid chromatography-mass spectrometry (LC-MS) and nuclear magnetic resonance (NMR) spectroscopy enable the identification and quantification of small molecules, secondary metabolites, and metabolic pathways involved in biocontrol (Hirsch *et al.,* 2020; Wang *et al.,* 2021). Metabolomic studies have identified bioactive compounds produced by Actinobacteria, including antibiotics, antifungal agents, and plant growth-promoting metabolites, contributing to biocontrol efficacy.In final, recent advancements in omics technologies have significantly enhanced our understanding of the molecular basis of biocontrol activity by Actinobacteria. Integrating multi-omics approaches allows for a comprehensive characterization of biocontrol mechanisms, facilitating the discovery of novel biocontrol agents and strategies for sustainable agriculture.

VI. Factors Influencing Efficacy:

Several factors influence the efficacy of Actinobacteria as biocontrol agents against plant pathogens. These factors encompass various biological, environmental, and agricultural aspects, shaping the effectiveness of biocontrol strategies.

Strain Selection: The choice of Actinobacteria strain plays a critical role in biocontrol efficacy. Different strains may exhibit varying levels of antagonistic activity against specific plant pathogens. Therefore, screening and selecting potent biocontrol strains with desirable traits are essential (Sharma *et al.,* 2021).

Antimicrobial Potential: The production of antimicrobial compounds by Actinobacteria is a key determinant of biocontrol efficacy. Actinobacteria strains capable of synthesizing a wide range of antimicrobial metabolites, such as antibiotics, antifungal agents, and lytic enzymes, exhibit enhanced biocontrol activity (Barka *et al.,* 2016; Vikram *et al.,* 2016).

Environmental Conditions: Environmental factors, including temperature, humidity, soil pH, and nutrient availability, significantly influence the growth and survival of Actinobacteria in the rhizosphere or phyllosphere. Optimal environmental conditions conducive to Actinobacteria proliferation are crucial for effective biocontrol (Ownley*et al.,* 2008).

Interactions with Plant Hosts: The ability of Actinobacteria to establish beneficial interactions with plant hosts is vital for biocontrol efficacy. Actinobacteria strains capable of colonizing plant roots or phyllosphere, promoting plant growth, and inducing systemic resistance against pathogens demonstrate superior biocontrol potential (Kwak *et al.,* 2018; Palazzini*et al.,* 2020).

Competitive Interactions: Actinobacteria must compete with indigenous microbial populations in the soil or plant rhizosphere for resources and niche colonization. Therefore, their competitiveness and persistence in complex microbial communities influence biocontrol efficacy (Pandi *et al.,* 2020).

Application Methods: The mode and timing of Actinobacteria application also affect biocontrol efficacy. Factors such as inoculum concentration, application frequency, and delivery methods (e.g., seed treatment, soil drenching, foliar spray) can impact the establishment and effectiveness of biocontrol agents (De Cal *et al.,* 2019).

Pathogen Diversity: The diversity and virulence of target plant pathogens influence biocontrol efficacy. Actinobacteria strains may exhibit differential antagonistic activity against various pathogens, necessitating tailored biocontrol strategies for specific disease management (Lahlali*et al.,* 2019).

Regulatory Considerations: Regulatory frameworks and policies governing the use of biocontrol agents in agriculture can impact their adoption and efficacy. Compliance with registration requirements, safety regulations, and labeling guidelines is essential for commercialization and widespread implementation of biocontrol products (Sharma *et al.,* 2021). In final, multiple factors, including strain selection, antimicrobial potential, environmental conditions, plant interactions, competitive interactions, application methods, pathogen diversity, and regulatory considerations, collectively influence the efficacy of Actinobacteria as biocontrol agents against plant pathogens.

VII. Innovative Approaches:

Innovative approaches in biocontrol entail the development and application of novel techniques and strategies to enhance the efficacy and sustainability of biocontrol agents against plant pathogens. These approaches leverage advancements in various scientific disciplines and technologies to address emerging challenges in agriculture while minimizing environmental impacts.

Microbial Consortia: Utilizing diverse microbial consortia composed of multiple beneficial microorganisms, including Actinobacteria, fungi, and bacteria, offers a promising approach to biocontrol. By harnessing synergistic interactions among different microbial species, microbial consortia can exhibit enhanced antagonistic activity against plant pathogens, increased nutrient cycling, and improved plant growth promotion (Berendsen *et al.,* 2012; Tyc*et al.,* 2014).

