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Endophytic Bacteria as Biocontrol Agents: Mechanisms and Applications in Plant Health

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ABSTRACT: Plant diseases and pest outbreaks pose a critical challenge to global food security, contributing to substantial crop yield losses. While synthetic pesticides have historically mitigated these threats, their long-term use has resulted in environmental degradation, human health risks, and the emergence of resistant pest populations. As a sustainable alternative, endophytic bacteria—microorganisms residing within plant tissues without causing harm—have emerged as promising biological control agents. These bacteria not only enhance plant growth and stress resilience by producing phytohormones, fixing nitrogen, and solubilizing nutrients, but also exhibit potent biocontrol properties through diverse mechanisms. Directly, they suppress pathogens via antibiotic production, secretion of hydrolytic enzymes, and emission of volatile organic compounds. Indirectly, they activate plant defense responses such as Induced Systemic Resistance (ISR), and outcompete pathogens by occupying ecological niches and sequestering essential micronutrients. With their ecological adaptability and compatibility with sustainable farming practices, endophytic bacteria represent a viable component of integrated pest and disease management (IPDM), offering a safer, environmentally friendly approach to crop protection.

Keywords: Endophytic bacteria, Biological control, Plant–microbe interaction, Biocontrol mechanisms, Plant disease management, Integrated pest management.

INTRODUCTION

The increasing global demand for food is significantly hindered by substantial losses due to plant diseases and pest outbreaks. According to Oerke (2006), crop yield reductions ranging from 17% to over 30% are observed in essential staples such as rice, wheat, maize, soybean, and potato. While synthetic pesticides have played a pivotal role in curbing these losses, their prolonged and widespread usage has raised environmental toxicity issues, pest resistance, and risks to human health (Pimentel & Burgess 2014). Consequently, research has increasingly turned towards more sustainable alternatives like the utilization of endophytic bacteria as biological control agents.

Endophytic bacteria are an ecologically diverse group of microorganisms that colonize the internal tissues of plants without causing any apparent harm. These bacteria establish symbiotic or mutualistic interactions and are known to inhabit roots, stems, leaves, flowers, and seeds. As described by Hallmann *et al.* (1997), endophytes enter host tissues through natural openings, wounds, or root zones and form species-specific or even genotype-specific associations (Kukreti *et al.*, (2024) comparative study of non-host endophytes in tomato (e.g., *Bacillus velezensis*, *Paenibacillus* spp., *B. pseudomycoides*) showed effective inhibition of *Alternaria solani* and activation of plant enzymes like peroxidase, polyphenol oxidase, and superoxide dismutase. Both ISR and antimicrobial metabolites were key in disease suppression and growth promotion

A prominent benefit of these endophytic bacteria is their role in enhancing plant growth and stress resistance. They produce growth-promoting substances such as indole-3-acetic acid (IAA), aid in nutrient acquisition by solubilizing phosphates, and fix atmospheric nitrogen (Santoyo *et al.*, 2016). Additionally, they help plants cope with abiotic stresses like drought, salinity, and heavy metal toxicity by triggering stress-resilient physiological responses (Compant *et al.*, 2010).

When it comes to biocontrol, endophytic bacteria operate through both direct and indirect mechanisms. Direct mechanisms involve the production of antibiotics, hydrolytic enzymes, and volatile organic compounds (VOCs) that suppress or eliminate pathogens. For example, Bacillus species synthesize lipopeptides like iturin and fengycin that disrupt fungal membranes (Ongena & Jacques 2008). According to (Ali *et. al.* 2024), detailed mechanisms—metabolite production, ISR, VOCs—across genera (*Bacillus*, *Paenibacillus*, *Pseudomonas*) and emphasizes the need for systematic screening of endophytes for both disease control and growth-promotion traits. Further they discussed the mechanisms of phytopathogenic fungi control and plant growth-promoting actions discovered in some major groups of beneficial endophytic bacteria such as Bacillus, *Paenibacillus*, and *Pseudomonas*. Most of the studied strains in these genera were isolated from the rhizosphere and soils, and a more extensive study of these endophytic bacteria is needed. Nibulkar *et al.* (2025) review highlights how endophytic bacteria produce a range of bioactive compounds—including phytohormones, siderophores, lipopeptides, volatile organic compounds (VOCs), and quorum-quenching enzymes—that modulate plant immunity, promote growth, and suppress pathogens via direct antagonism and induced systemic resistance (ISR). Indirectly, these bacteria trigger host defense responses, especially Induced Systemic Resistance (ISR), which is regulated by ethylene and jasmonic acid signaling pathways and enhances the plant's innate immune system against a broad range of pathogens (Van Wees *et al*., 2008).

