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BEHAVIORAL DUALISM OF ENDOPHYTES IN PLANT-MICROBE INTERACTION AND THEIR DIVERSE APPLICATIONS - A REVIEW

Pooja Singh[1], *Angkita Sharma*[1], *Preeti Arivaradarajan*[2], *Manobjyoti Bordoloi*[3], *Bidyut Kumar Sarmah*[4], *Shoma Paul Nandi*[1]*

Address(es):
[1] Amity Institute of Biotechnology, Amity University, Noida, Gautam Buddha Nagar- 201313, Uttar Pradesh, India.
[2] Department of Microbiology, Thiagarajar College, Madurai- 625009, Tamil Nadu, India.
[3] Department of Chemistry, Cotton University, Guwahati-781001, Assam, India.
[4] DBT-AAU Centre, Assam Agriculture University, Jorhat-785013, (Assam), India.

*Corresponding author: spaul@amity.edu

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ABSTRACT

Microbes are harmful as well as beneficial for the human, plants and environment. Plant-microbe interaction array depicts both mutualism and pathogenesis. This dual nature of microbes depends on their surrounding abiotic and biotic factors. Endophytes are plant symbionts, beneficial for plant health. Some microbes are harmful for plants and they also live inside the plants, are called pathogens. The interactions that exist between the endophytic communities have hardly been investigated. The microbes associated with the plants act mostly according to environmental factors. These factors have the ability to alter the nature of microbes from endophytes to pathogens and vice-versa. Thus, by modulating such environmental factors, these microbes can be designed to produce important secondary metabolites or desired products, either within the plants or under laboratory conditions. The plant-microbe interactions have immense research orientation in the near future. The international demand for medicinal plant-based resources has increased due to their augmented exploitation for research and development. Studies of such plants species having parallel phytochemical constituents or microbes producing similar constituents could be an effective way of circumventing this global demand gap. The present review gives a detailed description of the dual behavior that exists in plant endophytes. In addition, it details a state of coherence in their vivid mannerisms and various applications of microbes in different aspects, environmental safety, agriculture, and pollution control.

Keywords: Endophytes, Pathogen, Host plants, Secondary metabolites, Bioremediation, Plant- microbes interaction

INTRODUCTION

Endophytes arbitrate plant growth with the help of direct or indirect mechanisms. Endophytes begin their expedition as rhizospheric microbes, possibilities of them retaining their attributes inside plant remain. Plant habitat is classified into phyllosphere, endosphere and rhizosphere. Phyllospheres are aerial or terrestrial parts of plants such as leaves, stems and flowers that act as habitats for various microorganisms (phyllospheric microbes). Whereas, the rhizosphere is a small area of soil or substrate that is directly influenced by root exudates and associated soil microbiome (total rhizospheric microbes). Endosphere is microenviroment inside the plant and associated microbes are called endophytes. As endophytes network closer to plant than phyllosphere and rhizosphere microbes, their plant effects may be direct and intense. Phyllosphere region is Endophytes benefit plants directly by stimulating growth and/or indirectly with the help of a reduction in the plant disease incidence. For the purpose of endophyte multiplication, plant intercellular spaces are good sites because of the presence of nutrients like potassium, calcium, sulfur, chlorine, phosphorous and carbohydrates, amino acids and organic acids (**Madore and Webb, 1981; Canny and Huang, 1993; Canny and McCully, 1988**).
Modern times have seen a great deal of progress in the isolation of natural products from plants for drug discovery and development. The analysis of secondary plant products has progressed a lot in the past three decades. Studies showed that plant's secondary metabolite major classes such as benzopyranones, terpenoids, benzoquinones, flavonoids, steroids, alkaloids, and phenolics are endowed with interesting pharmacology activities (Figure 1) (**Kaushik *et al.*, 2021**).
Endophytes residing within living plant tissues are unique in character and exhibit multidimensional interactions with their host plants. The word 'endophyte' was devised first in **1866** by **De Bary**. By definition, it means any organism that lives inside the plant tissues. However, with time, the meaning of the word was subjected to differences in types, such as fungal and bacterial endophytes, and also on their mannerisms, like obligate or facultative with their host plants. The most fascinating quality of endophytes is that, unlike other organisms, the interactions of endophytes are multifaceted, from pathogenic to mutualistic, from symbiotic to saprophytic. Their most smart lifestyle includes both intercellular and/or intracellular mutualistic association along with their corresponding host plants (**Kandel *et al.*, 2017**). Recent studies have shown that the health and survival of plants usually depend on these endophytes (**Hardoim *et al.*, 2015**). One of the best endophytic relationships that have existed on the planet for more than sixty million years is the rhizobia-legume symbiosis (**Santoyo *et al.*, 2016**). This relationship governs the nitrogen sufficiency of the plants by their bacterial associates. Gene level studies of these endophytes show versatility and abundance of genes responsible for novel characters beneficial for the plant (**Ali *et al.*, 2014**).

