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Review

Therapeutic Potential of Endophytic Microbes: Emphasizing Both Fungal and Bacterial Endophytes

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Abstract: This review explores the diverse applications and therapeutic potential of endophytic microbes, emphasizing both fungal and bacterial endophytes. These microorganisms reside within plant tissues without causing harm and play an important role in enhancing plant growth, nutrient acquisition, and resistance to pathogens. They produce phytohormones, facilitate nutrient uptake, solubilize essential nutrients, fix nitrogen, and improve stress tolerance. Furthermore, endophytes contribute to agricultural sustainability by producing plant growth regulators, providing biocontrol against pathogens through antimicrobial compounds, and competing for resources. Integrating endophytic microbes into agricultural practices can reduce reliance on chemical fertilizers and pesticides, promoting eco-friendly and sustainable farming. This review highlights the dual role of endophytic microbes in fostering sustainable agriculture and providing novel therapeutic applications. By minimizing dependence on chemical inputs, endophytes support environmental health while boosting crop yields. The synthesis underscores the importance of leveraging endophytic microbes to tackle global food security and sustainability challenges.

Keywords: endophytic fungi; endophytic bacteria; agricultural applications; sustainability

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1. Introduction

Endophytic microbes, residing within plant tissues without causing harm, have garnered significant attention for their potential therapeutic applications in agriculture. These microorganisms form symbiotic relationships with their host plants, offering numerous benefits that can significantly enhance agricultural productivity and sustainability [1]. Endophytic microbes can enhance plant growth, improve resistance to diseases, and increase tolerance to environmental stressors, making them invaluable allies in the quest for sustainable agriculture [2].

One of the primary ways that endophytic microbes benefit plants is through the enhancement of nutrient uptake. These microorganisms can solubilize essential nutrients like phosphorus and nitrogen, making them more accessible to the plant. This improved nutrient availability leads to better plant growth and higher crop yields. Additionally, some endophytes produce plant growth-promoting hormones such as auxins, gibberellins, and cytokinins, further stimulating plant development and vigor [3].

Another significant benefit of endophytic microbes is their ability to improve plant disease resistance. Many endophytes produce antimicrobial compounds that can inhibit the growth of pathogenic microorganisms, providing a natural form of protection for the host plant. This biocontrol mechanism reduces the need for chemical pesticides, which are often harmful to the environment and human health. Moreover, endophytes can induce systemic resistance in plants, priming the plant's immune system to respond more effectively to pathogen attacks [4].

Endophytic microbes also play a crucial role in enhancing plant tolerance to abiotic stressors such as drought, salinity, and extreme temperatures. These microorganisms can modulate the plant's physiological responses, helping it to maintain water balance, stabilize cell membranes, and produce stress-related proteins [5,6]. For instance, some endophytes produce osmoprotectants that help plants retain water during drought conditions, while others can alter the plant's root architecture to improve water uptake.

By exploring the diverse roles and applications of endophytic microbes, researchers and farmers can develop innovative strategies to improve crop health and productivity. Biofertilizers and biopesticides can be made by incorporating endophytes into farming methods [3]. These are safer for the environment than traditional chemical inputs. This therapeutic approach not only benefits agricultural practices but also contributes to sustainable farming by reducing reliance on chemical fertilizers and pesticides [7].

Moreover, the use of endophytic microbes aligns with the principles of sustainable agriculture, which emphasize the need for practices that are environmentally sound, economically viable, and socially responsible. By reducing the dependence on chemical inputs, endophytes help mitigate the negative impacts of agriculture on the environment, such as soil degradation, water pollution, and loss of biodiversity. Additionally, the use of these microorganisms can improve soil health by enhancing microbial diversity and activity, leading to more resilient and productive agroecosystems [8].

Endophytic microbes, particularly fungi, establish symbiotic relationships with a variety of host plants, adapting to diverse environments and ecological niches. These endophytes are classified into several fungal phyla, including Ascomycota, Basidiomycota, and Mucoromycota, each contributing uniquely to plant health and growth [4]. The Ascomycota phylum is the largest and most diverse group of endophytic fungi, with species found in nearly every type of plant tissue. While Basidiomycota is less diverse in comparison, it also includes important endophytes that form mutualistic relationships with their hosts [9]. Mucoromycota, another key group, is typically associated with root-endophytes. Although Ascomycota remains the most widespread and diverse, all three phyla play vital ecological roles in plant health. Their diversity across plant tissues reflects their evolutionary adaptations, and understanding their roles is crucial for harnessing their potential in agriculture and plant health management [10]. This diversity allows fungi to form beneficial relationships with plants, enhancing nutrient uptake, promoting growth, and increasing resistance to environmental stressors [11].