Moreover, endophytes compete with pathogens by colonizing internal plant niches, thereby preventing pathogen establishment. They also sequester micronutrients like iron using siderophores, and in some cases, form biofilms that act as physical barriers against invading microbes (Lodewyckx *et al.,* 2002).

A growing number of studies have demonstrated the diversity and efficacy of endophytic bacteria in disease suppression across various crops. Their compatibility with eco-friendly farming practices and potential to reduce chemical pesticide reliance makes them promising agents in integrated pest and disease management (IPDM) strategies for sustainable agriculture.

COLONIZATION AND ESTABLISHMENT

Endophytic colonization is a complex, multi-step process that begins with the initial encounter between the bacterial endophyte and the plant surface, followed by bacterial attachment, penetration of plant tissues, internal migration, and final establishment within the host's internal compartments. Each of these stages involves a tightly regulated interplay of microbial traits and plant responses, often mediated by biochemical signaling and genetic determinants.

A. Initial Encounter and Attachment. The colonization process starts with the chemotactic attraction of bacteria towards plant exudates such as sugars, amino acids, and organic acids secreted by roots or other plant tissues. Motility structures like flagella and type IV pili play key roles in bacterial movement and attachment. For instance, *Azoarcus* sp. strain BH72 relies on twitching motility mediated by type IV pili for successful endophytic colonization of rice roots (Böhm *et al.*, 2007).

B. Adhesion and Surface Interaction. Bacteria attach to the surface of plant tissues using adhesins, pili, and exopolysaccharides. Quorum sensing molecules like N-acyl homoserine lactones (AHLs) regulate genes involved in biofilm formation and adhesion. These biofilms serve as a protective layer and enhance colonization efficiency (Olanrewaju *et al*., 2017).

C. Penetration into Plant Tissues. Endophytes can enter the plant through natural openings such as stomata, hydathodes, or root cracks, or via wounds. Some bacteria also produce cell wall-degrading enzymes like cellulases and pectinases to facilitate entry without triggering strong plant immune responses. For example, *Azoarcus* sp. uses an endoglucanase enzyme for the penetration of rice root cell walls (Reinhold-Hurek *et al*., 2006).

D. Internal Migration. Once inside, bacteria migrate through the apoplastic or symplastic pathways, colonizing different tissues such as the cortex, vascular bundles, and intercellular spaces. Successful migration requires evasion of plant defense mechanisms, often achieved through suppression of plant immunity or by residing in niche environments (Mushtaq *et al*., 2023).

ESTABLISHMENT AND SYSTEMIC SPREAD

After colonization, the bacteria establish stable populations by proliferating within plant tissues and forming long-term associations. The host plant may benefit from this interaction via improved nutrient uptake, growth promotion, or stress tolerance. Mutual recognition between the host and microbe often involves signaling molecules like reactive oxygen species (ROS), plant hormones (e.g., auxins, ethylene), and microbial elicitors (Santoyo *et al.*, 2016).

These stages are influenced by both host genotype and bacterial traits, dictating the specificity, efficiency, and sustainability of the symbiosis (Carmona *et al.*, 2021; Mushtaq *et al.*, 2023).