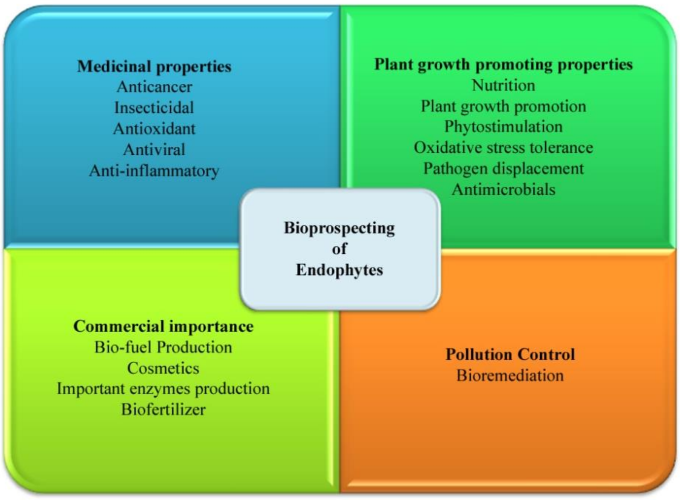

Figure 1 Illustration of versatile nature of endophytes.

For the endophytes to maintain a sustainable environment for stable symbiosis, they manufacture or trigger the host plants for secondary metabolite production which ultimately assists the plants to better adapt to their environment and improve plant health. Endophytes also help the plants to neutralize the reactive oxygen species (ROS), which are produced during biotic or abiotic stress. The 'Plant-Microbiome' altered the way scientists study the plant community around the globe. Microbes, which are an integral part of the plant ecosystem, must be considered together during coevolution of both -plants and microbes, rather than separately because their complex interaction have existed from initial stage of life on the earth (**Lyu *et al*., 2021**). Thus, this approach would help in understanding the benefits of their coexistence inside plant. The patterns and dynamics of endophytes are determined by gene expression in plants. Current approaches like next-generation sequencing (NGS), metagenomics, including meta-transcriptomics, and microarray have the ability to give a better picture of endophyte's way of life. Moreover, bacterial and fungal endophytic communities are separately studied. However, the interaction between them *in planta* can be an intriguing new field in endophytic research (**Berg *et al*., 2016**). This review meticulously analyses the dynamics of plant-microbe interaction in a variety of plants and the potential of their endophytic population.

Recognition of endophytic behavior and downstream signaling

Root exudates supplemented with nutrients and water is known to attract a varied range of microbes, including endophytes. Flavonoids play a big role as chemoattractants, and are one such metabolite exudated by different plants, which play a vital role in the interaction of the endophytes with host plant root hair. Flavonoids help in the colonization of endophytes *Azorhizobium* and *Serratia* sp. root in rice and wheat in a more effective way (**Balachandar *et al*., 2006; Webster *et al*., 1998**). Of late, strigolactone (SL) that is secreted by the roots of *Arabidopsis thaliana* playing the role of a signal molecule for endophytic colonization of *Mucor* sp. **López-Ráez *et al*.** in the year **2017** showed that this treatment also has the potential to activate the synthesis and release of short-chain oligomers of chitin. The signaling pathway of the plant can be stimulated by symbiosis. Moreover, arabinogalactan proteins play a crucial role which is necessary in plant-microbe interaction. Root exudates that include amino acids, sugars, phenolic compounds, organic acids are usually secreted from the plant roots. This process scrutinizes and invites the microbes, mainly the endophytes (**Chagas *et al*., 2017**).

