Perspectives and potential applications of endophytic microorganisms in cultivation of medicinal and aromatic plants

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Ensuring food and nutritional security, it is crucial to use chemicals in agriculture to boost yields and protect the crops against biotic and abiotic perturbations. Conversely, excessive use of chemicals has led to many deleterious effects on the environment like pollution of soil, water, and air; loss of soil fertility; and development of pest resistance, and is now posing serious threats to biodiversity. Therefore, farming systems need to be upgraded towards the use of biological agents to retain agricultural and environmental sustainability. Plants exhibit a huge and varied niche for endophytic microorganisms inside the planta, resulting in a closer association between them. Endophytic microorganisms play pivotal roles in plant physiological and morphological characteristics, including growth promotion, survival, and fitness. Their mechanism of action includes both direct and indirect, such as mineral phosphate solubilization, fixing nitrogen, synthesis of auxins, production of siderophore, and various phytohormones. Medicinal and aromatic plants (MAPs) hold a crucial position worldwide for their valued essential oils and several phytopharmaceutically important bioactive compounds since ancient times; conversely, owing to the high demand for natural products, commercial cultivation of MAPs is on the upswing. Furthermore, the vulnerability to various pests and diseases enforces noteworthy production restraints that affect both crop yield and quality. Efforts have been made towards enhancing yields of plant crude drugs by improving crop varieties, cell cultures, transgenic plants, etc., but these are highly cost-demanding and time-consuming measures. Thus, it is essential to evolve efficient, eco-friendly, cost-effective simpler approaches for improvement in the yield and health of the plants. Harnessing endophytic microorganisms as biostimulants can be an effective and alternative step. This review summarizes the concept of endophytes, their multidimensional interaction inside the host plant, and the salient benefits associated with endophytic microorganisms in MAPs.
Introduction

Plants perform a range of fundamental functions in helping all distinct forms of living beings and release chemical signals to communicate with them. The roots give anchorage to the plant in soil and assist in the acquisition of water and nutrients, as well as produce chemical compounds that induce various types of interactions. This constitutes mutualism with the microorganisms that include fungi in mycorrhizal associations, endophytes, and plant growth-promoting rhizobacteria (PGPRs) as well as parasitism with pathogenic microorganisms, other plants, and herbivores (Badri et al., 2009). The plant roots discharge tremendous quantities of chemical compounds to fight pathogens and attract advantageous microorganisms (Badri and Vivanco, 2009). Such plant–microbe interactions occur at different trophic levels within a sophisticated arrangement of communities (Yan et al., 2019). Approximately 470 million years ago, the evolution of aquatic plants into terrestrial organisms was made possible by cooperating with soil microbes, and many of those microbe–plant interactions still persist (Bhattacharya and Medlin, 1998; Palmer et al., 2004; Ni et al., 2012; Williams et al., 2013). Some plant–microbe interactions are commensalism, where no harm is done to the plant, but the microbe gains some advantage. Several distinct interactions are advantageous to both partners (e.g., they are called mutualistic). Lastly, another group of microorganisms are pathogens and parasites to their host plants. In all the incidents, the microbe and the plant have established the ability to communicate. The microorganism recognizes and responds to the chemical signaling molecules produced by the plants. This usually results in the discharge of microbial compounds that are in turn identified by the plant, thereby generating a two-way “communication” that uses a molecular lexicon. Once a plant–microbe relationship begins, microbes and plants continue to observe their partner’s physiology and coordinate their activities accordingly.

Medicinal and aromatic plants (MAPs) hold a crucial position within people’s healthcare systems throughout the world. Until the arrival of advanced medicines, an oversized population in emerging nations has traditionally relied upon the products obtained from plants, particularly from forests. Numerous medicinal and aromatic crops are being exploited for economic uses. Approximately 12.5% of the more than 422,000 plant species have been universally documented for medicinal properties; however, only a couple of hundreds are known to be in cultivation (Schippmann et al., 2002). There is a need to grow MAPs to maintain their steady supply and conservation amidst decreasing stocks from natural sources and rising global interest. Apart from increasing farmers’ income, MAPs cultivation also acts as insurance crops against the climate extremes. Its cultivation for essential oils and several phytopharmaceutically important compounds is an age-old aspect of agriculture; conversely, owing to the high demand for natural products, commercial cultivation of MAPs is on the upswing. Furthermore, the vulnerability to various biotic and abiotic perturbations (phytopathogens, drought, water-logging, salinity, temperature, etc.) enforces noteworthy production constraints to diminish both yield and overall quality of the crops. Until the arrival of today’s medicine, a large part of the population in developing nations traditionally depended on the products obtained from plants, particularly from forests, for administering human and livestock ailments. Some efforts have been made towards enhancing yields of plant crude drugs by improving crop varieties, cell cultures, transgenic plants, etc., but these are highly cost-demanding and time-consuming measures. Thus, it is vital to evolve efficient, eco-friendly, cost-effective simpler approaches for improvement in yield and health of the plants.

Plant growth-promoting endophytic microorganisms inhabit and proliferate inside the plants without any distinct symptoms of any diseases in-planta (Bacon et al., 2002), and their mechanism includes both direct and indirect actions such as mineral phosphate solubilization (Verma et al., 2001), fixing nitrogen (Alishahi et al., 2020), synthesis of auxins (Patten and Glick, 2002), production of siderophore (Lodewyckx et al., 2002), and various phytohormones (Costacurta and Vanderleyden, 1995). As many abiotic stresses induce multiple physiological disturbances, which include stomatal closure and stunted plant growth, this ultimately results in lesser crop yield. It has been well reported that ACC (1-aminocyclopropane-1-carboxylic acid) deaminase-containing microbes lower the effect of stress induced by higher ethylene levels of the host plant (Penrose et al., 2001; Sessitsch et al., 2005; Glick, 2005; Sun et al., 2009; Rashid et al., 2012). Therefore, microbial treatments can protect plants from the damaging effects of environmental perturbations (Ali et al., 2014). Changes in climatic conditions such as rainfall, ambient CO₂, and varying temperatures affect

Keywords

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Endophytes: Microbial entities for plant fitness

Endophytes, the Greek word having “endon” (within) and "phyton" (plant), was coined by De Bary (1879) for “any organism occurring within plant tissues”. Bacon and White (2000) have defined endophyte in the broadest and widely accepted manner that states that endophytes include those microbes colonizing living plant internal tissues and not causing any instant, obvious ill effects. Thus, most precisely, endophytes refer to microorganisms (fungi, bacteria, actinomycetes, etc.) that spend at least a part of their life cycle establishing a relationship with a plant that remains asymptomatic (Vanessa and Christopher, 2004). Microorganisms that require living cells to grow and complete their life cycle are known as “obligate” while the others that mainly thrive on the outside of the plant tissues are termed as “epiphytes” and sometimes may enter the plant endosphere, called “opportunist” (Hardoim et al., 2008). In this interaction, both plant and endophytic microbes live together, providing profound benefits to each other (Ting et al., 2009). These endophytes are often rhizospheric in nature, and preferable sites for their attachment and subsequent entry into the host plant could be apical root zone with thin-walled surface root layers and basal root zones with small cracks (Gagné, 1987). They proliferate in the entire host plant (Hallmann et al., 1997a), and reside within the cells, vascular tissues, or intercellular spaces (Patriquin and Dobereiner, 1978; Jacobs et al., 1985; Bell et al., 1995). Endophytic microbes could also enter through the stomata and vertically transmit from parent to offspring via seeds while roots have maximum colonization through epidermis formed by lateral root emergence (Roos and Hattingh, 1983; Agrawal and Shende, 1987). Which community of microbes are friends and which are foes? It is decided by the immune system of the plant itself (Zeilinger et al., 2016). The “balanced antagonism” with asymptomatic colonization between the host plant and endophytic microbes clearly shows that endophytes can live within the plant without activating any host defense mechanism and improves its self-sustenance through the production of the plant-like substances (Schulz et al., 1999; Schulz and Boyle, 2005).

The study of plant–microbe interactions helps us acknowledge natural events that influence our daily lives and could benefit befalling in sustainable resources, a smaller influence on the atmosphere and surroundings, and control of environmental pollution. The benefits of using these interactions for biotechnological applications are huge. The utilization of the pre-existing plant–microbe interactions for the promotion of growth of the plant and biocontrol diminishes the use of unnatural synthetic pesticides and fertilizers, resulting in lowering input costs and, more importantly, reducing the influence of chemical nutrients and pesticides on existing useful flora and fauna (Boddy et al., 2003; Elmer and Reglinski, 2006; Whipp and Gerhardson, 2007). The production of beneficial compounds of industrial and pharmaceutical importance through plant–microbe symbiosis reduces the requirement to supply expensive catalysts and precursors and is energy-saving (Wu et al., 2007; Del Giudice et al., 2008). Remediation by traditional methods is costly and laborious; however, plant–microbe remediation approaches are incredibly efficient and less interfering (Anderson et al., 1993). The carbon sequestration by the plant–rhizosphere methods is probably a sustainable approach for reducing atmospheric carbon (Wu et al., 2009).

As the name implies, endophytic microorganisms live within a plant in the intercellular spaces of various plant parts such as stems, roots, petioles, leaves, etc., without imposing any apparent symptoms of disease or ill health. The symbiotic relationship of the host and its endophytes has been studied in detail and is explained as the plant partner protecting and feeding the endophytes, which, “in return”, produce certain substances with bioactive capabilities (antiviral, plant growth promotion, antibacterial, antifungal, insecticidal, etc.) to augment the growth and competitiveness of the former under natural conditions. These endophytic entities defend their host plants from pathogens by secreting bioactive secondary metabolites under unfavorable environments (Azvedo et al., 2000; Strobel, 2003). The endophytic organisms are now recognized as a vital part of biodiversity, the allocation of endophytic microflora varies with the difference according to its host. Zhang et al. (2006a) suggested that almost all of the vascular plants are known to harbor endophytic entities, especially those with medicinal values that are thought to be related to the formation of therapeutic products. Endophytic microbes are not entirely explored yet, but several investigations present them as an enormous therapeutic compound source. Worldwide, about 300,000 plants grown in an unexplored region are a host of at least one or more endophytic microbes (Araújo et al., 2001). Therefore, functionally diverse endophytes’ occurrence offers a key role in ecosystems at the most plentiful biodiversity (Strobel, 2003). Survival of the endophytic microbes inside the host cell can be for a long duration. The ability of these microbes to produce bioactive secondary metabolites makes them interesting candidates to be studied and exploited in biotechnological aspects (Casella et al., 2013) to add on to the existing wealth of secondary metabolites. Such interest has been reflected in a number of recent reviews showcasing the secondary metabolite-producing abilities of these wonder
microbes (Müller, 2015). The growth and yield of several medicinal plants have been reported to be enhanced by many endophytes (Barnawal et al., 2012; Barnawal et al., 2014), especially by gene expression modulation regulated in important secondary metabolites’ biosynthesis. They have also been reported to impart tolerance to the plants against a range of biotic and abiotic stresses (Pandey et al., 2016a; Pandey et al., 2016b; Lata et al., 2018).

Chemical fertilizers’ indiscriminate use for boosting the productivity of crops is drastically destroying soil and environmental health (Tilman, 1998). Even then, the use of fertilizers is likely to increase further in agriculture to feed the ever-growing huge population (Vitousek et al., 1997; Frink et al., 1999). In the current scenario of global climate change, sustainable agriculture production proves to be a significant challenge. Some approaches such as the integration of microbes associated with plants in agriculture enhance the growth of the plant through different modes and alleviate several biotic and abiotic perturbations (Tanaka et al., 2005; Vega et al., 2008; Lata et al., 2018), and may serve as rescue practices under such situations.