A. Entry Mechanisms

Endophytic bacteria typically gain entry into plant tissues through various natural and opportunistic routes. These include natural openings such as stomata, hydathodes, and lenticels on aerial plant parts, as well as root-associated sites like zones of lateral root emergence and root hairs. Additionally, mechanical injuries or wounds resulting from cultivation practices, herbivory, or environmental stressors can serve as points of bacterial entry (Mahaffee, 1994; Lodewyckx *et al*., 2002).

The successful entry of endophytes is facilitated by several bacterial traits. Flagellar motility and chemotaxis allow bacteria to move toward plant-derived exudates such as sugars and amino acids in the rhizosphere. Upon reaching the plant surface, many bacteria secrete cell wall-degrading enzymes (CWDEs), including cellulases, pectinases, and xylanases, which weaken or soften the plant cell wall structure and enable penetration into deeper tissue layers without triggering a strong host immune response (Reinhold-Hurek *et al*., 2006; Santoyo *et al.,* 2016).

B. Early Colonization and Immune Evasion

Upon successful colonization, endophytic bacteria must overcome the plant's innate immune system, which relies on pattern recognition receptors (PRRs) to detect conserved microbial features known as microbe-associated molecular patterns (MAMPs). Recognition of MAMPs triggers MAMP-triggered immunity (MTI), which initiates a cascade of defense responses including reactive oxygen species (ROS) production, cell wall reinforcement, and expression of defense-related genes (Boller and Felix 2009).

To establish a successful endophytic lifestyle, bacteria deploy several strategies to suppress or evade host immune recognition. These include the secretion of effector molecules that interfere with host signaling pathways and dampen immune responses (Zamioudis and Pieterse 2012). Some endophytes modify their surface structures—such as lipopolysaccharides (LPS) or flagellin—to avoid recognition by plant PRRs (Trdá *et al.,* 2015). Others promote host tolerance by synthesizing phytohormone analogs such as indole-3-acetic acid (IAA), which modulate host development and immune balance, facilitating a more hospitable internal environment (Santoyo *et al*., 2016; Brader *et al.,* 2014).

C. Spatial and Temporal Colonization

Endophytic colonization is neither random nor uniform; it is governed by spatial and temporal factors that reflect plant physiology and microbial preferences. Spatially, endophytes exhibit tissue-specific colonization patterns influenced by nutrient gradients, the composition of plant exudates, and oxygen availability. For instance, oxygen-rich environments such as leaf intercellular spaces or root cortical regions may favor aerobic colonizers, whereas low-oxygen conditions within vascular tissues support microaerophilic or facultative anaerobic bacteria (Compant *et al.,* 2010).

Temporally, younger plant tissues are often more susceptible to colonization due to higher metabolic activity, softer cell walls, and reduced lignification, offering easier access to microbial invaders (Lòpez-Fernández et al., 2015). Endophytes commonly establish stable populations within the apoplast, xylem, phloem, or even intracellular spaces. Importantly, their colonization does not elicit visible disease symptoms or necrosis, underscoring their non-pathogenic and often mutualistic relationship with the host (Santoyo *et al*., 2016; Hardoim *et al.*, 2015).

D. Plant–Microbe Compatibility

The specificity of endophytic colonization is largely determined by intricate molecular crosstalk between microbial signaling molecules and host plant receptors. Bacterial surface adhesins and secreted effectors mediate initial recognition and attachment to plant tissues (Compant *et al*., 2010). Certain endophytes mimic rhizobial symbiosis by producing Nod factor-like molecules that can modify root hair development and branching patterns, thus facilitating internalization (Oldroyd, 2013).

Quorum sensing (QS) molecules, especially N-acyl homoserine lactones (AHLs), serve not only in intra-bacterial communication but also in inter-kingdom signaling. These molecules have been shown to modulate plant gene expression, enhancing root elongation, lateral root formation, and even defense priming (Mathesius *et al*., 2003; Hartmann and Schikora 2012).