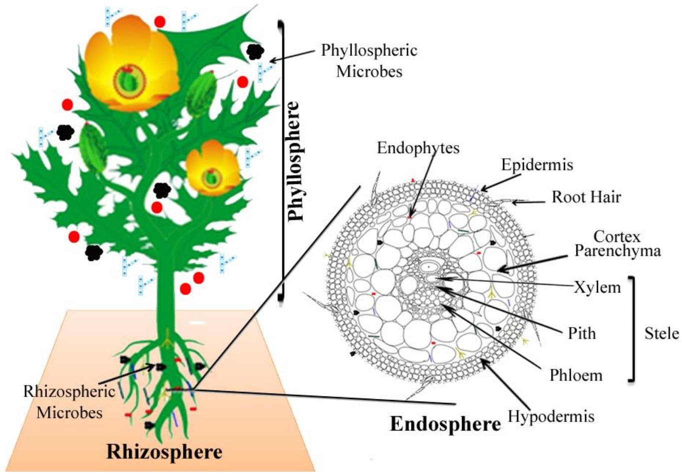

Figure 2 Pictorial representation of colonization and distribution of endophytes in the root of plant. Endophytes enter into endosphere from rhizosphere using different root parts.

The nature of microbes whether they act as endophytes or pathogens, is determined by the immune system of the plant that allows only beneficial microbes to enter the plant tissues. There is enough evidence to suggest that microbes govern the gene expression pathways. Nonetheless, certain signaling pathways like that of ethylene, jasmonic acid and salicylic acid work regardless of the microorganisms (**Kumar *et al*., 2020**). **Kusajima *et al*.** (**2018**) reported that the endophytic bacteria *Azospirillum* sp. stimulates systemic resistance to disease in rice. An interesting study showed that when the plant colonization by mutualistic partners occurs, there seems to be downregulation of plant defense pathways. These partners comprise of arbuscular mycorrhizal fungi or rhizobia (**Sarkar *et al*., 2016**). Yet, late ET/JA/SA signaling pathways induction stops the microbe from emasculating the plant when the mutualistic interactions take place.

Hardoim *et al*. (**2015**) showed the results of a comparative genomic analysis to investigate the endophytic behavior. They reported that anabolic pathway genes are plentiful among endophytes; nevertheless, in case of phytopathogens, catabolism-related genes, the ones involved in the assault of the host, are seen to be more prominent. The nitrogenase gene, along with ribulose bisphosphate carboxylase/oxygenase (RuBisCO) is a unique marker for endophytes together with nitrogen fixation capabilities (**Karpinets *et al*., 2014**). The researches in the field of mutualistic symbioses research show that *via* nutrient scrutinizing, plants identify if the conquering microbe is a parasite or is actually beneficial.

For the endophytes to enter the host plant, they need to pass through the preliminary line of the immune system of the plant defense. Plants denied the entry of microbes however plants rely totally on their innate immunity. For the detection of the danger, pathogens and pests, plants employ Pattern recognition patterns (PRPs). This process includes the recognition of many conserved molecules, known as microbe-associated molecular patterns (MAMPs) or pathogen-associated molecular patterns (PAMPs) by the plants (**Newman *et al*., 2013**). Most common MAMPS are lipopolysaccharides, Flagellin, peptidoglycan, bacterial cold shock proteins, BetaGlycan, bacterial superoxide dismutase, and elongation factor TU. PRPs of plants recognize these MAMPs on the surface of their cells. Endophytes have also designed strategies for their protection from these plant defense mechanisms.