Colonization of the endophytic microorganisms in plants

Plants exhibit a huge and varied niche for microorganisms inside the planta resulting in a closer association between them. Endophytes inhabit the internal plant tissue comprising different bacterial and fungal species that collectively form the “plant endomicrobiome” and can trigger various physiological responses in the plant. Colonization and benefits associated with endophytic microorganisms in plants are presented in Figure 1.

Colonization of the bacterial endophytes

Bacterial endophytes, sometimes considered a part of the population of rhizospheric microbes (Marquez-Santacruz et al., 2010), are present in various tissues such as the stem, root, leaf, tuber, and fruit, of different agricultural, horticultural, and forest species. As the endophytic bacteria are directly in contact with the plant tissues, they have the benefit of greater advantage than rhizospheric bacteria from the plants and offer more benefits to the plant other than bacteria in the rhizospheric region and outside the plants (Araujo et al., 2002). The wide-ranging and recurrent occurrence of such endophytic bacterial populations indicates that healthy plants recruit more endophytic populations (Hardoim et al., 2015) and provide these organisms with a huge and somewhat uncharted ecological niche.

The colonization of host-associated microbes occurs horizontally from the surroundings and might be vertical via parent to the progenies (Santoyo et al., 2016). Endophytic bacteria have several ways to enter inside the host plant tissues. Except for those microbes that are already established

![Figure 1](https://example.com/figure1.png)

**Figure 1** Colonization and benefits of endophytic microorganisms in plants.
inside the seeds of the plant (Truyens et al., 2014), the most frequent point of entry of endophytic bacterial endophytes inside the host plant is via the cracks on the roots and wounded root tissues formed as a result of growth and development of the plant (Sprent and De Faria, 1989; Sørensen and Sessitsch, 2006). This allows leakage of plant metabolites, which attract more bacteria towards it (Hallmann et al., 1997a). Other points of entry of endophytes could be lenticels present in root and shoot periderm (Scott et al., 1996), radicles of germinating seeds, or lateral root hair cells. For example, Hallmann et al. (1997b) showed that Enterobacter asburiae JM22, an endophytic bacterium in cotton plants, produces enzymes capable of hydrolyzing cellulose in the cell wall, assisting the entry of the bacterium inside the host plant.

Autofluorescent proteins (AFP) could be an important method as well as a tool for the visualization of the biofilm to study plant–microbe interaction. These visualization techniques also include gene expression studies using GFP (green fluorescent proteins) in which the GFP gene is integrated into the chromosome of bacteria and a plasmid containing GFP cloned cells which are visualized by confocal or epifluorescence or laser scanning microscopy (Villacieros et al., 2003; Germaine et al., 2004). In the β-glucuronidase (GUS) reporter system, staining helps in the visualization of bacterial movement and gene expression in the rhizosphere and phyllosphere, and entrance and site of pathogens can be studied by IVET (in vivo expression technology) (Preston et al., 2001; Leveau and Lindow, 2001; Zhang et al., 2006a).

Colonization of the fungal endophytes

For the recruitment of the endophytes, the host plant establishes symbiosis with large soil microbial diversity. Initially, attachment of the endophytic fungi might occur on the surface of roots and form structures called appressorium (Yedidia et al., 1999). After that, these attachments penetrate the outer root system and internally colonize the plant tissues (Viterbo and Chet, 2006; Nogueira-Lopez et al., 2018). Endophytic fungi mostly use two types of diffusion patterns; in the primary mechanism, fungi are vertically transmitted into progeny seed from maternal plants by which the offspring gets infected (Gagic et al., 2018). The endophytic fungi transmission among the host plants and the offspring is brought about under appropriate environmental conditions when infected seeds germinate and the endophytic fungi present inside the seed enter the seedlings after the germination of seeds (Hodgson et al., 2014).

Generally, endophytic fungi initiate from the nutrient-rich atmosphere of the rhizosphere, which also has insects and animal feeding processes, and air floating fungal spores (Rodriguez et al., 2009; Sasse et al., 2018). Many of the endophytic fungal microbes are transmitted through spores or hyphal fragments horizontally in aboveground tissues, by insects or herbivores (biotic) or rain or wind (abiotic dispersion agents) from plant to plant, thus establishing communication of fungal endophytes between several plant hosts (Wiewiora et al., 2015).

Microscopic observations of tomato roots on early colonization by the endophytic fungus Trichoderma illustrated no disturbance in cell integrity during this process (Chacón et al., 2007). However, in cucumber roots colonized by endophytes, various phenomena such as enhanced chitinase activity, necrosis of the penetration peg, and fluorescent products’ formation in the intercellular spaces were observed. This phenomenon might be due to copious extracellular enzyme production by endophytic fungi (Suryanarayanan et al., 2012).

How endophytic microorganisms benefit the plants

Not much information exists about the mechanisms of endophyte-mediated plant growth enhancement. Endophytes can mediate plant growth improvement both directly and indirectly (Figure 2). As rhizospheric bacterium initiates its development into endophytes, it is supposed that endophytes can maintain their characteristics inside the host plant.

Direct beneficial mechanisms

Endophytic microbes help host plants directly in many ways to promote the plant’s growth by improving the uptake of essential nutrients, which ultimately increases overall crop yield (Muthukumarasamy et al., 2002). A typical example is nitrogen fixation by particular endophytes in leguminous crops (Stacey et al., 2006). Additionally, several researchers have stated that endophytic bacteria effectively associate with non-leguminous crops to form a synergistic association intended for nitrogen fixation (Bhattacharjee et al., 2008; Saravanan et al., 2008; Mattos et al., 2008; Govindarajan et al., 2008; Oliveira et al., 2009). Plant growth enhancement may occur via many approaches that include plant hormone production, like gibberellins, IAA (indole-3-acetic acid), ethylene, and cytokinin regulation and activity. Many endophytes have shown to exhibit an activity of enzyme ACC (1-aminocyclopropane-1-carboxylate) deaminase to modulate physiology by reducing ethylene content (Hardoim et al., 2008; Barnawal et al., 2012) since ethylene in plant growth inhibitive hormone. In previous studies, Burkholderia phytofirmans, a plant growth-promoting endophytic strain, has been proven to enhance the yields of numerous crops (Lazarovits and Nowak, 1997; Sharma and Nowak, 1998; Sessitsch et al., 2005; Barka...
et al., 2006). Similarly, Mattos et al. (2008) showed that Burkholderia kururiensis, an endophytic bacterium, enhances IAA hormone production. Penicillium citrinum strain generated a large amount of physiologically active gibberellins than Gibberella fujikuroi (wild type), which offers to generate a biologically active source of gibberellic acid (GA3) (Khan et al., 2008). Various studies showed that a variety of fungal endophytes promoted height, biomass, and tiller number in numerous crops (Spiering et al., 2006; Zhang et al., 2007; Lowe et al., 2008). Stagonospora spp., a seed-borne endophytic fungus, increased the yield of Phragmites australis (Cav.) Trin. ex Steud. (Ernst et al., 2003), and endophytic fungus promoted growth in peppermint (Mucciarelli et al., 2003).

Some examples of endophytic microbes’ associated benefits in medicinal and aromatic plants are presented in Table 1.

**Indirect beneficial mechanisms**

Plants muddle through various unfavorable environmental conditions or abiotic stresses like cold, drought, hyper-salty situations, or pathogenesis. Endophytic microbes help the plant conquer such perturbations through some indirect mechanisms, which also promote the buildup of secondary metabolites (including drugs or important medicinal components) in plants.

The endophytic microbes support the host plants to defeat the before-mentioned stresses by some indirect mechanisms. They are also effective in bioremediation by various means, like they decrease heavy metal stress (Zhang et al., 2012), eliminating harmful greenhouse gases (Stepniewska and Kuźniar, 2013), and restricting the development of pests on plants (Azevedo et al., 2000). Endophytic microbes also support phytoremediation by reducing metal phytotoxicity. Simultaneously, for plants containing endophytes with requisite metabolic capabilities and degradation pathways for reducing phytotoxicity and magnifying degradation, the plant–endophyte relationships can be equipped to remediate wastelands and groundwater (Weyens et al., 2009). Rajkumar et al. (2009) reported that endophytic bacteria assist in promoting the extraction of heavy metals. Endophytes are also effective in the degradation of polycyclic aromatic hydrocarbon (PAH). Radwan (2009) documented the phytoremediation of oily soils using rhizobacteria, which appears to be a cheap and environmentally friendly method of cleaning the environment.

**Tolerance to biotic stresses**

Endophytic microorganisms have the ability to enhance plant resistance systems against pathogen infestation through antagonistic activity (Miller et al., 2002; Gunatilaka, 2006). Many studies showed that endophytes have a crucial role in regulating the gene expression of the host, modulating physiological responses and plant defense-related pathways (Van Bael et al., 2012; Estrada et al., 2013; Salam et al., 2017). Khare et al. (2016) illustrated that jasmonic acid and salicylic acid could greatly contribute to plant stress responses against phytopathogens. Ren and Dai (2012) described that inoculation with Gilmaniella sp. AL12 induces jasmonic acid defense responses against pathogenic fungi in Atractylodes lancea (Thunb.) DC. The gibberellins produced by endophytes enhance insect and phytopathogens’ resistance via salicylic and jasmonic acid pathways (Waqa et al., 2015a). An endophyte, Fusarium solani, elicits induced systemic resistance against a fungal pathogen, Septoria lycopersici, by stimulating gene expression.
TABLE 1 Benefits conferred by endophytic microorganisms in medicinal and aromatic plants.