The eventual interaction outcome—whether mutualistic, neutral, or mildly pathogenic—depends on a combination of microbial genotype, host plant species or cultivar, and environmental conditions (Brader *et al.*, 2017). For instance, a strain that promotes growth in one crop species might induce stress in another, highlighting the co-evolutionary basis of endophyte-host specificity.

E. Long-Term Persistence

Once established within host tissues, endophytic bacteria must secure their niche by outcompeting both indigenous microbial communities and opportunistic pathogens. To this end, many endophytes form structured biofilms on internal plant surfaces such as xylem vessels and intercellular spaces, enhancing their persistence and resistance to environmental stresses (Sessitsch *et al*., 2004). These biofilms act as physical barriers and coordinated microbial communities, often contributing to plant health and protection.

To suppress microbial competitors, endophytes may produce antimicrobial compounds including bacteriocins, lipopeptides, or antibiotics (Rosenblueth and Martínez-Romero 2006). For instance, strains of Bacillus and Pseudomonas are well-known for their production of secondary metabolites that inhibit phytopathogens within plant tissues (Santoyo *et al.*, 2016).

Successful colonizers also exhibit metabolic flexibility, allowing them to utilize diverse plant-derived substrates such as organic acids, amino acids, and sugars (Brader *et al.,* 2017). This metabolic adaptation ensures survival in varying tissue types and under shifting physiological conditions of the host.

Population dynamics of endophytes vary with the developmental stage of the plant, tissue-specific niches, and abiotic factors. Some endophytes exhibit vertical transmission, colonizing reproductive tissues and seeds, thereby ensuring early colonization of progeny and a competitive edge during seedling establishment (Johnston-Monje and Raizada 2011).

CLASSIFICATION OF BIOCONTROL MECHANISMS

Biocontrol mechanisms employed by endophytic bacteria can be broadly categorized into:

Direct mechanisms: These refer to the strategies employed by endophytic bacteria that directly affect the survival, growth, or virulence of plant pathogens. Direct inhibition or killing of pathogens can occur through the synthesis and release of antimicrobial substances such as antibiotics, lipopeptides, and volatile organic compounds. For instance, Bacillus and Pseudomonas species are known to produce bioactive compounds like iturin, fengycin, surfactin, and 2,4-diacetylphloroglucinol (DAPG), which interfere with fungal membrane integrity or disrupt essential cellular functions. Additionally, endophytes produce lytic enzymes including chitinases, glucanases, and proteases, which degrade fungal cell walls and structural proteins, leading to pathogen cell lysis. Some endophytes also produce siderophores that sequester iron, depriving pathogens of this essential nutrient, thereby inhibiting their growth. The net result is a reduction in the pathogenic load and prevention of infection within the plant system.

Indirect mechanisms: These mechanisms do not target pathogens directly but instead enhance the plant's innate ability to resist infection and outcompete harmful microbes. One of the main indirect strategies is the stimulation of the plant's immune system through a process called Induced Systemic Resistance (ISR). This defense pathway is typically regulated by signaling molecules such as jasmonic acid and ethylene and results in the production of pathogenesis-related proteins, reactive oxygen species, and lignin deposition, which collectively fortify the plant against pathogen attack. Another key aspect of indirect mechanisms is competitive exclusion, where endophytic bacteria occupy ecological niches within the plant tissues, such as intercellular spaces and vascular systems, effectively preventing pathogens from establishing themselves. Furthermore, endophytes can produce siderophores—iron-chelating compounds—that deprive pathogens of vital micronutrients. In some cases, endophytes form biofilms on plant surfaces, creating a physical barrier that impedes the attachment and invasion of pathogens. Collectively, these indirect strategies help maintain a balanced and resilient plant microbiome that contributes to overall plant health and disease suppression.