Studies have shown that plant genotype plays a significant role in shaping the composition of the rhizospheric, endophytic, or phyllospheric microbial communities (Figure 2). In our unpublished data, fungal metagenomics study of the root, shoot and rhizospheric soil has been done for *Argemone mexicana* and *Datura metel*, which suggested that genetic variation in plants and nutrition in rhizosphere soil are responsible for microbial diversity and richness. The soil microbes are attracted to root exudates of plants chemotactically, along with volatile organic carbon and rhizodeposition. These root exudates can be classified as organic acids, sugars, amino acids, flavonoids, enzymes. Root exudates attract the soil microbes because they are rich in nutrients and minerals. Some factors are there that affects on the quality and quantity of the root exudates. Temperature is key factor that affects the root exudates building, apart from soil moisture. Soil pH and nutrient availability such as carbon, nitrogen, and phosphate affect the release of root exudates and design a specific chemical niche. Certain soil microbes along with some antibiotics have been known to increase the exudation of organic materials, flexible cell permeability, and so on. Colonization of the endophytes inside plant tissues is basically dependent on some events along with cross-talk between plant - microbes and environmental factors. Endophytes have major application in agriculture, environment conservation and pharmaceutical industries.

ENDOPHYTES AS MAJOR PLAYER IN "ONE HEALTH"

Endophytes directly benefit plants and provide a vast array of support. These include antimicrobial metabolites, phosphate solubilizing compounds, insecticidal by-products, nitrogen fixing abilities, iron chelators. Endophytes produce plant growth-promoting hormones (such as, cytokinins, auxins, and gibberellins), which can alter the level of the growth-inhibiting phytohormone, for example, they can modulate ethylene level in the plants by producing 1-aminocyclopropane-1-carboxylate (ACC) deaminase activity and activate plant defense mechanism against biotic (For example, pathogens, herbivores, insects etc.) and abiotic stress (such as salt, water, temperature and heavy metals) (Figure 3). Moreover, many sulfur oxidizing endophytes oxidize elemental sulfur into sulfate, which are then used by plants (**Fadiji and Babalola, 2020**). There is wide range of applications of the microbes in sustainable environment, pharmaceuticals, alcoholic beverages production, biofuels production, baking industries, various industrial enzymes generation.

Plant secondary metabolites production by endophytes

Plant secondary metabolites are known for their pharmaceutical property but in the traditional view it is widely believed that the quality and quantity of crude drugs derived from medicinal plants are largely influenced by factors such as the genetic background of the plant concerned, environmental habitats and the nutrient content of the soil. On the other hand, plant based drugs are expensive owing to the fact that plants require huge area of land for farming, and downstream process is a tedious, grueling and time consuming. However, in recent years, it is gradually recognized that endophytes have played a very important role in affecting the quality and quantity of crude drugs through specific microbes-host interactions. Thus drug quality can be affected by modulating the plant endophytic microbiome. Inoculations of fungal cultures improved the physio-chemical prominence of plants and can increase the number of total flavonoids, reducing sugar, trans-resveratrol, total phenols, and phenylalanine ammonia-lyase activities. Conventionally, Taxol, anticancer drug, was extracted from the stem of ***Taxus brevifolia*** plant and the yield was very low. Endophytes can produce secondary metabolites same as their host plant. For instance, endophytic fungus, *Colletotrichum gleospoiroides* associated with ***Tectona grandis*** **have the ability to produce taxol at high yield in few days at controlled conditions.** Plant *Camptotheca* produces camptothecin (anticancer) drugs and endophytic fungus, *Fusarium solani* also produces camptothecin (**Fadiji and Babalola, 2020**). However, endophytic fungi associated with medicinal plants are major sources of bioactive metabolites. In another research, *Alternaria alternata* endophytic fungus from medicinal plant *Vitex negundo* was produced bioactive metabolite alternariol methyl ether, which is used in the treatment of hepatocellular carcinoma (**Palanichamy *et al*. 2018**). In a study, **Yang *et al*. (2016)**, reported that fungal endophytes, *Fusarium* sp. and *Nigrospora* sp. increased the metabolism of grape metabolism as compared to others.