In addition to fungi, endophytic bacteria are also incredibly diverse and abundant. They belong to several phyla, including Acidobacteria, Actinobacteria, Hadobacteria, Bacteroidetes, Firmicutes, Verrucomicrobia, and Proteobacteria [12]. These bacterial endophytes play crucial roles in plant health by promoting growth, improving nutrient acquisition, and providing protection against pathogens [13]. They produce a range of bioactive compounds, including antibiotics and growth hormones, which benefit their host plants [14].

The adaptability and diversity of endophytic microbes make them essential for sustainable agriculture. By exploring and harnessing their potential, we can develop innovative strategies to improve crop productivity, reduce dependency on chemical inputs, and enhance resilience against environmental stresses [15]. This approach not only benefits plant health but also supports ecological balance and soil health, contributing to more sustainable agricultural practices. Understanding and utilizing the complex interactions between endophytic microbes and plants holds great promise for advancing agricultural sustainability and food security in the face of global challenges [16].

Endophytic microbes offer a promising therapeutic approach to improving agricultural practices. Their ability to enhance nutrient uptake, increase disease resistance, and improve stress tolerance makes them valuable tools for sustainable farming. As research continues to uncover the myriad benefits of these microorganisms, their integration into agricultural systems is likely to play a key role in achieving food security and environmental sustainability in the future [17]. Figure 1 illustrates the symbiotic relationship between fungal and bacterial endophytes and plants. It shows how fungi like *Trichoderma* and bacteria like *Bacillus* colonize plant tissues, providing benefits such as growth promotion, disease resistance, and enhanced tolerance to both biological and environmental stresses. Their comprehensive involvement in plant health underscores the potential of endophytic microbes to foster more resilient and productive agricultural systems [18].