Direct Mechanisms of Biocontrol

1. Antibiosis. Antibiosis is a critical biological mechanism by which endophytic bacteria inhibit the growth of plant pathogens through the secretion of antimicrobial compounds. These include a wide array of bioactive molecules such as lipopeptides, polyketides, phenazines, and volatile organic compounds. These substances either directly kill pathogens or suppress their growth by interfering with vital cellular functions (Ongena and Jacques 2008). Among the best-studied endophytes exhibiting antibiosis are species of *Bacillus* and *Pseudomonas. Bacillus subtilis* is known for producing cyclic lipopeptides such as iturin and fengycin, which integrate into fungal membranes, causing pore formation and cell leakage that ultimately lead to fungal death (Weller, 2007). These lipopeptides exhibit a high degree of specificity toward phytopathogenic fungi and contribute significantly to plant protection.

Similarly, *Pseudomonas fluorescens* synthesizes 2,4-diacetylphloroglucinol (DAPG), a potent antifungal metabolite that inhibits spore germination, disrupts hyphal growth, and interferes with the pathogen's metabolic processes (Haas and Défago 2005). DAPG has been particularly effective against soil-borne pathogens such as *Fusarium*, *Rhizoctonia*, and *Pythium* spp., making it an integral component of biocontrol strategies.

These antimicrobial compounds can be volatile or non-volatile and act via diverse mechanisms, including membrane disruption, enzyme inhibition, and oxidative stress induction. The role of antibiotic-producing endophytes in sustainable agriculture and integrated disease management has been widely acknowledged (Raaijmakers *et al.*, 2002; Santoyo *et al.*, 2016).

2. Enzymatic Degradation. Endophytic bacteria play a crucial role in suppressing plant pathogens through the secretion of hydrolytic enzymes that degrade the structural components of fungal cell walls. These enzymes include:

- **Chitinases**, which target chitin, a major structural polysaccharide in fungal cell walls.
- **β-1,3-glucanases**, which hydrolyze β-glucans, essential glucopolymers in fungal membranes.
- **Proteases**, which break down structural and functional proteins essential for pathogen survival.

The enzymatic action compromises the integrity of the fungal cell wall and membrane systems, leading to cellular disintegration and death. This mechanism is especially effective against filamentous fungi and is considered a vital line of defense in the biological control arsenal of endophytic microbes.

Harman *et al.* (2004) demonstrated that microbial strains producing high levels of chitinases and glucanases are effective against a range of fungal pathogens, particularly *Fusarium*, *Rhizoctonia*, and *Sclerotinia* spp. Compant *et al.* (2005) further emphasized that such enzymes also aid in niche colonization by helping endophytes penetrate plant tissues and outcompete phytopathogens in the internal microenvironment.

The coordinated secretion of these enzymes not only disrupts the pathogen's defense structures but also facilitates the endophyte's establishment within plant tissues, making enzymatic degradation a dual-purpose strategy for both colonization and pathogen suppression.

3. Volatile Organic Compounds (VOCs). Volatile organic compounds (VOCs) produced by endophytic bacteria serve as potent antimicrobial agents, capable of inhibiting pathogenic fungi even in the absence of physical contact. Notably, endophytic species of *Bacillus*, such as *Bacillus subtilis* and *Bacillus amyloliquefaciens*, emit key volatiles like acetoin and 2,3-butanediol. These compounds disrupt fungal growth through mechanisms such as interference with membrane integrity, inhibition of spore germination, and modulation of fungal signaling pathways.

VOCs function at a distance, diffusing through the rhizosphere or internal plant tissues to create a hostile environment for pathogens. This remote antagonism allows for a broader spatial range of biocontrol activity compared to non-volatile antibiotics or enzymes. Studies by Ryu *et al.* (2003); Farag *et al*. (2006) have demonstrated the strong antifungal effects of these volatiles, which not only suppress pathogens but also promote systemic resistance and enhance plant growth.