| Endophytic microorganisms | Host plant | Associated benefits | References |
|---------------------------|------------|---------------------|------------|
| **Bacterial endophytes**  |            |                     |            |
| *Pseudomonas putida* BP25 | *Piper nigrum* (L.) | Inhibition of phytopathogens | Sheoran et al., 2015 |
| *Bacillus licheniformis*, *B. subtilis*, *B. circulan*, *B. amyloliquefaciens*, *B. licheniformis*, *Arthrobacter*, *Marinocilsa* sp., *Acinetobacte*, *Microbacterium*, *Kocuria* sp., *Janibacter* | *Papaver somniferum* (L.) | Plant productivity and alkaloid biosynthesis | Pandey et al., 2016a |
| *Gordonea terrae* | *Avicennia marina* (Forssk.) Vierh. | Plant growth promotion | Soldan et al., 2019 |
| *Pantoexsa, Pseudomonas, Enterobacter* | *Eleusine coracana* (L.) | Plant growth promotion | Miganaw et al., 2019 |
| *Burkholderia phytoformans* strain *PsJN* | *Vitis vinifera* (L.) | Plant growth promotion, enhancement of chilling resistance | Barka et al., 2006 |
| *Bacillus subtilis* LE24, *Bacillus amyloliquefaciens* LE109, *Bacillus tequilensis* F080 | *Citrus* (L.) | Biocontrol of pathogens | Daungfu et al., 2019 |
| *Enterobacter* sp. *SA187* | *Helianthus annuus* (L.) | Plant growth promotion and salinity stress tolerance | de Zelicourt et al., 2018 |
| *Burkholderia* sp. | *Helianthus annuus* (L.) | Calcium and phosphate solubilization | Ambrosini et al., 2012 |
| **Fungal endophytes** |            |                     |            |
| *Mucor* sp. | *Arabidopsis arenosa* (L.) Lawalrée | Metal toxicity tolerance | Domka et al., 2019 |
| *Colletotrichum tropicalis* | *Theobroma cacao* (L.) | Tolerance to Phytophthora | Mejia et al., 2008 |
| *Aspergillus fumigatus* TS1, *Fusarium proliferatum* BRL1 | *Osalia corniculata* (L.) | Plant growth promotion | Bilal et al., 2018 |
| *Yarrowia lipolytica* | *Euphorbia milii* Des Moul. | Plant growth promotion and salinity stress tolerance | Jan et al., 2019 |
| *Penicillium citrinum* LW4, *Aspergillus terreus* LW5 | *Helenium annuus* (L.) | Plant growth promotion, disease resistance | Waqas et al., 2015b |
| *Paecilomyces variotii*, *Penicillium purpurogenum* | *Carralluma acutangula* (Decne.) N.E.Br. | Plant growth promotion | Ali et al., 2019 |
| *Scelotrium* sp. | *Atractyls lancea* (Thunb.) DC. | Increases cell protection from desiccationin and leaf metabolic capability of host | Chen et al., 2008 |
| *Epulorhiza* sp. | *Amoecothecillus formosanus* Hayata | Enhances enzyme activities | Tang et al., 2008 |
| *Epulorhiza* sp., *Mycena anochotichula* | *Amoecothecillus raxburgii* (Wall.) Lindl. | Enhances enzyme activities | Yu and Guo, 2000; Chen et al., 2005 |
| *Pericormospora indica* | *Cymbidium aloifolium* (L.) Sw. | Plant growth promotion and abiotic stress tolerance | Shah et al., 2019a |
| *Mycena orchidicola* | *Cymbidium sinense* Wild. | Secretes phytohormones | Zhang et al., 1999 |
| *Fusarium* sp. | *Dendrobium moniliforme* (L.) Sw. | Plant growth promotion | Shah et al., 2019b |
| *Mycena dendrobii* | *Dendrobium candidum* Wall. ex Lindl. | Secretes phytohormones | Zhang et al., 1999 |
| *Epulorhiza sp., Mycena sp., Sebacinales, Cantharellales* | *Dendrobium nobile* Lindl., D. *chrysanthum* Wall. | Enhances the nutrient absorption in plants, promoting the seed germination of host | Chen and Guo, 2005 |
| *Aspergillus awamori* W11 | *Withania somnifera* (L.) | Plant growth promotion | Mehmoood et al., 2019 |
| *Aspergillus terreus*, *Penicillium laxicum*, *Sarocladium kilienes* | *Biosynthesis of withanolide* | | Kushwaha et al., 2019a |
| *Aspergillus terreus*, *Penicillium laxicum*, *Sarocladium kilienes* | *Plant growth promotion, enhances withanolide content* | | Kushwaha et al., 2019b |

(Continued)
linked to the pathogenesis (Kavroulakis et al., 2007). Foliar endophytic fungi, *Colletotrichum tropicale*, inoculated in *Theobroma cacao* (L.) enhance tolerance to *Phytophthora* (Mejia et al., 2008). The endophytic bacteria produce several antimicrobial compounds that can increase the resistance of the plants to various phytopathogenic fungi, bacteria, nematodes, etc. Endophytic *Pseudomonas putida* BP25 associated with black pepper inhibits a range of phytopathogens, viz., *Rhizoctonia solani*, *Phytophthora capsici*, *Gibberella moniliformis*, *Pythium myriatylum*, *Radopholus similis*, and *Colletotrichum gloeosporioides* by the production of several compounds (Sheoran et al., 2015). *Macrophomina phaseolina* causes charcoal rot disease in different crops and has been reported to be restricted by siderophore-producing *Rhizobium* (Arora et al., 2001). An endophyte, *Pseudomonas fluorescens*, having antagonistic effects against *Verticillium* was isolated by Mercado-Blanco et al. (2004) from olive plant roots. Yong et al. (1994) established the role of endophyte *Fusarium* spp. in the enhancement of growth and terpenoid content in *Euphorbia pekinensis* Rupr.

The endophytic fungus *Phomopsis cassia* associated with *Cassia spectabilis* enhances tolerance against phytopathogenic fungi *Cadosporium sphaeroaspernum* and *C. cladosporoides* by producing cadinane sesquiterpenoids, which are toxic to pathogens (Silva et al., 2006). Similarly, Wang et al. (2012) reported that an endophyte, *Chaetomium globosum* L18, inhibits pathogenic fungi by synthesizing some toxic chemicals in *Curcuma wenyujin* Y. H. Chen & C. Ling. In another study, Cao et al. (2009) identified endophytic microbes *Choironymes aboriginum*, *Stachybotrys elegans*, and *Cylindrocarpon* associated produces cell wall-degrading enzymes to kill pathogenic fungi in *Phragmites australis* (Cav.) Trin. ex Steud. Furthermore, an endophytic fungus, *Trichothecium roseum*, has a toxic chemical, “trichothechin”, which enhances tolerance to pathogenic fungi in *Maytenus hookeri* Loes. (Zhang et al., 2010). Similarly, *Bacillus subtilis* and *Myxormia* sp. also enhance tolerance against pathogenic fungi *Fusarium oxysporum* and *F. solani* in *Angelica sinensis* (Oliv.) Diels (Yang et al., 2012).

Endophytic microbes *Chaetomium cochliodes*, *Cladosporium cladosporioides*, and *Trichoderma viride* enhance insect resistance in creeping thistle *via* producing some chemicals toxic to pathogens (Gange et al., 2012). Similarly, Sumarah et al. (2010) reported that fungal endophytes enhance resistance against *Choristoneura fumiferana* insect in red spruce (*Picea rubens* Sarg.). An endophyte, *Leucocoprinus gongylophorus*, increases insect resistance by synthesizing some chemicals antagonistic to ants’ fungal symbiont (Bittleston et al., 2011). Furthermore, the endophyte *Chaetomium Ch1001* associated with cucumber enhances tolerance against root-knot nematode by producing abscisic acid affecting the motility of the second-stage juveniles of insects (Yan et al., 2011). According to the study undertaken by Gómez-Vidal et al. (2009), endophytes *Beauveria bassiana*, *Lecanicillium dimorphum*, and *L. cf. Psalliota* increase insect resistance to *Phoenix dactylifera* by modulating the expression of cell division-related proteins in the host plant. Strobel et al. (1999) reported that in thunder god vine (*Tripterygium wilfordii* Hook. f.), an endophyte, *Cryptosporiopsis cf. quericina*, produces “cryptocin” and “cryptocandin” toxic to pathogenic fungi

**TABLE 1 Continued**

| Endophytic microorganisms | Host plant | Associated benefits | References |
|---------------------------|------------|---------------------|------------|
| Mycena dendrobii, *M. omnundicola*, *Mycena orchidicola*, *M. anevochili* | Gastrodia elata Blume | Secretes phytohormones, promoting seed germination | Guo and Wang, 2001 |
| Epulorhiza sp., *Fusarium sp.* | Pectobacterium susmae (L.) Raf. | Enhances NPK absorption plants promoting the seed germination of host | Chutima et al., 2011 |
| Penicillium sp., *Aspergillus sp.* | Monachoria vaginalis (Burm.f.) C.Presl ex Kunth | Secretes gibberellins | Ahmad et al., 2010 |
| Dark septate endophytic fungi (DSEF) | Pedicularis (L.) | Increases their nutrient utilization efficiency | Li and Guan, 2007 |
| Ceratobasidium sp. | Rehmannia glutinosa Steud. | Secretes IAA | Chen et al., 2011a |
| Sebacina vermifera | Nicotiana attenuata Steud. | Enhances absorption of nutrient and promote the growth and fitness by inhibiting ethylene signaling | Baranzani et al., 2007 |
| Funneliformis mosseae, *Rhizopus intraradices*, *Cladozymogamus etunicatum* | Sesbania sesban (L.) Merr. | Secretes phytohormones | Abd Allah et al., 2015 |
| Chaetomium globosum, *Aspergillus proliferans*, *Periplococillium blacicum* | Papaver somniferum (L.) | Enhances plant productivity and benzylisoquinoline alkaloid (BIA) biosynthesis | Pandey et al., 2016a |
| Curvularia sp., *Choanephorha infundibulifera* | Catharanthus roseus (L.) | Terpenoid indole alkaloid biosynthesis | Pandey et al., 2016b |

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Pyricularia oryzae in host plant. Daungfu et al. (2019) recently identified several endophytes, Bacillus subtilis LE24, Bacillus amyloliquefaciens LE109, and Bacillus tequilensis PO80, isolated from citrus plant having antagonistic effects against pathogens, which might be helpful in the biocontrol of pathogens. All these findings strongly confirm that the presence of endophytes in the host has the potential to increase their tolerance to pathogens through several mechanisms. Conversely, in resistance stimulation to disease facilitation, the process wherein endophytes invade plant tissues affects endophyte–pathogen interactions, perhaps producing facilitation (positive induction of pathogens), negatively strengthening host resistance, or having no effect at all (Suryanarayanan et al., 2009; Schmidt et al., 2014; Adams et al., 2015). These require further research for confirmation.

Tolerance to abiotic stresses

Abiotic stressful conditions, viz., drought, water-logging, salinity, cold, heat, and heavy metal toxicity, may cause adverse effects on soil and environmental health (Wang et al., 2003; Khare and Arora, 2015). Endophytes have a vital function in increasing tolerance against abiotic perturbations in plants (Wani et al., 2016). Waqas et al. (2012) reported that stomatal closure mediated by abscisic acid (ABA) might have a key function in the regulation of plant growth by reducing other abiotic stresses, including osmotic stress.

Under drought stress, an endophytic bacterium, Sinorhizobium meliloti, upregulated FeSOD and Cu/ZnSOD, promoting drought tolerance in Medicago sativa (L.) (Naya et al., 2007). Similarly, Arbuseular mycorrhiza improves nutrient absorption and modifies Salvia’s metabolic activities to boost drought tolerance (Meng and He, 2011). An endophytic microbe, Trichoderma hamatum DIS 219b, delayed drought-induced alterations in stomatal conductance and net photosynthesis, promoting drought tolerance in Theobroma cacao (L.) (Bae et al., 2009). According to Sziderics et al. (2007), a fungal endophyte, Piriformospora indica, enhances osmotic stress tolerance via encoding enzyme ACC oxidase and lipid transfer protein. Wang et al. (2009) reported that Arbuseular mycorrhiza and Penicilium griseofulvum reduce injury of water stress by increasing the activity of protective enzymes and osmota contents, thereby enhancing tolerance against salt and drought stress in Glycyrrhiza uralensis. Liu et al. (2011) reported that soluble protein concentration and peroxidase activity (POD) are altered by Chaetomium globosum and Botrytis sp. Under salt stress in Chrysanthemum morifolium (Ramat.) Hemsl. A fungal endophyte, Yarrowia lipolytica, promotes salinity stress tolerance in Euphorbia milii Des Moul. (Jan et al., 2019).