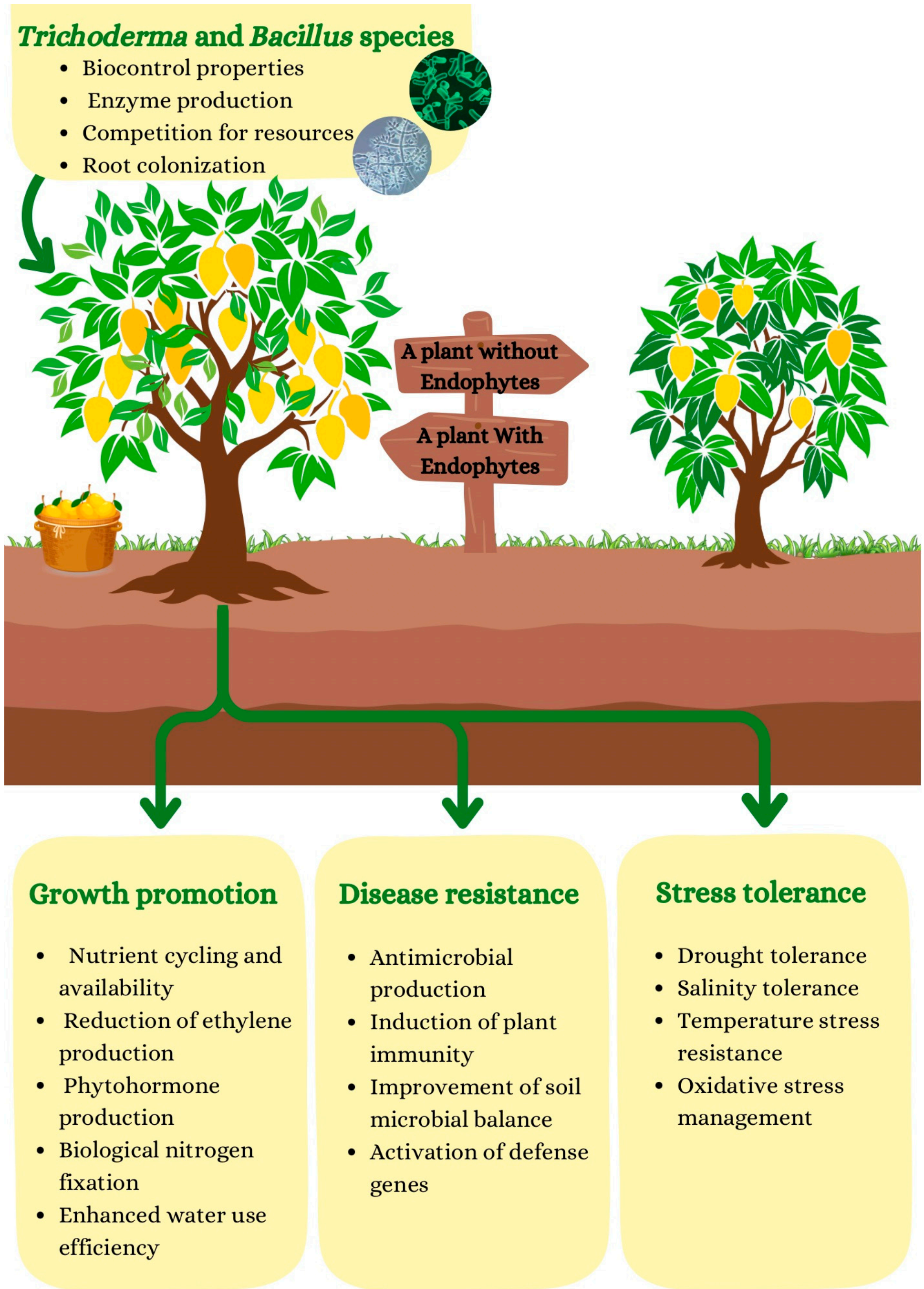

Figure 1. Symbiotic relationship between fungal and bacterial endophytes and plants.

2. Endophytic Fungi

Endophytic fungi, mainly from the Ascomycota phylum, colonize the healthy tissues of host plants either for part or the entirety of their life cycle, influencing plant ecology, fitness, and evolution. These fungi coexist with plant tissues in a mutualistic relationship, providing benefits such as enhanced resistance and growth promotion without causing significant harm to the host [19]. The distinction between "host" and "plant" lies in the fact that while the plant is the organism, the host refers to the plant as a living environment for the endophyte, which may reside in various plant tissues like roots, stems, or leaves. They have been found in a wide range of plants, including trees, grasses, algae, and herbaceous species, with isolations reported from crops such as mustard, rice, chili, wheat, tomato, citrus, maize, soybean, potato, common bean, pea, cotton, sunflower, strawberry, and chickpea [20].

Researchers have studied endophytes in about 300,000 plant species, discovering that nearly all plants harbor at least one type of endophyte. While it is estimated that around 1.5 million fungal species exist within plants, only 70,000–100,000 species have been identified, accounting for just 7% of fungal endophytes. These findings underscore the need for additional research to uncover the fungal endophytes linked to plant species in different environments and geographic areas [21]. It is possible to isolate these fungi from plant tissues and culture them on agar, revealing significant diversity within the phyla Ascomycota and Basidiomycota. Studies [22–24] have documented a vast array of endophytic fungal species belonging to genera like *Aspergillus*, *Claviceps*, *Colletotrichum*, *Alternaria*, *Curvularia*, *Geomyces*, *Fusarium*, *Leptospora*, *Glomus*, *Neotyphodium*, *Microdochium*, *Penicillium*, *Paecilomyces*, *Piriformospora*, *Phaeomoniella*, *Trichoderma*, and *Rhizopus* [25]. Research has also indicated that some endophytic fungi are host-specific. For example, *Gibberella zeae* is associated with maize (*Zea mays*) [26], *P. glabrum* with barley (*Hordeum vulgare*) [27]; *C. capsici*, *Phoma herbarum*, and *C. boninense* with soybean (*Glycine max*) [28]; *F. verticillioides*, *Diaporthe endophytica* and *Metarhizium brunneum* with sugarcane (*Saccharum officinarum*) [29]; and *Pleospora herbarum*, *Talaromyces flavus*, and *T. atroviride* with wheat (*Triticum aestivum*) [30,31].

Endophytic fungi that colonize the leaves of grasses are classified within the clavicipitaceous system, which belongs to the Ascomycota phylum and the Clavicipitaceae families. These fungi are typically divided into two main groups: clavicipitaceous endophytes (CEs) and non-clavicipitaceous endophytes (NCEs). Clavicipitaceous (CEs) primarily colonize plant rhizomes and shoots, while NCEs are found in the shoots or roots of many plants. These groups can be further categorized based on their host range, biodiversity, functional benefits, and the plant tissues they inhabit [25].

While clavicipitaceous fungi are generally considered mutualistic, some species, particularly those in the *Epichloë* genus, can exhibit pathogenic behavior under certain conditions. Environmental changes or plant stress can disrupt the symbiotic relationship, leading to negative effects on the plant. Additionally, species of *Neotyphodium* (the anamorph of *Epichloë*) are known to produce toxic alkaloids that can harm herbivores consuming infected plants. Despite these potential harmful effects, clavicipitaceous fungi are mainly viewed as beneficial rather than pathogenic [32].