Indirect Mechanisms of Biocontrol

1. Induced Systemic Resistance (ISR). Induced Systemic Resistance (ISR) is a crucial defense mechanism in plants that primes their immune systems to respond more robustly upon subsequent pathogen attack. Unlike Systemic Acquired Resistance (SAR), which is typically activated through salicylic acid (SA) signaling and is often associated with pathogen infection, ISR is governed primarily by jasmonic acid (JA) and ethylene (ET) signaling pathways. Endophytic bacteria, notably strains of *Bacillus velezensis*, have demonstrated a strong ability to elicit ISR in host plants such as tomato and rice (Kloepper *et al.*, 2004; Choudhary *et al.*, 2007). This immune priming results in the transcriptional activation of several plant defense-related genes and the increased production of pathogenesis-related proteins and enzymes, including peroxidase, phenylalanine ammonia-lyase (PAL), and chitinase (Pieterse *et al.*, 2014).

The ISR-eliciting capacity of endophytes often correlates with their production of microbe-associated molecular patterns (MAMPs), lipopeptides, and other secondary metabolites that modulate host hormone signaling. This resistance is systemic, long-lasting, and environmentally sustainable, offering an effective complement or alternative to chemical pesticides in integrated pest management (IPM) strategies.

2. Competition. Endophytic bacteria play a pivotal role in plant defense by effectively outcompeting pathogenic microorganisms for limited resources such as nutrients and colonization sites within host tissues. One critical factor in this competition is the availability of iron, an essential micronutrient for nearly all living organisms. Endophytes produce high-affinity iron-chelating compounds known as siderophores, which scavenge ferric ions (Fe^{3+}) from the plant environment, making them unavailable to competing pathogens. This iron depletion strategy leads to the inhibition of pathogen growth and virulence. In addition to nutrient competition, endophytes occupy ecological niches on root and shoot surfaces and within intercellular spaces, thereby preventing pathogen establishment through physical exclusion—a process known as competitive exclusion. Loper and Buyer (1991) demonstrated that siderophore-producing fluorescent *Pseudomonas* spp. could suppress soil-borne root pathogens effectively by limiting iron availability in the rhizosphere.

3. Biofilm Formation. Biofilm formation is a critical indirect mechanism through which endophytic bacteria protect host plants from pathogen invasion. A biofilm comprises a structured microbial community embedded in a self-produced matrix of extracellular polymeric substances (EPS), including polysaccharides, proteins, and extracellular DNA. This matrix not only facilitates stable adhesion of bacteria to plant surfaces—such as roots, stems, and even internal tissues—but also acts as a physical barrier that restricts pathogen access and colonization. Furthermore, biofilms enhance bacterial resistance to abiotic stresses like desiccation, pH fluctuations, and antimicrobial agents. In agricultural systems, biofilm-forming endophytes such as *Bacillus subtilis* and *Pseudomonas fluorescens* have demonstrated enhanced persistence and prolonged biocontrol efficacy against soil-borne pathogens like *Fusarium* spp. and *Rhizoctonia* spp. As noted by Ramey *et al*. (2004), biofilm formation facilitates robust root colonization and serves as a platform for coordinated microbial behaviors via quorum sensing. This signaling system regulates the synchronized expression of key biocontrol traits, including antibiotic production and the induction of systemic resistance (ISR). Thus, biofilms function both as defensive structures and as regulatory hubs crucial for sustained plant-microbe symbiosis and effective biological control.

Representative Endophytic Bacteria

Table 1: Endophytic Bacteria with Biocontrol Activity.

Strain	Origin	Target Pathogens	Mechanism	Reference
B. subtilis CB2	Wheat	*F. graminearum*	Iturin	Taheri *et al.* (2023)
B. velezensis QSE-21	Tomato	*B. cinerea*	ISR	Xu *et al.* (2021)
P. polymyxa SF05	Maize	*R. solani*	ISR	Chen *et al.* (2022)
P. fluorescens HP72	Bentgrass	*R. solani*	DAPG	He *et al.* (2004)

Molecular and Genomic Insights. Recent advances in genomics have significantly enhanced our understanding of the molecular mechanisms underpinning the biocontrol activity of endophytic bacteria. Central to this activity are biosynthetic gene clusters (BGCs), which encode the enzymes required for the production of bioactive metabolites such as antibiotics, siderophores, and signaling molecules involved in the induction of systemic resistance (ISR). Particularly important are genes encoding non-ribosomal peptides (NRPs), polyketides, lipopeptides (e.g., iturin, fengycin), and siderophores (e.g., bacillibactin). These compounds not only exhibit potent antimicrobial properties but also modulate plant immune responses and enhance microbial colonization efficiency.