Fungal secondary metabolites include terpenoids, alkaloids, isocoumarins, steroids, quinones, lignans, flavonoids, phenylpropanoids, peptides, aliphatics, phenolics, volatile organic compounds, and have immense pharmaceutical prospects. An interesting point here is that when compared, these compounds are identical to the ones produced by the particular host plants. This suggests a plausible genetic cross-talk existing between the host plant and the endophytes (**Jia *et al*., 2016**). The work of **Stierle *et al*. (1993)** is considered a major breakthrough

for endophytes, when it was established that an endophytic fungus, *Taxomyces andreana* for the first time isolated from *Taxus brevifolia*, also produced paclitaxel. Paclitaxel is the multibillion-dollar worth anticancer compound, extracted from the fungal endophytes, same as from the main source of paclitaxel, the yew plant (Table 1). Therefore, this unique characteristic of the endophytic fungus is an interesting character and can be used as a substitute for plant-based secondary metabolites. A number other studies have proven the production of host-mimicking bioactive metabolites with the help of their respective endophytic fungal allies (**Jia *et al*., 2016; Zhao *et al*., 2010; Stierle *et al*., 1993**). These metabolites besides taxol are camptothecin, diosgenin, hypericin, podophyllo toxin, vinblastine, vazadirachtin and rohitukine. Nineteen different genera of endophytic fungi (*Alternaria*, *Botryodiplodia*, *Aspergillus*, *Botrytis*, *Ectostroma*, *Cladosporium*, *Fusarium*, *Monochaetia*, *Metarhizium*, *Mucor*, *Papulaspora*, *Ozonium*, *Periconia*, *Pestalotiopsis*, *Phyllosticta*, *Pithomyces*, *Pestalotia*, *Taxomyces*, and *Tubercularia*) isolated from plants producing taxol, have been shown to produce paclitaxel and its analogs (i.e. baccatinIII, 10-deacetylbaccatin III) (Table 1)(**Zhao *et al*., 2010**).
Another major example is the anti-leukaemic compound vincristine produced by the endophytic fungus in association with *Catharanthus roseus* (**Yang *et al*., 2004**). Also, a crucial precursor of major anticancer agents, podophyllotoxin, is produced by *Trametes hirsuta*, a fungal endophyte from the plant *Podophyllum hexandrum* and *Phialocephala fortinii*, which are associated with *Podophyllum peltatum* (**Puri *et al*., 2006; Eyberger *et al*., 2006**). *Shiraia* sp. Slf14, an endophytic fungus isolated from the plant *Huperzia serrata* is known to produce huperzine. Fungal endophytes extracted from the stems of the plant *Hypericum perforatum* have been shown to produce emodin and hypericin (**Kusari *et al*., 2009**). Many secondary metabolites such as huperzine A, β-irone, α-irone, hypericin, diosgenin, and toosendanin, are extracted from various endophytic fungi (**Zhao *et al*., 2010**). The anticancer alkaloid, camptothecin (CPT), has been isolated from plants *Ophiorrhiza pumila*, *O. liukiuensis*, and *Camptotheca acuminata* but it can be extracted from the various endophytic fungus. *Neurospora* sp. and *Entrophospora infrequens* associated with *Nothapodytes foetida*, can synthesize camptothecin (**Aswini *et al*., 2018; Bhalkar *et al*., 2016; Rehman *et al*., 2008**). Manufacture of CPT, 9-methoxy camptothecin and 10-hydroxycamptothecin was reported by **Kusari *et al*. (2009)** from the fungal endophyte *Fusarium solani* in alliance with *C. acuminate*. **Shweta *et al*. (2013)** showed the endophytes induced manufacture of camptothecin from the *Miquelia dentata*, plant, with the maximum quantity of the metabolite in the fruits (Table 1).
Even though there are a large number of studies shows that fungal endophytes produce a gamut of host-mimicking bioactive metabolites, but to date, studies have not been able to prove them as a useful source or alternative of the bioactive metabolites originally from plants (**Priti *et al*., 2009**). Axenic sub-culturing of commercially important microbes is known to reduce the potential of its secondary metabolite production, which is a major challenge in achieving the optimal manufacture of important compounds. This process, which is also stated as attenuation, is a phenomenon that is seen in bacteria, fungi, and viruses. In this regard, an example may be cited of consecutive sub-culturing of the fungal endophyte *Periconia* sp. sequestered from the plant *Torreya* sp. had major attenuated production of taxol (Table 1). Similarly, consecutive culturing of endophytic fungi that were isolated from the plant *Nothapodytes nimmonian*, resulted in the reduction in the production of camptothecin (**Gurudatt *et al*., 2010**). Thus, this attenuation problem of fungal endophytes has become a real matter of disablement for the use of fungal endophytes as alternate resources of plant metabolites. Among many suggested hypotheses, it is postulated that the weakening could be because of the loss of stimuli from the host when the endophytes are grown in axenic medium or because of silencing of the genes in these axenic cultures (**Priti *et al*., 2009**). Various efforts to remedy this problem by enhancing these axenic cultures along with extracts of their respective host plants have not yielded many positive results.