Moreover, ABA-mediated signaling pathways and their biosynthesis during salinity stress are altered by several microbes in the plant endosphere and may help plant growth. B. phytofirmans (PsJN) altered gene expression for a cell surface signaling element, which passes signals to bacteria about the alteration in environmental conditions and consequently improves their metabolism (Sheibani-Tekerji et al., 2015). Fernandez et al. (2012) reported in PsJN bacterized grapevine that stress-induced gene expression in addition to metabolite levels improved over control at a lower temperature by balancing carbohydrate metabolism. Recently, de Zélicourt et al. (2018) reported that Enterobacter sp. (SA187), an endophyte, colonizes Arabidopsis root and shoot tissues and stimulates tolerance against salt stress by synthesizing KMBA (2-keto-4-methylthiobutyric acid). Marquez et al. (2007) reported that at high soil temperatures, Curvularia proteobate, an endophytic fungus, has been linked to Dichanthelium lanuginosum for its survival. Wan et al. (2012) reported that endophytes can also reduce the heavy metal-promoted oxidative injury. Earlier studies suggested endophytic bacteria’s function in enhancing tolerance to metal toxicity through diverse mechanisms such as sequestration, intracellular accumulation, and extracellular precipitation or alteration of toxic metal ions to a minimum or non-toxic form (Ma et al., 2016; Mishra et al., 2017). Luo et al. (2012) discovered that a bacterial endophyte, Bacillus sp. SLS18, reduces heavy metal toxicity via root tillers and biomass accumulation in Solanum nigrum (L.) and Phytolacca acinosa Roxb. Recently, Domka et al. (2019) identified an endophytic fungus, Mucor sp., which enhances metal toxicity tolerance in Arabidopsis arina (L.) Lawalère. Some examples of endophytes enhancing the tolerance of crop plants against abiotic and biotic stresses are presented in Table 2.

Endophytic microorganisms producing secondary metabolites/bioactive compounds in the host plant

The diversity of bioactive compounds varies according to the habitats of the host plants; for example, in a tropical rain forest, limited resource availability leads to great competition among plants and their endophytes; thus, selection pressure is at the peak, resulting in the production of many novel molecules as compared to temperate forests (Reddell and Gordon, 2000). Isolation of indigenous microbes from different plant parts and their interaction with the host plant may divulge applicant microbes to promote plant growth and as biocontrol agents. Such microbial inoculants have the potential to provide resistance against environmental perturbations without affecting the indigenous microbial equilibrium (Palaniyandi et al., 2013).
Many endophytic microbes can synthesize a notable variety of secondary metabolites like antioxidant, anticancer, immunosuppressive, antidiabetic, antioomycete, antifungal, antibacterial, antiviral, and nematicidal agents (Gunatilaka, 2006; Zhang et al., 2006b; Verma et al., 2009; Aly et al., 2011). Shimizu (2011) reported that endophytic actinobacteria synthesize antibiotics, which is useful in plant growth promotion and improves the tolerance of plants to stress. Endophytes also have been in the limelight during the last decade or so because of their capability in producing several secondary metabolites that are bioactive (Tan and Zou, 2001; Schulz et al., 2002; Strobel, 2003; Prado et al., 2013). These compounds extracted from endophytes belong to the various chemical groups like xanthones, terpenoids, phenols, steroids, benzopyranones, isooumarins, chinones, cytochalasins, tetralones, and enniatines (Schulz et al., 2002). Sometimes, these endophytic microbes may cause variation in well-known structural compounds like fungal steroids, ergosterol, or plant

| Endophytic microorganisms         | Host plant                  | Type of stresses       | Mechanism                                                                 | References                      |
|----------------------------------|-----------------------------|------------------------|---------------------------------------------------------------------------|--------------------------------|
| Bacillus subtilis, Myxormia sp.  | Angelica sinensis (Oliv.)   | Pathogenic fungi: Fusarium oxysporum and F. solani | Produce some chemicals toxic to pathogens                                | Yang et al., 2012               |
| Gilmansia sp. AL12.              | Atractylodes lancea (Thunb.) DC. | Pathogenic fungi      | Produce jasmonic acid inducing defense responses                           | Ren and Dai, 2012               |
| P. indica                        | Capparis annum (L.)          | Osmotic stress         | Encodes enzyme ACC oxidase, encodes a lipid transfer protein             | Sziderics et al., 2007          |
| Phomopsis cassis                 | Cassia spectabilis DC.       | Pathogenic fungi: Cadosporium sphaerospermum, C. cladosporioides       | Produce cadinane sesquiterpenoids toxic to pathogens                      | Silva et al., 2006              |
| Chaetomium globosum, Botrytis sp.| Chrysanthemum morifolium (Ramat.) Hetol. | Salt stress           | Increase POD activity and soluble protein content                          | Liu et al., 2011                |
| Chaetomium cochliodes, Cladosporium cladosporioides, Trichoderma versl. | Cirsium arvense (L.) Scop. | Insect                  | Produce some chemicals toxic to pathogens                                  | Gange et al., 2012               |
| Leucopepinsus gongophorius       | Cordia alliodora Cham.       | Insect                  | Produce some chemicals antagonistic to ants’ fungal symbiont              | Bettleston et al., 2011          |
| Chaetomium Ch1001                | Cucumis sativis (L.)         | Insect: root-knot nematode Meloidogyne incognita                     | Produced abscisic acid affecting motility of the second stage juveniles of insects | Yan et al., 2011                |
| Chaetomium globosum L18          | Curcuma wenyujin Y.H.        | Pathogenic fungi       | Produce some chemicals toxic to pathogens                                  | Wang et al., 2012               |
| Arbuesedur myccorrhiza, Penicillium griseofulvum | Glycyrrhiza uralensis (L.) Fisch. ex DC. | Drought and salt stress | Reduce injury of water stress by increasing protective enzymes’ activity and osmotica contents | Wang et al., 2009               |
| Trichothecium roseum             | Maytenus hookeri Loes.       | Pathogenic fungi       | Produce trichothecin toxic to pathogens                                     | Zhang et al., 2010              |
| Sinanthizium melilati            | Medicago sativa (L.)         | Drought stress         | FeSOD and CU/ZnSOD are upregulated                                         | Naya et al., 2007               |
| Pseudomonas koreensis            | Miscanthus sinensis Andersson | Heavy metal toxicity (Zn, Cd, As, and Pb)                           | Through extracellular sequestration, increased catalase and SOD activities in plants | Babu et al., 2015               |
| Beauveria bassiana, Lecanicillium dimorphum, L. cf. Psalliotae | Phoenix dactylifera (L.) Scop. | Insect                  | Modulate the expression of cell division-related proteins in host         | Gómez-Vidal et al., 2009         |
| Chaetomycyes aberginiun, Stachybryts elegans, Cylindocrine | Phragmites australis (Cav.) Steud. | Pathogenic fungi       | Produce cell wall-degrading enzymes to kill pathogenic fungi               | Cao et al., 2009                |
| 150 foliar fungal endophytes     | Picea rubens Sarg.           | Insects: Choristoneura fumiferana                                  | Produce some chemicals toxic to insects                                    | Sumarah et al., 2010            |
| Arbuesedur myccorrhiza            | Sabia nitarrisirrhiza Bunge   | Drought stress         | Increase the absorption of nutrient and alter metabolic activities in root | Meng and He, 2011               |
| Bacillus sp. SLS18                | Salomon nigrum (L.), Phyloccasia acinosa Roxb. | Heavy metal toxicity (Mn and Cd) | Accumulation of root tillers and biomass                                    | Luo et al., 2012                |
| Trichoderma hamatum DIS 219b     | Theobroma cacao (L.)         | Drought stress         | Delayed drought-induced changes in stomatal conductance and net photosynthesis | Bae et al., 2009               |
| Crypsoспорiose cf. quercina       | Tripterygium wilfordii Hook.f. | Pathogenic fungi: Pyricularia oryzae                               | Produce cryptocin and cryptocandin toxic to pathogens                      | Strobel et al., 1999            |
hormone indole-3-acetic acid (Lu et al., 2000). Several endophytes can also be attributed to providing protection of plants against pests because of the compounds occurring in them (Poling et al., 2008).

There are many reports that have shown that host secondary metabolism can be induced by endophytes, but such interaction has not been much explored. Qawasmeh et al. (2012) reported that when endophytes (from the Clavicipitaceae family) interact with grasses, there is a production of phenolic compounds, which are mainly defense-related. However, secondary metabolites could remain unchanged or get reduced depending on which type of endophyte interacts with the host plant. A well-known example of a high-demanding anticancerous molecule is “taxol” isolated from Taxomyces andreanae, a taxol-producing fungal endophyte of Taxus species (Stierle et al., 1995). An example showed that bacterial endophytes have methanol dehydrogenase genes, which were known to express furanone biosynthesis and localized especially in vascular tissues of strawberry receptacles and plant achenes cells (Nasopoulos et al., 2014). Likewise, Koskimaki et al. (2009) have reported that fungal endophyte Paraphaeosphaeria sp. increased the accumulation and biosynthesis of flavan-3-ols phenolic acids and oligomeric proanthocyanidins in Vaccinium myrtillus. In Artemisia annua (L.), an endophytic bacterium, Pseudomonas sp., has been reported to increase artemisinin synthesis by upregulating the cytochrome P450 monoxygenase (CYP71AV1) and cytochrome P450 oxidoreductase (CPR) genes, and this also activated a defense mechanism (Wang et al., 2006). It has also been found that endophytes may act as upregulators of the specific gene expression for tissue-specific roles, e.g., foliar endophytes enhanced primary metabolites, crop yields could be increased by root endophytes, and endophytes isolated from the capsule could upregulate key genes of benzylisoquinoline alkaloid (BIA) biosynthesis in Papaver somniferum (L.) (Pandey et al., 2016a). Tiwari et al. (2010) found an improved content and yield of essential oils in holy basil. In the Chinese medicinal plant Atractylodes lancea (Thunb.) DC., the endophytic bacterium P. fluorescens could enhance the generation of ROS (reactive oxygen species), which resulted in an increase of sesquiterpenoids (Zhou et al., 2015). Endophytic bacteria Aranicola proteolytica, Bacillus cereus, B. thuringiensis, B. licheniformi, and Serratia liquefaciens recovered from Pinellia ternata (Thunb.) Makino could produce inosine and guanosine alkaloids similar to their host plant in fermentation media (Liu et al., 2015). Tiwari et al. (2013) found that endophyte Micrococcus sp. and Staphylococcus sciuri inoculated plant had significantly higher amounts of ajmalicine, serpentine, and vindoline in Catharanthus roseus (L.) G. Don. Kumar et al. (2014) reported that the endophytic bacterium Azotobacter chroococcum could enhance the yield of curcumin in rhizomes of turmeric.

Endophytic microflora encompasses a high potential for the synthesis of an ample range of unidentified, undepicted novel secondary metabolites within or without host plants. It is needed to identify which type of mechanism or cryptic genes and what circumstances for the evolution of the genome are involved in the synthesis of novel compounds in endophytes as well as in planta. Some examples of endophytes producing secondary metabolites in host plants are presented in Table 3.