High-throughput genomic techniques, including whole genome sequencing, RNA-Seq-based transcriptomics, and comparative proteomics, have enabled the comprehensive identification and functional annotation of these BGCs. For instance, genome analysis of *Bacillus amyloliquefaciens* FZB42 revealed that over 10% of its genome is dedicated to secondary metabolite biosynthesis, encompassing clusters for fengycin, iturin, and bacillomycin D (Chen *et al.*, 2007; Koumoutsi *et al*., 2004). Similarly, the genome of *Pseudomonas fluorescens* disclosed the presence of BGCs for biocontrol-relevant metabolites such as 2,4-diacetylphloroglucinol (DAPG), pyoluteorin, and hydrogen cyanide (Paulsen *et al.,* 2005).

These molecular insights are instrumental in the identification of elite bacterial strains with superior biocontrol potential. They also support the engineering of strains with enhanced traits using genome-editing technologies like CRISPR-Cas systems. Furthermore, such knowledge facilitates the development of predictive models for tripartite microbe–plant–pathogen interactions, thereby increasing the field-level efficacy and reliability of endophytic bacteria in sustainable agriculture.

Application in Agriculture. Endophytic bacteria are being used in various formulations to enhance their delivery and efficacy in agricultural practices:

Seed coatings: This method involves applying a thin layer of endophytic bacteria directly onto the surface of seeds before planting. The coated seeds facilitate early colonization of the plant by the beneficial microbes, ensuring that the bacteria establish themselves as the plant grows. This approach promotes early root colonization and offers protection against soil-borne pathogens from germination onwards.

Soil drenches: In this technique, a liquid suspension of endophytic bacteria is applied directly to the soil surrounding the root zone. The bacteria then penetrate the roots and colonize internal tissues. This method is particularly effective for treating already established plants and for enhancing root health and nutrient uptake.

Foliar sprays: Here, bacterial formulations are sprayed onto the plant's leaves, allowing entry through stomata or wounds. Foliar application is effective for targeting above-ground plant parts and can help in inducing systemic resistance or directly combating foliar pathogens. It also enables repeated treatments as part of an integrated pest and disease management program.

They are compatible with integrated pest management (IPM) and organic farming. Commercial examples include:

a. Serenade (based on *B. subtilis*)

b. BioYield (based on *Pseudomonas* sp.)

Challenges and Limitations

Despite their promising potential, the widespread adoption of endophytic bacteria as biocontrol agents in sustainable agriculture faces several scientific, technical, and regulatory hurdles.

Inconsistent Field Performance: Perhaps the most pressing issue is the variable efficacy of endophytic strains under different field conditions. Factors such as soil composition, temperature, humidity, plant genotype, and existing microbial communities significantly affect colonization success and biocontrol activity. These inconsistencies reduce the reliability of outcomes across diverse agroecological zones (Sessitsch *et al.*, 2004; Hardoim *et al.*, 2015).

Host Specificity and Compatibility: Endophytic colonization is often restricted by host plant specificity. Certain strains display a preference or compatibility with specific cultivars or species, complicating the development of broad-spectrum biocontrol solutions. This necessitates crop-specific screening and formulation, increasing cost and complexity (Compant *et al.*, 2010).

Regulatory and Biosafety Constraints: The environmental release of live microbial agents is subject to strict biosafety evaluations and regulatory approval. Regulatory frameworks vary between countries and often involve extensive documentation, risk assessments, and field trials. These requirements, although necessary, can slow innovation and discourage commercial investment (Berg *et al.*, 2013).