Precision Agriculture: Precision agriculture techniques, such as remote sensing, geographic information systems (GIS), and sensor-based monitoring, enable targeted and site-specific application of biocontrol agents. By accurately mapping disease hotspots and environmental conditions, precision agriculture facilitates optimized deployment of biocontrol agents, minimizing input costs and maximizing efficacy (Rao and Senthilkumar, 2016; Pandey *et al.,* 2021).

Biostimulants and Plant Growth Promoters: Integrating biostimulants and plant growth-promoting substances with biocontrol agents enhances plant resilience and defense mechanisms against pathogens. Biostimulants, such as seaweed extracts, humic acids, and beneficial microorganisms, promote plant growth, root development, and stress tolerance, thereby complementing the biocontrol activity of microbial agents (Colla *et al.,* 2015; García-Gutiérrez *et al.,* 2020).

Nanoformulations: Nanotechnology-based formulations offer novel delivery systems for biocontrol agents, enhancing their stability, bioavailability, and target specificity. Nanoformulations protect biocontrol agents from environmental stresses, improve adhesion to plant surfaces, and enable controlled release of active ingredients, resulting in enhanced biocontrol efficacy and reduced environmental impact (Raliya *et al.,* 2018; Li *et al.,* 2020).

Plant-Microbe-Soil Interactions: Understanding complex interactions among plants, microbes, and soil components is crucial for developing innovative biocontrol approaches. Harnessing plant-microbe-soil interactions through ecological engineering, soil microbiome manipulation, and rhizosphere engineering can promote beneficial microbial communities, suppress pathogen proliferation, and enhance plant health and productivity (Berendsen *et al.,* 2018; De Coninck *et al.,* 2018).

Synthetic Biology: Synthetic biology techniques enable the design and engineering of microbial strains with customized biocontrol traits and functionalities. By engineering microbial biosynthetic pathways, regulatory circuits, and communication systems, synthetic biology offers unprecedented opportunities to create tailor-made biocontrol agents with improved efficacy, specificity, and environmental safety (Xiao *et al.,* 2018; Schmidt-Dannert, 2019). In final, innovative approaches in biocontrol leverage advancements in microbial ecology, precision agriculture, nanotechnology, and synthetic biology to develop sustainable and effective strategies for managing plant diseases. These approaches hold great promise for addressing the evolving challenges of modern agriculture while promoting environmental sustainability and food security.

VIII. Importance Of Sustainability:

The importance of considering ecological factors and promoting sustainable agricultural practices in developing Actinobacteria-based biocontrol agents cannot be overstated. Sustainable agriculture aims to meet the needs of the present without compromising the ability of future generations to meet their own needs. In the context of biocontrol, sustainability entails the development and implementation of strategies that minimize negative environmental impacts, preserve biodiversity, and ensure long-term efficacy.

Preservation of Ecosystem Health: Actinobacteria-based biocontrol agents should be developed with a holistic understanding of ecosystem dynamics. By targeting specific plant pathogens while preserving beneficial microbial communities and natural habitats, biocontrol agents can contribute to the overall health and resilience of agroecosystems (Singh *et al.,* 2020).

Reduction of Chemical Inputs: One of the key benefits of biocontrol agents is their ability to reduce reliance on chemical pesticides and fungicides. Actinobacteria-based biocontrol offers a sustainable alternative by harnessing natural antagonistic mechanisms to suppress pathogen populations, thereby minimizing environmental contamination and reducing health risks associated with chemical exposure (Gopalakrishnan *et al.,* 2017).

Enhancement of Soil Health: Actinobacteria play crucial roles in soil nutrient cycling, organic matter decomposition, and soil structure maintenance. Developing biocontrol agents that promote soil health and fertility can contribute to sustainable agriculture by improving soil structure, enhancing water retention, and increasing nutrient availability for plant growth (Lakshmanan *et al.,* 2014).

Promotion of Biodiversity: Sustainable biocontrol strategies should prioritize the conservation of biodiversity by preserving natural enemy populations and enhancing habitat diversity. Actinobacteria-based biocontrol agents can be integrated into biodiversity-friendly farming systems, such as agroforestry and polyculture, to promote beneficial insect and microbial diversity while reducing monoculture-associated pest pressures (Gurr *et al.,* 2017).

Adaptation to Climate Change: Climate change poses significant challenges to agricultural productivity and food security. Sustainable biocontrol practices, including the use of Actinobacteria-based agents, can contribute to climate change mitigation and adaptation by fostering resilient agroecosystems, improving carbon sequestration, and reducing greenhouse gas emissions associated with conventional agricultural practices (Bakker *et al.,* 2021).