Phytoremediation

Phytoremediation is the most efficient and eco-friendly system for restoring natural soil conditions when various environmental pollutants have contaminated it. In the past two decades, endophytes’ usage in the phytoremediation of diverse environmental pollutants has received more attention (Sheng et al., 2008; McGuinness and Dowling, 2009; Weyens et al., 2009; Weyens et al., 2010; Hur et al., 2011; Segura and Ramos, 2013; Wei et al., 2014; Anyasi and Atagana, 2018). Such research has shown the potential of plant–microbe interaction in the restoration of polluted regions and may be helpful in designing efficient environmental pollutant removal systems. One of the reasons could be attributed to the complicated relationship between endophytes and their hosts. In contrast, the other reason has to do with the fact that it is practically impossible to comprehend the mechanisms of existence and situations of endophytes to be able to replicate them. It is impractical to exaggerate the role of endophytes in both management and harnessing the natural environment. Unfortunately, the holistic view of these taxa has been constrained by them. Such constraints include the fact that the process of isolation of endophyte relies on culture dependence, while several microorganisms exist that cannot be cultured. This emphasizes nonculture-dependent innovation as the barrier to understanding endophytes.

Agronomic practical application of endophytic microorganisms

The most frequently used inoculation technique in agriculture includes the use of endophytes; culture, facilitated by a carrier, is combined with the synthetically manufactured sticky seeds and sown. Moreover, several commercial formulations include liquid cultures directly applied or with the granular fertilizer or seed applications. Other techniques have also been used, including seed priming, seed coating, foliar spraying, root dipping, pelleting, and direct soil application (O’Callaghan, 2016). Given the presence of endophytic microbes, seed inoculation can accomplish this goal. Still, its effectiveness is constrained by the lengthy engaging period, subsequent physical abrasion, and competition with other soil microbes. Root dipping or seedling treatments with microbial
### TABLE 3  Endophytic microorganisms producing plant secondary metabolites in host plants.

| Endophytic microorganisms | Host plant | Plant secondary metabolite | Bioactivity of secondary metabolite | References |
|---------------------------|------------|----------------------------|-------------------------------------|------------|
| **Bacterial endophytes**  |            |                            |                                     |            |
| Jishengella endophytica   | Xylocarpus granatum J. Koenig | Per洛lyrine                 | Antiviral effect                    | Wang et al., 2014 |
| Streptomyces sp. TP-A0569 | Allium fistulosum (L.)       | Fistupryne                  | Protection against pathogenic fungi | Bernardi et al., 2019 |
| Streptomyces sp. TP-A0556 | Aucuba japonica Thunb.       | Coumarins TPU-0031-A and B  | Antibiotic activity against Gram-positive and Gram-negative bacteria | Bernardi et al., 2019 |
| Streptomyces hygroscopicus TP-A0451 | Pteridium aquilinum (L.) Kuhn | Pteridic acids A and B, Pterocidin | Plant growth-promoting properties | Bernardi et al., 2019 |
| Taxomyces andreanae       | Taxus brevifolia Nutt.       | Taxol                       | Anticancer                          | Strobel et al., 1993 |
| Streptomyces griseus      | Kandelia candel (L.) Druce   | p-Aminoacetophenonic acids  | Antimicrobial                        | Guan et al., 2005 |
| Streptomyces NRRL 30562   | Kennedia nigricans Lindl.    | Munumbicins Munumbicin D    | Antibiotic Antimarial                | Castillo et al., 2002 |
| Serratia marcescens       | Rhyzohalaxis penicillata    | Oocystin A                  | Antifungal                          | Strobel et al., 2004 |
| Pseudomonas fluorescens   | Atractylodes lancea (Thunb.) DC. | Increases enzymic sesquiterpenoid content | Triggers generation of ROS | Zhou et al., 2015 |
| Azotobacter chroococcum   | Curculia longa (L.)         | Curcumin                    | Anti-inflammatory, anti-tumor, and antioxidant | Kumar et al., 2014 |
| Stenotrophomonas maltophilia | Papaver somniferum (L.)     | Enhance alkaloid and morphine contents | Narcotic analgesics | Limón et al., 2015 |
| Pseudomocardia sp.        | Artemisia annua (L.)         | Artemisinin                 | Antimalarial                         | Sato and Kumagai, 2013 |
| **Fungal endophytes**     |            |                            |                                     |            |
| Acremonium sp., Shiraia sp. | Huperzia serrata (Thunb.) Trevis | Huperzine A                   | Anticholinesterase                    | Li et al., 2007 |
| Alternaria sp.            | Phellodendron amurense Rupr. | Berberine                   | Antibiotic                           | Duan et al., 2009 |
| Alternaria sp.            | Sabina vulgaris Antoine     | Podophyllotoxin              | Antitumor                            | Lu et al., 2006 |
| Aspergillus fumigatus     | Podocarpus sp. Pers.         | Paclitaxel                   | Antitumor                            | Sun et al., 2008 |
| Aspergillus nidulans, A. oryzae | Ginkgo biloba (L.)         | Quercetin                    | Anti-inflammatory                     | Qiu et al., 2010 |
| Blastomyces sp., Botrytis sp. | Phlegmariurus cryptomerianus | Huperzine A                  | Anticholinesterase                    | Ju et al., 2009 |
| Botryodiadema theobroma, Fusarium lateritium, Monochaetia sp., Pestalotia bicilia | Taxus baccata (L.) | Paclitaxel                    | Antitumor                            | Venkatachalam et al., 2008 |
| Cephalosporium corda      | Fritillaria uasuriensis (Maxim.) | Sipeimine                   | Antibechic and anti-ulcer            | Yin and Chen, 2008 |
| Cephalosporium sp., Paecilomyces sp. | Paris polyphylla var. yunnanensis (Franch.) Hand.-Mazz. | Diosgenin                  | Antitumor, anti-inflammatory, cardiovascular protection | Cao et al., 2007 |
| Chaetomium globosum       | Hypericum perforatum (L.)    | Hypericin                    | Anti-depressant                       | Kusari et al., 2008 |
| Cladosporium cladosporio  | Taxus media Rehder           | Paclitaxel                   | Antitumor                            | Zhang et al., 2009 |
| Cochliobolus niakadei     | Cinnamomum camphora chvar. Borneol | Borneol                    | Anti-inflammatory, antioxidant        | Chen et al., 2011b |
| Colletotrichum gloeosporioides | Piper nigrum (L.) | Piperine                  | Antimicrobial, antidepressant, anti-inflammatory, and anticancer | Chitra et al., 2014 |
| Entrophosporia infrequens, Neurospora sp. | Nothapodytes foetida (Wight) Steunier | Camptothecin               | Antitumor                            | Amna et al., 2006; Rehman et al., 2008 |
| Fusarium oxysporum        | Juniperus recurva Buch.-Ham. ex D.Don | Podophyllotoxin            | Antitumor                            | Kour et al., 2008 |

(Continued)
suspension are also susceptible to contamination and handling issues. The application of endophytes in bulk populations is made possible by pelleting or direct soil application. However, there is still an issue with the lack of homogeneity in the field and exposure to environmental perturbations. Despite using every conventional method, the microbes still need to endure for a few weeks before they may enter the plant after root hair emergence. Even while some endophytes’ facultative character suggests the prospect of further colonization if they can endure in the rhizosphere, the ecological constraint exists. Seed priming with a predetermined duration can help the microbe’s entrance during imbibitions. However, several scientific and technical difficulties are still associated with applying endophytes to seeds via coatings, sprays, granules, and capsules. Moreover, a seemingly simple procedure like plate counting also seems to have some technical problems, e.g., the “viable but not culturable” bacteria may not be detected by plate counting. The formulation should facilitate the microorganism’s penetration and colonization of the host while minimizing dosage and cost. It should also increase microbe establishment in the soil and close to or on the plant. The application of endophytes requires a thorough knowledge of the physicochemical and biological environment, including the phyllosphere, soil, seed surface, and rhizosphere, as well

| Endophytic microorganisms | Host plant | Plant secondary metabolite | Bioactivity of secondary metabolite | References |
|---------------------------|------------|---------------------------|-----------------------------------|------------|
| Fusarium oxysporum        | Ginkgo biloba (L.) | Ginkgolate B | Antishock, anti-inflammatory, and antiallergic | Cui et al., 2012 |
| Fusarium redolens         | Fritillaria whebuenensis S.Y. Teng & S.C. Yueh | Peiminsine and imperialine-3β-D-glucoside | Get rid of sputum, cough, and antitumor | Pan et al., 2015 |
| Fusarium solani           | Apodytes dimiduata E.Mey. ex Arn. | Camptothecin | Antitumor | Shweta et al., 2010 |
| Fusarium solani           | Camptotheca acuminata Deane | Camptothecin | Antitumor | Kusari et al., 2009 |
| Fusarium solani           | Taxus celebica (Warr.) H.L. Li | Paclitaxel | Antitumor | Chakravarti et al., 2008 |
| Fusarium solani, Metarhizium anisopliae, Mucor rouxianus | Taxus chinensis Roxb. | Paclitaxel | Antitumor | Deng et al., 2009; Liu et al., 2009 |
| Monilia sp., Penicillium implication | Dussova veitchii (Hemsl. & E.H.Wilson) L.K.Fu ex T.S.Ying | Podophyllotoxin | Antitumor | Yang et al., 2003 |
| Osorium sp., Alternaria alternata, Botrytis sp., Ectenospora sp., Fusarium mairei, Papulaspora sp., Tubercularia sp. | Taxus chinensis var. mairei (Lemee & Levli) W.C. Cheng & L.K. Fu | Paclitaxel | Antitumor | Zhou et al., 2007; Guo et al., 2009; Wu et al., 2013 |
| Penicillium chrysogenum   | Lycopodium serratum Thunb. | Huperzine A | Anticholinesterase | Zhou et al., 2009 |
| Penicillium implicatum    | Diphyllela sinensis H.L.Li | Podophyllotoxin | Antitumor | Zeng et al., 2004 |
| Penicillium sp., Phialocephala fortinii, Trametes hirsuta, Alternaria neesex | Sinopodophyllum hexandrum (Royle) Ying | Podophyllotoxin | Antitumor | Li, 2007 |
| Pestalotopsis microspora, Sporormia minima, Trichotheccium sp. | Taxis wallachiana Zucc. | Paclitaxel | Antitumor | Shrestha et al., 2001 |
| Pestalotopsis pauciseta   | Cardiospermum helicacabum (L.) | Paclitaxel | Antitumor | Gangadevi et al., 2008 |
| Pestalotopsis terminaliae | Terminalia arjuna (Roxb. ex DC.) Wight & Arn. | Paclitaxel | Antitumor | Gangadevi and Muthumary, 2009 |
| Phomopsis sp., Dlaporthe sp., Schizothyphum sp., Penicillium sp., Fomitopsis sp., Arthrinium sp. | Cinchona ledgeriana Bern. Moens | Cinchona alkaloids: quinine, quinidine, cinchonidine, cinchonine | Antipyretic and antimalarial, analgesic and anti-inflammatory | Maehara et al., 2012 |
| Phylosticta citricarpa     | Citrus medica (L.) Cupressus (L.) | Paclitaxel | Antitumor | Kumaran et al., 2008 |
| Phylosticta spinarum      | Hibiscus ros-sinensis (L.) | Paclitaxel | Antitumor | Kumaran et al., 2009 |
| Phylosticta dioscoreae    | Eucommia ulmoides Oliv. | Chlorogenic acid | Antimicrobial and antitumor | Chen et al., 2010 |
| Sordariomycete sp.        | Salvia miltiorrhiza Bunge | Tanshinone IIa and tanshinone I | Antibacterial and anti-inflammatory | Ming et al., 2011 |
as the cultivation and formulation of the biologicals to prolong shelf life. In the context of mycorrhiza, progress has been made in understanding the molecular plant–microbe interaction that needs to be integrated into novel formulation and application strategies. In other circumstances, such endophytic entomopathogenic fungi do not clearly understand how they invade and colonize. Basic research studies only use straightforward water-spore mixtures instead of more advanced and practical application methods.