Formulation Stability and Shelf Life: Ensuring the stability and viability of bacterial formulations under field conditions poses significant technical challenges. Endophytes are susceptible to stress from UV light, desiccation, and temperature extremes. Current formulations often suffer from reduced shelf life and diminished efficacy, particularly when stored or transported under suboptimal conditions (Pillay & Nowak 1997; Malusá *et al.*, 2012).

Knowledge Gaps in Microbial Ecology and Mechanisms: Although mechanisms such as antibiosis, competition, and ISR have been characterized in controlled environments, our understanding of the dynamic interactions between endophytes, host plants, and pathogens under natural field conditions remains incomplete. This lack of ecological insight hinders the development of predictive models and optimized application strategies (Hardoim *et al.*, 2015).

Addressing these limitations will require integrated, interdisciplinary approaches that combine plant microbiome ecology, genomics, molecular biology, agronomy, and bioengineering. Advances in formulation technology, precision agriculture, and regulatory harmonization will be equally essential to realize the full potential of endophytic bacteria in sustainable plant protection.

Future Prospects

The future of endophytic bacterial biocontrol hinges on the integration of biological insights with cutting-edge technological innovations to overcome existing limitations and optimize field performance. Several promising strategies are being actively explored:

Development of Multi-Strain Consortia: Rather than relying on single-strain inoculants, future biocontrol formulations are likely to feature rationally designed microbial consortia. These consortia combine strains with complementary functional traits—such as antimicrobial compound production, induction of Induced Systemic Resistance (ISR), phosphate solubilization, and nitrogen fixation—thereby enhancing efficacy and ecological resilience under diverse environmental conditions. Synergistic interactions among consortium members may also expand host compatibility and suppress a broader range of pathogens (Finkel *et al*., 2020).

Genome Engineering via CRISPR-Cas Systems: CRISPR-Cas genome editing offers an unprecedented opportunity to enhance the biocontrol potential of endophytic bacteria with precision. This includes the targeted activation or insertion of biosynthetic gene clusters (BGCs) responsible for producing antimicrobial metabolites, the enhancement of colonization-related genes, and improved stress resistance. Importantly, such modifications can be made without introducing foreign DNA, easing regulatory constraints (Borriss, 2020).

Advanced Delivery Systems and Formulations: Innovations in delivery platforms are critical for ensuring endophyte viability and colonization success. Encapsulation methods such as alginate beads, biodegradable hydrogels, nano-formulations, and biochar-based carriers offer physical protection and controlled release. Moreover, smart formulations responsive to plant exudates or environmental cues can enhance targeting and persistence in planta (Bashan *et al*., 2014; Malusá *et al.*, 2012).

Integration with Digital Agriculture and Precision Tools: Emerging digital agriculture tools—such as remote sensing, AI-based disease prediction models, and site-specific application systems—can be harnessed to fine-tune the spatial and temporal application of endophytic inoculants. Such integration will enable data-driven decisions on the optimal timing, location, and dosage of microbial biocontrol agents, maximizing efficacy and minimizing waste (Chaudhary *et al*., 2022).

By synergizing microbiological research with synthetic biology, formulation science, and digital technologies, endophytic bacterial biocontrol can transition from experimental trials to scalable, field-ready solutions. These innovations are expected to play a pivotal role in building climate-resilient, resource-efficient, and sustainable agroecosystems.

CONCLUSIONS

Endophytic bacteria offer a promising and sustainable alternative to chemical pesticides. Their multifaceted mechanisms—ranging from direct antagonism to systemic defense activation—make them effective biocontrol agents. Continued research and field validation are essential for their wider adoption in modern agriculture.

FUTURE SCOPE

The potential of endophytic bacteria as biological control agents remains largely untapped. Future research should focus on unraveling the molecular mechanisms underlying host-microbe interactions, identifying novel endophytes with broad-spectrum antagonistic activity, and developing effective formulation technologies for field application. Integrating omics tools and genome editing techniques can enhance strain specificity and efficiency. Moreover, large-scale field validation and commercialization pathways are essential for translating laboratory success into sustainable agricultural practices.

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