Clavicipitaceous endophytes (CEs), which include fungi from the genera *Epichloë* and *Balansia* (corresponding to the anamorphs *Neotyphodium* and *Ephelis*), establish systemic intercellular infections along the plant axis, forming a hyphal gradient. These fungi are primarily transmitted vertically via seeds. In contrast, non-clavicipitaceous endophytes (NCEs) belong to the Agaricomycotina and Pucciniomycotina classes (Basidiomycota) and the Pezizomycotina class (Ascomycota), such as *Phoma* spp. and *Arthrobotrys* spp. These fungi are transmitted both vertically and horizontally, providing various habitat-specific and general benefits to the plant host [33].

The extensive diversity and adaptability of endophytic fungi underscore their potential in sustainable agriculture. By enhancing nutrient uptake, promoting plant growth, and increasing resistance to environmental stressors and pathogens, these fungi offer valuable solutions for improving crop productivity and sustainability. Future research should continue to explore the complex interactions between endophytic fungi and their host plants to fully harness their benefits for agricultural advancements [29].

Fungal endophytes have significant biotechnological potential as biological control agents and sources of secondary metabolites, including antitumor compounds [34], antimicrobial agents, immunosuppressants [35], antibiotics, natural antioxidants [36], antidiabetic compounds [25], and antiviral compounds [37]. Their abundant reservoir of bioactive metabolites has led to the isolation of numerous novel compounds, including steroids, alkaloids, peptides, terpenoids, flavonoids, polyketides, and phenols, with applications in agriculture, medicine, and industry [38].

In recent decades, plant scientists have emphasized the importance of endophytic fungi as biofertilizers. These fungi can provide essential nutrients to crops, enhancing yield and potentially replacing chemical fertilizers with multifaceted plant growth-promoting (PGP) endophytic fungi for sustainable agriculture. Fungal endophytes produce bioactive growth regulators, such as phytohormones and other substances, that exhibit antibacterial, antifungal, antiviral, and anticancer activities. Natural products from endophytic fungi continue to play a crucial role in novel agricultural applications due to their non-toxic and cost-effective nature revised in [39].

Endophytic fungi attract attention for their diverse applications, including agricultural control and plant growth stimulation, drawing interest from ecologists, taxonomists, chemists, and agronomists. Screening methods for PGP attributes of endophytic fungi involve the production of phytohormones, gibberellic acid, indole-3-acetic acid, ACC deaminase, and the solubilization of phosphorus, potassium, and zinc. Utilizing endophytic fungi in agriculture offers new methods to improve nutrient supply and manage fields sustainably [40,41].

3. Endophytic Bacteria

Bacterial endophytes are a diverse group of microorganisms that reside within healthy plant tissues without causing any harm to their host plants. These bacteria typically form symbiotic relationships with plants, thriving in intercellular spaces rich in amino acids, carbohydrates, and inorganic nutrients. Initially, scientists believed these endophytic bacteria to be potential pathogens, but recent research has revealed their significant beneficial roles, including enhancing plant resistance to parasites and pathogens and promoting growth [42,43].

Endophytic bacteria have gained significant interest in recent years due to their positive impact on crop production [44]. These bacteria influence plant growth across various species and strains, making them a focal point in agricultural research. Their role as biological fertilizers is particularly important, as they adapt metabolically within the host plant to promote growth and nutrient uptake. Endophytic bacteria are ubiquitous in most plant species, encompassing multiple genera and species within a single host, as well as being specific to certain plant species [45]. These bacteria can also exist on the plant surface as epiphytes at certain stages of their life cycle. For instance, many endophytic bacteria may initially colonize the surface of the plant (as epiphytes) before they enter the plant's tissues and establish themselves as endophytes. This transition can occur due to environmental factors or when the plant's physical barriers allow the bacteria to penetrate and move into the internal tissues [46].

The composition of bacterial endophytic communities is primarily dominated by four phyla: *Proteobacteria* (54%), *Actinobacteria* (20%), *Firmicutes* (16%), and *Bacteroidetes* (6%) [47]. Common genera of bacterial endophytes include *Bacillus*, *Pseudomonas*, *Stenotrophomonas*, *Burkholderia*, *Micrococcus*, *Microbacterium*, and *Pantoea* [48].The population dynamics of endophytic bacteria are influenced by several key factors. These include the plant species, as different plants may support distinct microbial communities, and the specific plant part being analyzed, as certain areas, like roots or leaves, may harbor different bacterial populations. Additionally, the plant's developmental stage plays a significant role, as bacteria may interact differently with juvenile versus mature tissues. Environmental conditions, such as temperature, moisture, and soil composition, also affect bacterial growth [49]. Furthermore, plant-genotype variations can alter susceptibility to specific bacterial communities, shaping the microbiome. Lastly, interactions with other organisms, such as pathogens or other microbes, can significantly influence endophyte dynamics.

Bacterial endophytes enter plant tissues through various pathways, including germinating radicles, secondary roots, stomata, or foliar damage [50]. They can either remain localized at the entry point or spread throughout the plant once inside. In general, these bacteria use hydrolytic enzymes such as pectinase and cellulase to penetrate plant tissues, entering through natural openings or wounds [51].