The last few decades have shown several studies that confirm, endophytic microbiome and endophytes secrete the bioactive metabolites the same as their host plant. For example, more than nineteen different fungal genera, which were extracted from various species of Taxus were known to produce taxol *in vitro*. The taxonomy and phylogeny of the fungi were very diverse and but manufactured the same compound. It is rather improbable that a collaboration like this between the diverse fungi and the host could have ascended through either a mutualistic or symbiotic relationship. Podophyllotoxin, a metabolite of *Podophyllum* species and some other plant species, is also isolated from the endophytic microbes (*Fusarium* sp., *Aspergillus* sp., *Alternaria* sp. *Penicillium* sp., and *Chaetomium* sp.) from the different plants (**Kusari *et al*., 2009; Lu *et al*., 2006**). In another study, it was isolated from *Fusarium oxysporum* allied with the medicinal plant *Juniperus recurva* from the Himalayas (**Kour *et al*., 2008**). In yet another study, it was isolated from *Aspergillus fumigates* in association with the plant *Juniperus communis* L. *Horstmann* (**Kusari *et al*. 2009**).
A species of *Xylaria* sp. with the role of a fungal endophyte allied with the Manchurian fir *Abies holophylla* is known to produce both the metabolites dechlorogriseofulvin and griseofulvin when grown in culture. These compounds were studied for their antifungal activity *in vivo* to fight various major fungi acting as plant pathogens. The compound Griseofulvin showed greater antifungal activity in both *in vivo* and *in vitro* and proficiently measured the growth of blight of rice sheath (*Corticium sasaki*), rice blast, *Magnaporthe grisea*, and barley powdery mildew (*Blumeria graminis* f. sp. *hordei*) wheat leaf rust (*Puccinia recondita*) (**Park *et al*., 2005**). Brefeldin A is another bioactive compound having significant antiviral, antifungal, and anticancer activities. Along with these properties, it also acts as an inhibitor of protein transport. This compound has been extracted from a variety of fungal species, which include *Alternaria*, *Curvularia*, *Ascochyta*, *Penicillium*, *Cercospora*, and *Phyllosticta*. It was first described as a bioactive metabolite of *Eupenicillium brefeldianum* (**Harri *et al*., 1963**). Decumbin, an identical bioactive compound was first informed in 1958 dihydroxy-α, β-unsaturated lactone in the crystalline form. *Penicillium* allied with spoiled corn also produced this metabolite. Cyanein isolated from *P. cyaneum* is another identical metabolite along with ascotoxin, which was isolated from *Ascochyta imperfect* (**Fen *et al*., 1994**).
Sequoiatones A and B are the two novel polyketides that were extracted from the endophyte *Aspergillus parasiticus*. These are associated with the *Sequoia sempervirens* bark. An unusual dimeric quinine Torreyanic acid is isolated from *Pestalotiopsis microspora*, which is an endophyte of the plant *Torreya taxifolia*. The endangered plant *Juniperus cedrus* (Canary Island Juniper) fungal endophyte produces Nodulosporins (**Dai *et al*., 2006**). A type of *Penicillium* sp. that was isolated from the plant *Taxus brevifolia* produced the phomopsolides. These are a series of polyketides that has an ester side chain of tiglic acid. *Phomopsis oblonga*, a fungus, which is known to confer protection against infestations of elm bark beetle, originally produced Phomopsolide. Rugulosin is a bis-anthraquinoid yellow pigment that is isolated from *Hormonema dematioides*. It is a fungal endophyte that is allied with the Canadian balsam fir.*Piper nigrum*, belonging to the family Piperaceae is extremely extraordinary as the alkaloid piperine is present in the same. Piperine is described to have broad bioactive properties that range from antidepressant, antimicrobial, antioxidative, anti-inflammatory to anticancer activities. It also plays a major role in amassing the bioavailability of many drugs. The study conducted by **Chithra *et al*.** in the year **2014** identified piperine producing endophytic fungus from *Piper nigrum* L, which was a member of *Colletotrichum gloeosporioides* and was confirmed by HPLC and LCMS.
In a study conducted by **Ebrahim *et al*. 2012**, chemical investigation of the ethyl acetate extract of *Corynespora cassiicola*, which was isolated from leaf tissues of the Chinese mangrove medicinal plant *Laguncularia racemosa*, produced four new secondary metabolites. These included three decalactones, xestodecalactones as well as corynesidone, in addition to four known compounds. One- and two-dimensional NMR spectroscopy as well as by high-resolution mass spectrometry showed the structures of the new compounds. These compounds belong to the (11*S*) series of xestodecalactones, opposite to the (11*R*) configuration of the known xestodecalactones. When the compounds were tested against a panel of human protein kinases, showed that among the isolated compounds, two inhibited several kinases such as IGF1-R and VEGF-R2 with IC_{50} values mostly in the low micromolar range.
In another study, different endophytic fungi isolated from the plant Himalayan Yew were tested for their ability for taxol production. BAPT gene was involved in the taxol biosynthetic pathway was used as a molecular marker in order to screen taxol-producing endophytic fungi. Taxol extracted from fungal strain *Fusarium redolens* based on the morphology and internal transcribed spacer region of nrDNA analysis. Quantification by HPLC methods of fungal taxol showed that *F. redolens* was able to produce 66 µg/l of taxol in fermentation broth. The antitumour activity of the fungal taxol was tested using *Agrobacterium*. The results showed that PCR amplification of genes involved in taxol biosynthesis is an effective and reliable method for prescreening taxol-producing fungi (**Garyali *et al*., 2013**). These studies suggested that plant based drugs can be produced by the endophytes and it is time saving, cost effective and less laborious. These qualities of the endophytes make them a good source of plant drugs.