In finally, considering ecological factors and promoting sustainable agricultural practices are imperative in the development and implementation of Actinobacteria-based biocontrol agents. By prioritizing ecosystem health, reducing chemical inputs, enhancing soil fertility, promoting biodiversity, and adapting to climate change, sustainable biocontrol strategies can contribute to the transition towards environmentally friendly and resilient agricultural systems.

IX. Challenges And Future Directions:

Challenges and future directions in the development and application of Actinobacteria-based biocontrol agents pose both opportunities and hurdles in sustainable agriculture. These aspects shape the trajectory of research and innovation aimed at addressing plant diseases while ensuring environmental stewardship.

Commercialization Hurdles: Despite promising research outcomes, the commercialization of Actinobacteria-based biocontrol agents faces several challenges. Regulatory requirements, high production costs, and limited market acceptance hinder widespread adoption. Overcoming these hurdles requires collaborative efforts among researchers, policymakers, and industry stakeholders to streamline registration processes and develop cost-effective production methods (Ghorbanpour *et al.,* 2021).

Efficacy and Persistence: Ensuring consistent efficacy and persistence of biocontrol agents under diverse environmental conditions remains a significant challenge. Actinobacteria-based formulations may exhibit variable performance due to interactions with soil microbiota, fluctuations in temperature and moisture, and pathogen diversity. Enhancing the stability, shelf-life, and adaptability of biocontrol agents through formulation optimization and genetic engineering holds promise for overcoming these challenges (Hassan *et al.,* 2019).

Understanding Microbial Interactions: Deciphering the complex interactions among Actinobacteria, plant hosts, and pathogens is crucial for optimizing biocontrol efficacy. Elucidating the mechanisms of action, signaling pathways, and ecological dynamics of microbial consortia in the rhizosphere and phyllosphere requires interdisciplinary approaches integrating genomics, metabolomics, and ecological modeling (Finkel *et al.,* 2020).

Climate Change Resilience: Climate change poses new challenges to agricultural sustainability, altering disease dynamics, pest pressures, and microbial community composition. Actinobacteria-based biocontrol strategies must adapt to changing environmental conditions and evolving pathogen populations. Developing climate-resilient biocontrol agents and implementing precision agriculture techniques can mitigate the impacts of climate change on crop health (Meena *et al.,* 2021).

Public Awareness and Acceptance: Promoting public awareness and acceptance of biocontrol agents is essential for their successful integration into mainstream agriculture. Educating farmers, policymakers, and consumers about the benefits of sustainable biocontrol practices, their safety, and their role in reducing chemical inputs is crucial for fostering adoption and market demand (Pineda *et al.,* 2021).

Ethical Considerations: Ethical considerations, such as intellectual property rights, equitable access to biocontrol technologies, and socioeconomic implications for smallholder farmers, must be addressed to ensure the equitable distribution of benefits and promote social justice in agricultural innovation (Kolady and Choudhary, 2021).

X. Conclusion:

In conclusion, Actinobacteria-based biocontrol agents hold immense potential for sustainable agriculture by offering effective alternatives to chemical pesticides and fungicides. Throughout this exploration, we have underscored the significance of Actinobacteria in suppressing plant pathogens, promoting plant growth, and fostering ecological balance in agroecosystems. Despite the promising prospects, several challenges remain to be addressed to realize the full benefits of Actinobacteria-based biocontrol.From regulatory hurdles to efficacy concerns and climate change resilience, overcoming these challenges requires concerted efforts from researchers, policymakers, industry stakeholders, and farmers. Embracing interdisciplinary approaches, leveraging technological innovations, and promoting public awareness are essential for advancing the development and adoption of Actinobacteria-based biocontrol strategies.

As we navigate towards a more sustainable and resilient agricultural future, it is imperative to prioritize ecological integrity, biodiversity conservation, and ethical considerations. By integrating Actinobacteria-based biocontrol into holistic farming practices, we can mitigate the environmental impacts of conventional agriculture, enhance food security, and safeguard the health of ecosystems and communities.In essence, Actinobacteria-based biocontrol represents a promising avenue for sustainable agriculture, offering innovative solutions to combat plant diseases while preserving environmental health and promoting agricultural sustainability. With continued research, collaboration, and commitment, we can harness the power of Actinobacteria to cultivate thriving and resilient agricultural systems for generations to come.

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