Furthermore, designing formulations having high microbial inoculant concentration and survivability during storage is crucial for developing potent inoculants. Since it is impossible to test out every potential combination of parameters throughout the formulation process, it is challenging to determine the most critical variables. Nevertheless, it is challenging to maintain sterility throughout the formulation process for an extended period, which could lead to contamination. Even though we can find entomopathogenic fungi in nature in this form, their poor recovery rate from plants reveals that these organisms do not occur naturally.

### Conclusion

Plant–microbe interactions benefit the all-embracing vicinity of agricultural applications. Microorganisms are abundantly present in nature and primarily colonized *in planta*. Plant–endophyte interaction is mostly considered beneficial, having profound effects on the physiology of the host plant and the overall performance by promoting growth, development, and imparting fitness to the host plants against different biotic and abiotic stresses. They play a vital function in agricultural sustainability by providing eco-friendly inputs to enhance crop productivity and quality while minimizing harmful chemical fertilizers. The study of these plant–microbe interactions helps us acknowledge natural events that influence our daily lives and could benefit befalling in sustainable resources, a smaller influence on the atmosphere and surroundings, and control of environmental pollution. The benefits of using these interactions for biotechnological applications are huge. The utilization of the pre-existing plant–microbe interactions for the promotion of growth of the plant and biocontrol diminishes the use of unnatural synthetic pesticides and fertilizers, resulting in lowering input costs and, more importantly, reducing the influence of chemical nutrients and pesticides on existing useful flora and fauna. Moreover, the production of beneficial compounds of industrial and pharmaceutical importance through plant–microbe symbiosis reduces the requirement to supply expensive catalysts and precursors and is energy-saving. In recent years, MAPs are being paid considerable attention worldwide due to their vast economic potential, primarily in the field of herbal medicine. Until the arrival of advanced medicines, an oversized population in emerging nations has traditionally relied upon the products obtained from plants. Furthermore, about 12.5% of the more than 422,000 plant species have been universally documented for medicinal properties; however, only a couple of hundreds are known to be in cultivation. There is a need to grow MAPs to maintain their steady supply and conservation amidst decreasing stocks from natural sources and rising global interest.

### Limitations and further investigations

Endophytic microorganisms are tissue specific in nature; their establishment and functionality within the host are affected by several factors such as tissue type, host's genotype, and surrounding conditions. The lack of knowledge about the widespread presence of endophytic microorganisms’ communities in plant tissues has been a hindrance in advancing research on endophytes in various fields. It should be noted that the development of successful endophyte application technologies would fully depend on improving our understanding of how they enter and colonize *in planta*. Consequently, to guarantee reproducibility, reliable methods of endophytic inoculum delivery should be developed for better productivity of MAPs. Leveraging the relationship between plants and endophytes can be crucial for advancing sustainable development (Ryan et al., 2008); extensive research investigations are required to accept or refute this hypothesis. Therefore, in-depth future studies are needed to demonstrate an improved comprehension of the organism in its host to advance the viability of endophyte-assisted biological applications, especially in the field. The persistent reliance on the deployment of a generic method in their processing was inferred to be a hindrance to the capability to fully grasp the interaction between endophytes and their host concerning their utilization in biological activities. Since most organisms prefer to eschew them due to transformations, they cannot be recognized using those general techniques. Thus, using complex molecular processes in their processing will lead to a better understanding and enable the use of the endophytic application in agriculture/food processing, medicine, and environmental management.
Author contributions

AK and AT conceived and planned this review article. AT and PP wrote the original draft of the manuscript. ST helped in review and data collection. PP prepared the figures. All authors reviewed and agreed on the final version.

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References

Abd Allah, E. F., Hashem, A., Alqarawi, A. A., Bahkali, A. H., and Abwhibi, M. S. (2015). Enhancing growth performance and systemic acquired resistance of medicinal plant sesbania sesban (L.) merr using arbuscular mycorrhizal fungi under salt stress. Saudi J. Biol. Sci. 22 (3), 274–283. doi: 10.1016/j.sjbs.2015.03.004

Adame-Alvarez, R. M., Mendiola-Soto, J., and Heil, M. (2014). Order of arrival shifts endophyte-pathogen interactions in bean from resistance induction to disease facilitation. FEMS Microbiol. Lett. 355, 100–107. doi: 10.1111/1574-6966.12454

Agarwal, S., and Shende, S. T. (1987). Tetrazolium reducing microorganisms inside the root of brassica species. Curr. Sci. 56, 187–188. Available at: https://www.currentscience.ac.in/Volumes/56/04/0187.pdf

Ahmad, N., Hamayun, M., Khan, S. A., Khan, A. L., Lee, I. J., and Shin, D. H. (2010). Gibberellin-producing endophytic fungi isolated from monochoria vaginalis. J. Microbiol. Biotechnol. 20 (12), 1744–1749. Available at: https://korescience.kr/article/JAKO20101886405953.page

Ali, S., Charles, T. C., and Glick, B. R. (2014). Amelioration of high salinity stress damage by plant growth-promoting bacterial endophytes that contain ACC deaminase. Plant Physiol. Biochem. 80, 160–167. doi: 10.1016/j.plaphy.2014.04.003

Ali, S., Khan, S. A., Hamayun, M., Iqbal, A., Khan, A. L., Hussain, A., et al. (2019). Endophytic fungi from caralluma acutangula can secrete plant growth promoting enzymes. Frenesia. Environ. Bull. 28, 2688–2696. Available at: https://www.cabdirect.org/cababstracts/abstract/2019531732

Alishahi, F., Alkhaldi, H. A., Khoshkholgh-Sima, N. A., and Etemadi, H. (2020). Mining the roots of various species of the halophyte suseda for halotolerant nitrogen-fixing endophytic bacteria with the potential for promoting plant growth. int. J. Microbiol. 23, 415–427. doi: 10.1155/2012/019-00115-y

Aly, A. H., Debbah, A., and Proksch, P. (2011). Fungal endophytes: unique plant inhabitants with great promises. Adv. Appl. Microbiol. 70 (6), 1829–1845. doi: 10.1016/S0065-2113(11)70016-3

Ambrosini, A., Beneduzzi, A., Stefanis, T., Pinheiro, F. G., Vargas, L. K., and Passaglia, L. M. (2012). Screening of plant growth promoting rhizobacteria isolated from sunflower (Helianthus annuus L.). Plant Soil 356 (1-2), 245–264. doi: 10.1007/s11104-011-1079-1

Anma, T., Puru, S. C., Verma, Y., Sharma, J. P., Khajuria, R. K., Musarrat, J., et al. (2006). Biocontrol studies on the endophytic fungus entrophospora infrequens for the production of an antiancer alkaloid camptothecin. Can. J. Microbiol. 52 (3), 189–196. doi: 10.1139/w05-122

Anderson, T. A., Guthrie, E. A., and Walton, B. T. (1993). Bioremediation in the rhizosphere. Environ. Sci. Technol. 27 (13), 2630–2636. doi: 10.1021/es00049a001

Anyasi, R. O., and Atagana, H. I. (2018). Screening of plant growth promoting rhizobacteria isolated from leaf tissues of citrus rootstocks. Can. J. Microbiol. 47 (3), 229–236. doi: 10.1139/w00-146

Araujo, W. L., Maccheroni, W., van Elsas, J. D., van Vuure, J. W., and Azevedo, J. L. (2002). Diversity of endophytic bacterial populations and their interaction with xylella fastidiosa in citrus plants. Appl. Environ. Microbiol. 68 (10), 4906–4914. doi: 10.1128/AEM.68.10.4906-4914.2002

Arora, N. K., Kang, S. C., and Maheshwari, D. K. (2001). Isolation of siderophore-producing strains of rhizobium melliloti and their biocontrol potential against macrophomina phaseolina that causes charcoal rot of groundnut. Curr. Sci. 81, 673–677. Available at: https://www.currentscience.ac.in/Volumes/81/06/673.pdf

Azevedo, J. L., Maccheroni, W. Jr., Pereira, J. O., and de Araujo, W. L. (2000). Endophytic microorganisms: a review on insect control and recent advances on tropical plants. Electron. J. Biotechnol. 3 (1), 15–16. doi: 10.2225/vol3-issue1-fulltext-4

Babu, A. G., Shea, P. J., Sudhakar, D., Jung, I. B., and Oh, B. T. (2015). Potential use of pseudomonas koreensis AGB-1 in association with miscanthus sinensis to remediate heavy metal (loid)-contaminated mining site soil. J. Environ. Manage. 151, 160–166. doi: 10.1016/j.jenvman.2014.12.043

Bacon, C. W., Glenn, A. E., and Hinton, D. M. (2002). “Isolation, in planta detection and culture of endophytic bacteria and fungi,” in Manual of environmental microbiology, 2nd edn. Eds. C. J. Hurst, R. L. Crawford, M. J. Mcnerney, G. R. Kudsen and L. D. Stettenbach (Washington DC: ASM Press).

Bacon, C. W., and White, J. (2000). Microbial endophytes (New York, Basel: Switzerland: CRC Press). doi: 10.1201/9781420077302

Badri, D. V., and Vivanco, J. M. (2009). Regulation and function of root exudates. Plant Cell Environ. 32, 666–681. doi: 10.1111/j.1365-3040.2009.01926.x

Badri, D. V., Weir, T. L., van der Lehe, D., and Vivanco, J. M. (2009). Rhizosphere chemical dialogues: plant-microbe interactions. Curr. Opin. Biotechnol. 20 (6), 642–650. doi: 10.1016/j.copbio.2009.09.014

Baek, H., Sicher, R. C., Kim, M. S., Kim, S. H., Strem, M. D., Melnick, R. L., et al. (2009). The beneficial endophyte trichoderma hamatum isolate D219b promotes growth and delays the onset of the drought response in theobroma cacao. J. Exp. Bot. 60 (11), 3279–3295. doi: 10.1093/jxb/erp165

Bararani, O., von Dahl, C. C., and Baldwin, I. T. (2007). Sebacinia vermifera promotes the growth and fitness of nicotiana attenuataa by inhibiting ethylene signaling. Plant Physiol. 144 (2), 1223–1232. doi: 10.1104/pp.107.097543

Bartha, E. A., Nowak, J., and Climent, C. (2006). Enhancement of chilling resistance of inoculated grapevine plantlets with a plant growth-promoting rhizobacterium, burkholderia phytofirmans strain PsJN. Appl. Environ. Microbiol. 72 (11), 7246–7252. doi: 10.1128/AEM.01047-06

Barnawal, D., Bharti, N., Maji, D., Chanotiya, C. S., and Kalra, A. (2012). 1-Aminocyclopropane-1-carboxylic acid (ACC) deaminase-containing rhizobacteria protect ocimum sanctum plants during waterlogging stress via reduced ethylene generation. Plant Physiol. Biochem. 58, 227–235. doi: 10.1016/j.plaphy.2012.07.008

Barnawal, D., Bharti, N., Maji, D., Chanotiya, C. S., and Kalra, A. (2014). ACC deaminase-containing arborhacter protopromiae induces NaCl stress tolerance

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Kumaran, R. S., Muthumary, J., Kim, E. K., and Hur, B. K. (2009). Production of taxol from phylothecia dioecorea, a leaf spot fungus isolated from hibiscus rosasinensis. *Biotechnol. Bioprocess Eng.* 14 (1), 76–83. doi:10.1007/s12257-008-0041-4

Kumar, A. Singh, R., Giri, D. D., Singh, P. K., and Pandey, K. D. (2014). Effect of azotobacter chroococcum CL13 inoculation on growth and curcumin content of turmeric (Curcuma longa). *Int. J.Curr. Microbiol. Appl. Sci.* 3 (9), 275–283.