The beneficial roles of endophytic bacteria extend beyond just plant growth promotion. These bacteria can also enhance the plant's tolerance to abiotic stressors like drought, salinity, and extreme temperatures. By modulating the plant's physiological responses, endophytic bacteria help maintain water balance, stabilize cell membranes, and produce stress-related proteins. Some endophytes produce osmoprotectants that assist plants in retaining water during drought conditions, while others alter root architecture to improve water uptake [43].

Endophytic bacteria are also pivotal in sustainable agriculture by reducing the need for chemical fertilizers and pesticides. Their ability to promote nutrient uptake and provide biocontrol against pathogens supports more eco-friendly farming practices. By integrating these bacteria into agricultural systems, farmers can improve crop resilience and productivity, contributing to more sustainable and environmentally friendly farming practices.

Understanding and leveraging the complex interactions between endophytic bacteria and plants holds great promise for advancing agricultural sustainability and ensuring food security in the face of global challenges [52]. Further research into the diverse roles and applications of these microorganisms will continue to uncover their potential to enhance crop health and productivity, ultimately benefiting agricultural practices and the environment [53,54].

Endophytic nitrogen-fixing bacteria, such as *Acetobacter diazotrophicus* and *Herbaspirillum* spp. in sugar cane, *Azoarcus* spp. in kallar grass, and species of *Alcaligenes*, *Azospirillum*, *Bacillus*, *Enterobacter*, *Herbaspirillum*, *Klebsiella*, *Pseudomonas*, and *Rhizobium* in rice, play a crucial role in enhancing plant health and agricultural productivity [55]. These bacteria produce nitrogenase enzymes, which are essential for nitrogen fixation, converting atmospheric nitrogen (N2) into a form that plants can use. The symbiotic relationship between these bacteria and plants significantly contributes to plant growth and nutrient uptake. These endophytic bacteria are also capable of solubilizing essential nutrients like phosphorus, nitrogen, and potassium from complex compounds, making them more accessible to plants [56]. The ability to solubilize phosphorus is particularly important, as it enhances nutrient availability and supports plant growth [5]. Emphasized that microbial fertilizers, including Rhizobium and phosphate-solubilizing bacteria (PSB), improve the availability of nitrogen and phosphorus, thereby promoting agricultural sustainability.

Increasing nutrient levels in the rhizosphere, biological nitrogen fixation, and root surface area elongation are key functions of many marketable biofertilizers.

Endophytes significantly contribute to plant growth by enhancing microbial processes that increase the availability of nutrients, making them easily assimilable by plants. These beneficial bacteria improve soil fertility by fixing nitrogen and converting insoluble phosphates and potassium into soluble forms. Endophytic microbes residing inside plant tissues utilize various mechanisms to promote plant growth [28,57].

Bacterial endophytes promote plant growth directly by facilitating the uptake of nutrients like potassium, nitrogen, phosphorus, and iron, or by regulating plant hormones such as cytokinin, auxin, and ethylene, thereby modifying plant growth [58]. Indirectly, endophytic bacteria produce metabolites that reduce plant damage and infection from pathogens. Nitrogen, essential for synthesizing vital biomolecules, is supplied to agricultural lands as chemical fertilizer. However, biological nitrogen fixation by endophytic microorganisms offers an alternative [59].

Endophytic biofertilizers include both rhizobial and non-rhizobial bacteria such as *Achromobacter*, *Burkholderia*, *Azoarcus*, *Gluconoacetobacter*, *Klebsiella*, *Herbaspirillum*, and *Serratia*, with *Azoarcus* recognized for its potential in nitrogen fixation [60]. Phosphorus is an essential macronutrient for metabolic processes like photosynthesis, biological oxidation, nutrient uptake, and cell division. Endophytic bacteria can solubilize phosphates, enhancing soil fertility by converting insoluble phosphorus to soluble forms through the release of organic acids. Additionally, certain endophytic bacteria such as *Pseudomonas*, *Acidothiobacillus ferrooxidans*, and various *Bacillus* species have demonstrated the ability to release soluble potassium from soils. To show how important endophytic bacteria are for sustainable agriculture, [61] talk about plant growth-promoting bacteria (PGPB) and their subset, PGPBEs. These bacteria affect plant growth in several different ways, such as fixing atmospheric nitrogen, synthesizing plant hormones (e.g., auxins, cytokinins), and solubilizing essential nutrients like phosphorus. This phenomenon also protects plants from pathogens by producing antimicrobial compounds, outcompeting harmful microbes, and inducing systemic resistance in plants. Additionally, these beneficial bacteria help plants tolerate environmental stresses like drought and salinity, making them valuable tools for sustainable agriculture by reducing the need for chemical fertilizers and pesticides [57].

To utilize endophytic bacteria as biofertilizers, they must be isolated from host plant tissues, cultivated, and then refined into a condensed form suitable for field application. People view the use of beneficial microbiota, such as endophytic microbes, as a viable solution to lessen dependency on chemical fertilizers, thereby reducing environmental stress and boosting food production. Leveraging the services of endophytic microbes is undoubtedly essential for achieving economic goals and ensuring environmental sustainability by reducing excessive agrochemical use [62].

4. Fungi and Bacteria Endophytes: Natural Allies in Controlling Plant Pathogens

Endophytes have garnered significant attention in recent years for their potential to control plant pathogens. These endophytic organisms, including both fungi and bacteria, form symbiotic relationships with plants, often enhancing their growth, improving stress tolerance, and crucially, providing protection against a range of pathogens [63]. The use of endophytes in sustainable agriculture presents a promising alternative to chemical pesticides, offering environmentally friendly solutions to managing plant diseases.

Endophytes can be broadly categorized into fungal and bacterial endophytes, both of which colonize plant tissues such as roots, stems, leaves, and seeds. Unlike pathogens, endophytes do not cause disease in their host plants. Instead, they contribute to the host's overall health, often enhancing its ability to resist biotic and abiotic stresses [64].

Fungal Endophytes are more commonly associated with grasses and other plants, where they have been observed to provide protection against herbivores, pathogens, and environmental stressors like drought. These fungi may produce bioactive compounds that deter pathogens or enhance the plant's immune responses [65].

Bacterial Endophytes inhabit the same plant tissues and contribute to plant health by promoting growth, facilitating nutrient uptake, and protecting against pathogens. These bacteria often produce antibiotics or other antimicrobial compounds, which can inhibit the growth of plant pathogens directly [66].

4.1. Mechanisms of Pathogen Control

Endophytes control plant pathogens through several mechanisms as follow:

A. Antibiosis: is a biological phenomenon where one organism produces substances that inhibit or kill another organism, often as a means of competing for resources or territory. In the context of plant-microbe interactions, antibiosis typically refers to the production of bioactive compounds, such as antibiotics, that target and suppress the growth of harmful pathogens. These compounds can be produced by various microorganisms, including bacterial endophytes, which reside within plant tissues and contribute to plant health by protecting against pathogens [67,68]. Bacterial endophytes, such as *P. fluorescens*, *A. brasilense*, and *B. subtilis*, are known to produce a variety of bioactive compounds, including antibiotics, siderophores, and enzymes, which directly inhibit pathogen growth. For example, siderophores are molecules that bind to iron, sequestering it from the environment. Since iron is essential for pathogen growth, the production of siderophores by beneficial bacteria can limit pathogen growth by making iron unavailable. This mechanism of competition for iron is a form of antibiosis, as it prevents pathogens from thriving. Studies, such as those by [69], have demonstrated the role of bacterial endophytes in controlling plant pathogens through antibiosis, highlighting their potential in sustainable agriculture by reducing reliance on chemical pesticides. By promoting plant health and resisting infections, endophytic bacteria can contribute to more resilient crops.

B. Competition for Resources: Endophytes help protect plants from pathogens by outcompeting them for vital resources, including nutrients, water, and space within plant tissues. These beneficial microbes colonize areas where pathogens would normally thrive, blocking access and preventing pathogen establishment. One example is *A. brasilense*, which colonizes the root systems of grasses like maize, outcompeting pathogens such as *Rhizoctonia solani* [70]. By depleting available nutrients and occupying ecological niches, *Azospirillum* limits pathogen growth and prevents infections. Another example is *Bacillus amyloliquefaciens*, which has been shown to outcompete pathogens like *Colletotrichum* and *Botrytis* in tomatoes and other crops [71]. These endophytes produce antimicrobial compounds, including lipopeptides, which inhibit pathogen growth. Additionally, *T. harzianum* is an endophytic fungus that can protect plants like tomatoes and cucumbers from soil-borne pathogens such as *Fusarium oxysporum* by colonizing the root zone and reducing pathogen access to resources [72]. *Trichoderma* also prevents pathogen establishment by outcompeting harmful microbes for nutrients and by producing enzymes that break down pathogen cell walls. This competitive exclusion strategy is widely used in integrated pest management (IPM), where beneficial microbes are introduced to enhance plant protection, reduce pathogen populations, and decrease reliance on chemical pesticides, promoting sustainability in agriculture [73].