Kusari, S., Lamboth, M., Zülhike, S., and Speitler, M. (2008). An endophytic fungus from hypericum perforatum that produces hypericin. *J. Natural Prod.* 71 (2), 159–162. doi:10.1360/070669k

Kusari, S., Zülhike, S., and Speitler, M. (2011). An endophytic fungus from *Camptotheca acuminate* that produces camptothecin and analogues. *J. Nat. Prod.* 74 (2), 2–7. doi:10.1021/np100812m

Kushwaha, R. K. Singh, S., Pandey, S. S., Kalra, A., and Babu, C. V. (2019a). Fungal endophytes attenuate withanolide biosynthesis in withania somnifera, prime to enhanced withanolide a content in leaves and roots. *World J. Microbiol. Biotechnol.* 35 (2), 20. doi:10.1007/s11274-019-2933-7

Kushwaha, R. K. Singh, S., Pandey, S. S., Rao, D. V., Nagegowda, D. A., Kalra, A., et al. (2019b). Compatibility of inherent fungal endophytes of withania somnifera with trichoderma viride and its impact on plant growth and withanolide content. *J. Plant Growth Regul.* 38 (4), 1228–1242. doi:10.1007/s10995-019-09928-7

Lata, R., Chowdhury, S., Gond, S. K., and White, J. F. (2018). Induction of abiotic stress tolerance in plants by endophytic microbes. *lett. Appl. Microbiol.* 66 (8), 268–276. doi:10.1111/lam.13185

Lazarovits, G., and Nowak, J. (1997). Rhizobacteria for improvement of plant growth and establishment. *HortSci* 32 (2), 188–192. doi:10.21273/HORTSCI.32.2.188

Leevaeu, J., and Hound, S. E. (2001). Appetite of an epiphytic: quantitative monitoring of bacterial sugar consumption in the phyllosphere. *Proc. Natl. Acad. Sci.* 98 (6), 3446–3453. doi:10.1073/pnas.061829998

Li, C. (2007). Fermentation conditions of *strophanthus griseus* subsp. *hyacinthoides* endophytic fungi on production of podophytoin. *Food Ferment. Ind.* 33 (9), 28.

Li, A. R., and Guan, K. Y. (2007). Mycorrhizal and dark sepalate endophytic fungi of pedicularis species from northwest of yunnan province, China. *Mycorrhiza* 17 (2), 103–109. doi:10.1007/s00253-006-0081-6

Limón, R. I., Petans, E., Tortino, M. I., Martínez-Villaluenga, C., Duertas, M., and Fras, J. (2015). Fermentation enhances the content of bioactive compounds in kidney bean extracts. *Food Chem.* 172, 343–352. doi:10.1016/j.foodchem.2014.09.084

Liu, K., Ding, X., Deng, B., and Chen, W. (2009). Isolation and characterization of endophytic taxol-producing fungi from *tamarix chinensis*. *J. Ind. Microbiol. Biotechnol.* 36 (9), 1171. doi:10.1007/s10295-009-0588-9

Liu, Y., Liu, W., and Liang, Z. (2015). Endophytic bacteria from pinellia ternata, a new source of purine alkaloids and bacterial manure. *Pharmacol. Biol.* 53 (10), 1545–1548. doi:10.1016/j.pharma.2015.10.0580

Liu, X., Song, W., Zhang, K., and Ye, Y. (2011). Effects of two kinds of endophytic fungi infection on water stress of seedlings of chrysanthemum morifolium. *Acta Horticultica Sin.* 38 (5), 335–342.

Li, W., Zhou, J., Lin, Z., and Hu, Z. (2007). Study on fermentation condition for production of huperzine a from endophytic fungus *corydalis chinensis* by huperzia serrata. *Chin. Med. Biotechnol.* 2 (4), 254–259.

Lodewyckx, C., Vangronsveld, J., Porteous, F., Moore, E. R., Taghavi, S., Megezay, M., et al. (2002). endophytic bacteria and their potential applications. *Crit. Rev. Plant Sci.* 21 (6), 583–606. doi:10.1080/07352680290044377

Lewe, K. F., Bowdler, T. M., Hume, D. E., Casey, N. D., and Tapper, B. A. (2008). The effect of the endophyte on the performance of irrigated perennial ryegrasses in subtropical Australia. *Aust. J. Agric. Res.* 59 (6), 567–577. doi:10.1071/AR08019

Lu, L., He, J., Yu, X., Li, G., and Zhang, X. (2006). Studies on isolation and identification of endophytic fungus strain SC13 from pharmaceutical plant *sabina vulgaris* ant. and metabolites. *Ji Bei Nong Ye Xue Bao.* 15, 85–89. doi:10.3969/j.issn.1008-2086.2006.05.021

Luo, S., Xu, T., Chen, L., Chen, J., Rao, C., Xiao, Y., et al. (2012). Endophyte-assisted promotion of biomass production and metal uptake of energy crop sweet sorghum by plant-growth-promoting endophyte *bacillus sp.* *SL-58*. *Appl. Microbiol. Biotechnol.* 93 (4), 1745–1753. doi:10.1007/s00253-011-3483-0

Hu, L., Zhou, W. X., Meng, J. C., Hu, J., and Tan, R. X. (2000). New bioactive metabolites produced by *colletotrichum sp.*, an endophytic fungus in artemisia annua. *Plant Sci.* 151 (1), 67–73. doi:10.1016/S0168-9452(99)00199-5

Maehara, S., Simanpunjak, P., Maetani, Y., Kitamura, C., Ohashi, K., and Shihiya, H. (2014). Ability of endophytic filamentous fungi associated with cinchona ledgeriana to produce cinchona alkaloids. *J. Nat. Med.* 67 (2), 421–423. doi:10.1007/s10995-014-0701-8

Máquez, L. M., Redman, R. S., Rodríguez, R. I., and Roossinck, M. J. (2007). A fungus in a fungus: a three-way symbiosis required for thermal tolerance. *Science* 315 (5811), 513–515. doi:10.1126/science.1136237

Tripathi et al. 10.3389/fpls.2022.985429
with diazotrophic bacteria. Eur J Soil Biol. 45 (1), 106–113. doi: 10.1016/j.ejsobi.2008.04.004

Palanivand, S. A., Yang, S. H., Zhang, L., and Suh, J. W. (2013). Effects of actinobacteria on plant disease suppression and growth promotion. Appl. Microbiol. Biotechnol. 97 (22), 9621–9636. doi: 10.1007/s00253-013-5206-1

Palmer, J. D., Solis, D. E., and Chase, M. W. (2004). The plant tree of life: an overview and some points of view. Am. J. Bot. 91 (10), 1437–1445. doi: 10.3732 ajb.h091.1437

Pandey, S. S., Singh, S., Babu, C. V., Shanker, K., Srivastava, N. K., and Kalra, A. (2016a). Endophytes of opium poppy differentially modulate host plant productivity and genes for the biosynthetic pathway of benzyloquinoline alkaloids. Planta 243 (5), 1097–1114. doi: 10.1007/s00225-016-2467-9

Pandey, S. S., Singh, S., Babu, C. V., Shanker, K., Srivastava, N. K., Shukla, A. K., et al. (2016b). Fungal endophytes of catharanthus roseus enhance vindoline content by modulating structural and regulatory genes related to terpenoid indole alkaloid biosynthesis. Sci. Rep. 6, 26583. doi: 10.1038/srep26583

Pan, X. W., Han, L., Zhang, Y. H., Chen, D. F., and Simonsen, H. T. (2015). Sclareol production in the moss Physcomitrella patens and observations on growth and terpenoid biosynthesis. Plant Biotechnol. Rep. 9 (3), 149–159. doi: 10.1007/s12259-015-0353-8

Patrigni, D. G., and Dobereiner, J. (1978). Light microscopy observations of tetrazolium-reducing bacteria in the endorhizosphere of maize and other grasses in Brazil. Can. J. Microbiol. 24 (6), 734–742. doi: 10.1139/m78-122

Patten, C. L., and Glick, B. R. (2002). Role of pseudomonas putida indoleacetic acid in development of the host plant root system. Appl. Environ. Microbiol. 68 (8), 3795–3801. doi: 10.1128/AEM.68.8.3795-3801.2002

Penrose, D. M., Moffat, B. A., and Glick, B. R. (2001). Determination of 1-aminoacyclopentane-1-carboxylic acid (ACC) to assess the effects of ACC deaminating-containing bacteria on roots of canola seedlings. Can. J. Microbiol. 47 (1), 77–80. doi: 10.1139/w99-128

Poling, S. M., Wicklow, D. T., Rogers, K. D., and Glor, J. B. (2008). Acremonium zea, a protective endophyte of maize, produces dihydroresorcylic and 7-hydroxydihydroresorcylic. J. Agricult. Food Chem. 56 (9), 3006–3009. doi: 10.1021/jf071327f

Prado, R., Vendramim, J. D., Bicalho, K. U., dos Santos Andrade, M., Fernandes, J. B., de Andrade Moral, R., et al. (2013). Amanoa rucoasa Jacq.(Amanoaceae): a promising source of bioactive compounds against sitophilus zeamais Mots.(Coleoptera: Curculionidae). J. Stored Prod. Res. 55, 6–14. doi: 10.1016/j.jspr.2013.06.001

Preston, G. M., Bertrand, N., and Rainey, P. B. (2001). Type III secretion in plant growth-promoting pseudomonas fluorescens SBW25. Mol. Microbiol. 41 (5), 999–1014. doi: 10.1042/0962-9243-25.20560.s

Qawasmeh, A., Obied, H. K., Raman, A., and Wheatley, W. (2012). Influence of fungal endophyte infection on phenolic content and antioxidant activity in grasses: interaction between loliere perenne and different strains of neotyphodium lolii. J. Agricult. Food Chem. 60 (13), 3388–3388. doi: 10.1021/jf301774y

Qiu, M., Xie, R. S., Shi, Y., Zhang, H., and Chen, H. M. (2010). Isolation and identification of two flavonoid-producing endophytic fungi from ginkgo biloba 1. Ann. Microbial. 60 (1), 143–150. doi: 10.12313/10-016-015-5

Radvan, S. (2009). “Phytoremediation for oil desert soils,” in Advances in applied bioremediation (Berlin, Heidelberg: Springer). [pp. 279–298]. doi: 10.1007/978-3-540-89620-1_15

Rajkumar, M., Ae, N., and Freitas, H. (2009). Endophytic bacteria and their potential to enhance heavy metal phytoextraction. Chemosphere 72 (7), 153–160. doi: 10.1016/j.chemosphere.2009.06.047

Rashid, S., Charles, T. C., and Glick, B. R. (2012). Isolation and characterization of new plant growth-promoting bacterial endophytes. Appl. Soil Ecol. 61, 217–224. doi: 10.1016/j.apsoil.2011.09.011

Redd, P., and Gordon, V. (2000). Lessons from nature: can ecology provide new leads in the search for novel bioactive chemicals from tropical rainforests? in biodiversity: New leads for the pharmaceutical and agrochemical industries. Proc Int Meeting Held 5-8 September 1999 Univ St Andrews UK, 205–212. doi: 10.3893/9781847550231-00205

Rehman, S., Shaval, A. S., Kour, A., Andrabi, R., Sudan, P., Sultan, P., et al. (2008). An endophytic neosporella sp. from nothapodytes foetida producing antifungal endophyte in tropics. Appl. Soil Ecol. 34 (2), 203–209. doi: 10.1016/j.apsoil.2007.04.013

Ren, C. G., and Dai, C. C. (2012). Jasmonic acid is involved in the signaling pathway for fungal endophyte-induced volatile oil accumulation of atractylodes lancea plantlets. BMC Plant Biol. 12 (1), 128. doi: 10.1186/1471-2229-12-128

Roldiguez, J. R., White, J. J., Arnold, A. E., and Redman, A. R. A. (2009). Fungal endophytes: diversity and functional roles. New Physiol. 182 (2), 314–330. doi: 10.1093/18190.1479.1.1437

Roos, I. M., and Hattingh, M. J. (1983). Scanning electron microscopy of pseudomonas syringae pv, mosoprornorum on sweet cherry leaves. J. Phytopathol. 108 (1), 18–25. doi: 10.1111/j.1439-0434.1983.tb00559.x

Frontiers in Plant Science
Mital, D. (1998). The greening of the green revolution. Nature 396 (6708), 211–212. doi:10.1038/362254
Ting, A. S. Y., Meon, S., Kadir, J., Radu, S., and Singh, G. (2009). Induced host resistance by non-pathogenic fusarium endophyte as a potential defense mechanism in fusarium wilt management of banana. Pest Technol. 3 (1), 67–72.
Tripathi, R., Awasthi, A., Mall, M., Shukla, A. K., Srivinas, K. S., Syamasundar, K. V., et al. (2013). Bacterial endophyte-mediated enhancement of plants content of key terpenoid indole alkaloids and growth parameters of callatharnus roseus. Ind. Crops Prod. 43, 306–310. doi:10.1016/j.indcrop.2012.07.045
Tripathi, R., Kalra, A., Darokar, M. P., Chandra, M., Aggarwal, N., Singh, A. K., et al. (2010). Endophytic bacteria from oxonium sanctuary and their yield enhancing capabilities. Curr. Microbiol. 60 (3), 167–171. doi:10.1007/s00284-009-9520-x
Truyen, S., Jambon, I., Crous, S., Jansen, J., Weyens, N., Mench, M., et al. (2014). The effect of long-term cd and Ni exposure on seed endophytes of agrostis capillaris and their potential application in phytoremediation of metal-contaminated soils. Int. J. Phytoremed. 17 (6-8), 643–659. doi:10.1080/10296618.2013.870327
Van Bael, S. A., Seid, M. A., and Wicso, W. T. (2012). Endophytic fungi increase the processing rate of leaves by leaf-cutting ants (Atta). Ecol. Entomol. 37 (4), 318–321. doi:10.1111/j.1365-2319.2012.01364.x
Vanessa, M. C., and Christopher, M. M. F. (2004). Analysis of the endophytic actinobacterial population in the roots of wheat (Triticum aestivum l.) by terminal restriction fragment length polymorphism and sequencing of 16S rRNA clones. Curr. Microbiol. 49 (4), 258. doi:10.1007/s00284-006-0333-3
Venkatachalam, R., Subban, K., and Paul, M. (2008). Taxol from botryodiplodia theobromae (BT 115)-an endophytic fungus of taxus baccata. J. Chem. Res. 1794.2004
Vega, F. E., Rosado, F., Aime, M. C., Viterbo, A. D. A., and Chet, I. (2006). TasHyd1, a new hydrophobin gene from Fasciola hepatica. J. Biotechnol. 107 (1), 23–31. doi:10.1016/j.jbiotec.2005.09.024
Villaricos, M., Power, B., Sánchez-Conteras, M., Lloret, J., Orueabal, R. I., Martin, M., et al. (2003). Colonization behaviour of pseudomonas fluorescens and sinorhizobium meliloti in the alfalfa (Medicago sativa) rhizosphere. Plant Soil 251 (1-2), 127–141. doi:10.1023/A:102394708794
Viterbo, A. D. A., and Chet, I. (2006). Analysis of the endophytic actinobacterial population in the roots of wheat (Triticum aestivum l.) by terminal restriction fragment length polymorphism and sequencing of 16S rRNA clones. Curr. Microbiol. 49 (4), 258. doi:10.1007/s00284-006-0333-3
Wang, J. W., Zheng, L. P., and Tan, R. X. (2006). The preparation of an elicitor metabolites from chaetomium globosum L18, an endophytic fungus in the flax. Mar Drugs 161111.
Wang, L., Han, T., Li, W., Jia, M., Xue, L., Rahman, K., et al. (2013). Geographic and tissue influence on the production of useful compounds, remediation and carbon sequestration. Microb. Biotechnol. 2 (4), 428–440. doi:10.1111/j.1754-6299.2010.00109.x
Wu, C. H., Bernard, S. M., Andersen, G. L., and Chen, W. (2009). Developing microbe-plant interactions for applications in plant growth-promotion and disease control, production of useful compounds, remediation and carbon sequestration. Microb. Biotechnol. 2 (4), 428–440. doi:10.1111/j.1754-6299.2010.00109.x
Wu, L., Han, T., Li, W., Jia, M., Xue, L., Rahman, K., et al. (2013). Geographic and tissue influence on the production of useful compounds, remediation and carbon sequestration. Microb. Biotechnol. 2 (4), 428–440. doi:10.1111/j.1754-6299.2010.00109.x
Xie, W., and Gerhardsson, B. (2007). Biological pesticides for control of seed-and soil-borne plant pathogens. Modern Soil Microbiol. CRC Press Boca Raton pp, 479–501. Available at: https://cris.icr.ac.id/1750854175615702528
Yi, D., and Li, Y. (2015). The vertical transmission of neotyphodium lolii in perennial ryegrass: the only possible way to the spread of endophytes. PLoS One 10 (2), e0117231. doi:10.1371/journal.pone.0117231
Williams, T. A., Foster, P. G., Cox, C. J., and Embly, T. M. (2013). An archaeal origin of eukaryotes supports only two primary domains of life. Nature 504 (7479), 231–236. doi:10.1038/nature12733
Wu, C. H., Bernard, S. M., Andersen, G. L., and Chen, W. (2009). Developing microbe-plant interactions for applications in plant growth-promotion and disease control, production of useful compounds, remediation and carbon sequestration. Microb. Biotechnol. 2 (4), 428–440. doi:10.1111/j.1754-6299.2010.00109.x
Wu, L., Han, T., Li, W., Jia, M., Xue, L., Rahman, K., et al. (2013). Geographic and tissue influence on the production of useful compounds, remediation and carbon sequestration. Microb. Biotechnol. 2 (4), 428–440. doi:10.1111/j.1754-6299.2010.00109.x
Yang, N. Y., Jiang, S., Shang, X. E., Tang, Y. P., and Duan, J. A. (2012). A new phyllostensamamine alkaloid produced by an endophyte bacillus subtilis isolated from angelia sinensis. J. Chem. Res. 36 (11), 647–647. doi:10.3184/174751912X5345681422
Yi, D., and Wang, S. J., and Chen, W. S. (2005). Induced host resistance by non-pathogenic fusarium endophyte as a potential defense mechanism in fusarium wilt management of banana. Pest Technol. 3 (1), 67–72. doi:10.1007/s00284-009-9520-x
Yin, H., and Chen, J. L. (2008). Sipeimine-producing endophytic fungus isolated from Commelina communis L. J. Chem. Res. 32, 422. doi:10.3969/j.issn.1001-6880.2003.05.012
Yin, H., and Chen, J. L. (2008). Sipeimine-producing endophytic fungus isolated from Commelina communis L. J. Chem. Res. 32, 422. doi:10.3969/j.issn.1001-6880.2003.05.012
Zeng, S., Shao, H., and Zhang, L. (2004). An endophytic fungus producing a neurotoxin. J. Biotechnol. 171. doi:10.1007/s00284-009-9520-x
Zeng, S., Shao, H., and Zhang, L. (2004). An endophytic fungus producing a neurotoxin. J. Biotechnol. 171. doi:10.1007/s00284-009-9520-x
Zeng, S., Shao, H., and Zhang, L. (2004). An endophytic fungus producing a neurotoxin. J. Biotechnol. 171. doi:10.1007/s00284-009-9520-x
Zhang, H., Bai, X., and Wu, B. (2012). Evaluation of antimicrobial activities of extracts of endophytic fungi from artemisia annua. *Bangladesh J. Pharmacol.* 7 (2), 120–123. doi: 10.3329/bjp.v7i2.10951

Zhang, X. X., George, A., Bailey, M. J., and Rainey, P. B. (2006b). The histidine utilization (hut) genes of pseudomonas fluorescens SBW25 are active on plant surfaces, but are not required for competitive colonization of sugar beet seedlings. *Microbiology* 152 (6), 1867–1875. doi: 10.1099/mic.0.28741-0

Zhang, X., Li, G., Ma, J., Zeng, Y., Ma, W., and Zhao, P. (2010). Endophytic fungus trichothecium roseum LZ93 antagonizing pathogenic fungi *in vitro* and its secondary metabolites. *J. Microbiol.* 48 (6), 784–790. doi: 10.1007/s12275-010-0173-z

Zhang, C. L., Liu, S. P., Lin, F. C., Kubicek, C. P., and Druzhinina, I. S. (2007). *Trichoderma taxi* sp. nov., an endophytic fungus from Chinese yew taxus mairei. *FEMS Microbiol. Lett.* 270 (1), 90–96. doi: 10.1111/j.1574-6968.2007.00659.x

Zhang, H. W., Song, Y. C., and Tan, R. X. (2006a). Biology and chemistry of endophytes. *Nat. Prod. Rep.* 23 (5), 753–771. doi: 10.1039/b609457b

Zhang, J., Wang, C., Guo, S., Chen, J., and Xiao, P. (1999). Studies on the plant hormones produced by 5 species of endophytic fungi isolated from medicinal plants (Orchidacea). *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* 21 (6), 460–465.

Zhang, P., Zhou, P. P., and Yu, L. J. (2009). An endophytic taxol-producing fungus from taxus media, cladosporium cladosporioides MD2. *Curr. Microbiol.* 59 (3), 227. doi: 10.1007/s00284-008-9270-1

Zhou, X., Wang, Z., Jiang, K., Wei, Y., Lin, J., Sun, X., et al. (2007). Screening of taxol-producing endophytic fungi from taxus chinensis var. mairei. *Appl. Biochem. Microbiol.* 59 (3), 227. doi: 10.1134/S000368380704014X

Zhou, S. L., Yang, F., Lan, S. L., Xu, N., and Hong, Y. H. (2009). Huperzine a producing conditions from endophytic fungus in SHB huperzia serrata. *J. Microbiol.* 3, 32–36. doi: 10.3969/j.issn.1005-7021.2009.03.006

Zhou, J. Y., Yuan, J., Li, X., Ning, Y. F., and Dai, C. C. (2015). Endophytic bacterium-triggered reactive oxygen species directly increase oxygenous sesquiterpenoid content and diversity in atractylodes lancea. *Appl. Environ. Microbiol.* 82 (5), 1577–1585. doi: 10.1128/AEM.03434-15