C. Induced Systemic Resistance (ISR): is a defense mechanism where endophytes activate a plant's immune system, priming it to respond more quickly and effectively to future pathogen attacks. This process involves the production of signaling molecules such as jasmonic acid (JA), salicylic acid (SA), and ethylene by the endophyte [74]. These molecules trigger the plant's defense pathways, which include the activation of pathogenesis-related proteins, enhanced production of antimicrobial compounds, and the fortification of plant cell walls. One of the key aspects of ISR is that it "primes" the plant's defense system, meaning the plant's immune response is heightened and ready to respond faster when a pathogen challenge occurs. For instance, *P. fluorescens*, a well-studied endophyte, induces ISR in plants by producing acetoin and other volatile compounds that trigger the plant's immune system [75]. In rice and wheat, these compounds have been shown to increase resistance to fungal pathogens like *Rhizoctonia* and *Pythium* [76]. Unlike traditional resistance mechanisms, ISR is typically more generalized and can protect plants against a wide range of pathogens. This makes it a sustainable method of crop protection, reducing the need for chemical pesticides while enhancing plant health and resilience to environmental stressors.

D. Parasitism of Pathogens: certain endophytic fungi and bacteria can parasitize or directly attack plant pathogens, providing an effective means of pathogen control [77]. These parasitic relationships are often established through the production of enzymes that degrade the cell walls or other essential components of the pathogen. For example, species of *Trichoderma*, such as *T. harzianum*, are well known for their ability to parasitize pathogenic fungi by secreting chitinases and glucanases, enzymes that break down the cell walls of the fungi [78]. This parasitism effectively kills the pathogens, preventing them from establishing infections in plants. *Trichoderma* can colonize plant roots and other tissues, forming a protective barrier against soil-borne pathogens like *Fusarium* and *Verticillium* spp. In addition bacteria like *Bacillus subtilis* also exhibit parasitic behavior. They can attack pathogenic bacteria and fungi by competing for space and resources or by producing bacteriocins and lytic enzymes that directly kill the pathogen. For instance, *Bacillus* strains have been shown to control bacterial wilt in tomatoes and other crops by directly attacking the pathogen *Ralstonia solanacearum* [79]. The parasitic ability of endophytes offers a promising biological control strategy, reducing the need for chemical pesticides and supporting sustainable farming practices.

4.2. Examples of Fungal and Bacterial Endophytes in Pathogen Control

Endophytes are microorganisms, including fungi and bacteria. These microorganisms have evolved various mechanisms to protect their host plants from a wide array of pathogens, making them valuable allies in sustainable agriculture. Below are examples of fungal and bacterial endophytes that play significant roles in controlling plant pathogens.

A. *Trichoderma* spp.: *Trichoderma* is one of the most studied fungal endophytes for its biocontrol properties. These fungi are known to colonize plant roots and protect against soil-borne pathogens like *R. solani* and *F. oxysporum*. *Trichoderma* produces a range of enzymes, such as chitinases and glucanases, that degrade the cell walls of pathogenic fungi. Additionally, *Trichoderma* can outcompete pathogens for nutrients and space, reducing their ability to infect the plant [80].

B. *Piriformospora* spp.: This root-colonizing endophytic fungus is known for its ability to enhance plant growth and confer resistance to a variety of pathogens. *P. indica* has been shown to protect plants like barley and maize from root rot caused by *Fusarium* species. The fungus induces systemic resistance in the host plant and produces antimicrobial compounds that inhibit the growth of the pathogen [81].

C. *Epichloë* spp.: These fungal endophytes are found in grasses, where they form mutualistic relationships. *Epichloë* species produce alkaloids that deter herbivores and inhibit the growth of fungal pathogens. In tall fescue grass, for example, *E. coenophiala* has been shown to protect against pathogens such as *Bipolaris sorokiniana*, which causes leaf spot diseases [82].

D. *Bacillus* spp.: *Bacillus* species are widely recognized for their role in biocontrol. These bacteria produce a variety of antimicrobial compounds, including lipopeptides and antibiotics, that inhibit the growth of fungal and bacterial pathogens. *B. subtilis*, for example, has been used to control diseases like bacterial wilt in tomatoes and rice blast caused by *Magnaporthe oryzae*. The bacterium also induces systemic resistance in plants, making them more resilient to future pathogen attacks [83].

E. *Pseudomonas* spp.: *P. fluorescens* is a well-known bacterial endophyte that provides protection against a range of soil-borne pathogens. It produces antibiotics like pyoluteorin and 2,4-diacetylphloroglucinol, which inhibit the growth of pathogens such as *Pythium* and *Fusarium*. *Pseudomonas* species also promote plant growth by producing phytohormones and enhancing nutrient availability [84].

F. *Streptomyces* spp.: These endophytic bacteria are notable for their ability to produce a wide range of antibiotics, making them effective against various plant pathogens. *Streptomyces griseoviridis*, for example, has been used to control diseases like potato scab caused by *Streptomyces scabies* and damping-off in seedlings caused by *R. solani.* In addition to producing antibiotics, *Streptomyces* species can also degrade pathogen cell walls and induce systemic resistance in plants [85].

5. Applications in Sustainable Agriculture

The application of endophytes in sustainable agriculture is an emerging strategy that aligns with the growing need for environmentally friendly and economically viable farming practices. As concerns about chemical pesticide resistance, environmental degradation, and food security increase, endophytes provide a promising alternative. These microorganisms, which live within plant tissues, offer several advantages in sustainable agriculture, including the ability to specifically target plant pathogens without harming non-target organisms [86]. Unlike conventional chemical pesticides, which can disrupt ecosystems and harm beneficial organisms, endophytes often act in a highly specific manner, reducing collateral damage and promoting the overall health of the ecosystem. For instance, certain bacterial endophytes such as *P. fluorescens* and *B. subtilis* produce bioactive compounds like antibiotics and siderophores that can inhibit the growth of harmful pathogens, making them effective biocontrol agents. These beneficial bacteria can also improve nutrient uptake by plants, enhancing growth and resilience to stressors such as drought and salinity. This makes endophytes valuable for integrated pest management (IPM) systems, where they complement other biocontrol agents, such as predatory insects or nematodes, to provide a holistic approach to pest control and reduce dependence on chemical pesticides [87].

Endophytes are also being explored for their role in the development of crops that are naturally resistant to diseases and environmental stresses. Research into selecting or genetically engineering plants that harbor beneficial endophytes holds great promise for creating crops that require fewer external inputs like fertilizers, pesticides, and water. For example, *Trichoderma* species, which are widely used in agriculture, not only protect plants from soil-borne pathogens but also stimulate plant growth through the production of growth-promoting compounds like plant hormones and enzymes. In addition to disease control, endophytes can enhance the plants' ability to absorb nutrients from the soil and protect them against environmental stresses, such as heavy metals, drought, and high salinity. In particular, *Bacillus* and *Azospirillum* species have been demonstrated to improve nitrogen fixation in plants, reducing the need for chemical fertilizers and enhancing soil fertility [70]. These microorganisms can be applied as seed treatments, soil amendments, or foliar sprays, making them versatile and easy to integrate into current agricultural practices. Moreover, the incorporation of endophytes into broader IPM strategies, alongside resistant crop varieties and sustainable cultural practices like crop rotation, offers a path toward reducing pesticide use and increasing crop productivity in an eco-friendly manner. The combined effect of these strategies contributes to the overall sustainability of agricultural systems, improving soil health, reducing chemical inputs, and enhancing biodiversity. Through ongoing research and development, the agricultural industry can further optimize the use of endophytes, ensuring their effective role in promoting sustainable, resilient farming systems [1].

6. Challenges and Future Prospects

While the potential of endophytes in controlling plant pathogens is promising, several challenges remain. The effectiveness of endophytes can be influenced by environmental conditions, plant species, and the presence of other microorganisms. Additionally, there is a need for more research to understand the complex interactions between endophytes, pathogens, and host plants [88].

Future research should focus on identifying new endophytic strains with biocontrol potential, understanding the mechanisms of pathogen suppression, and developing methods to enhance the colonization and persistence of beneficial endophytes in plants. Advances in molecular biology and genomics are likely to play a key role in these efforts, enabling the development of more effective and targeted biocontrol strategies [89].

7. Conclusions

This review underscores the diverse applications and significant therapeutic potential of endophytic microbes, particularly fungal and bacterial endophytes. These microorganisms, which reside harmlessly within plant tissues, play an essential role in enhancing plant growth, nutrient acquisition, and pathogen resistance. By producing phytohormones, facilitating nutrient uptake, solubilizing essential nutrients, fixing nitrogen, and improving plant stress tolerance, endophytes contribute to more sustainable agriculture. Their ability to offer biocontrol against pathogens and reduce reliance on chemical fertilizers and pesticides highlights their value in promoting eco-friendly and sustainable farming practices.

Fungal and bacterial endophytes represent a powerful tool in the fight against plant pathogens. Through mechanisms such as antibiosis, competition, induced systemic resistance (ISR), and parasitism, these microorganisms provide significant protection to their host plants, reducing the need for chemical pesticides. Endophytic microbes not only promote sustainable agriculture but also hold potential for discovering new therapeutic applications, making them vital in addressing global challenges related to food security and environmental sustainability. Leveraging these microbes in agricultural systems is crucial for achieving a more resilient and productive future in farming, as they are likely to play an increasingly important role in global efforts to ensure food security and environmental sustainability.

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