Endophytes in sustainable Agriculture

Endophytes play crucial role in plant growth promotion and disease management. Therefore, endophytes are used as bio-inoculants for improving the crop productivity. There are many reports on the application of endophytes to improve plant disease resistance and promote plant growth.

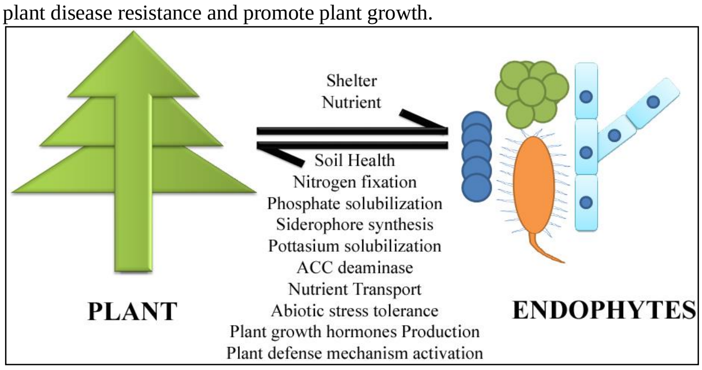

Figure 3 Schematic representation is showing symbiotic relationship between plant and endophytes.

Endophytes promote plant growth promotion via their participation in plant root elongation through IAA production, phosphate solubilization, siderophore synthesis, potassium solubilization, nitrogen fixation, ROS neutralization, abiotic and biotic stress tolerance (Figure 3) (**Amr *et al.*, 2015**). In another study, *Aspergillus niger* CSR3, an endophytic fungus, was isolated from the plant *Cannabis sativa*, was screened for growth-promoting activities like phosphate solubilization, presence of siderophores, production of IAA and gibberellins. It was further examined for its ability to cause the promotion of growth of mutant *waito*-C rice. All the plant growth attributes examined were significantly enhanced by treatment with CSR3m which was due to the presence of various types of gibberellins and IAA in the filtrate. (**Lubna *et al.*, 2018**). Endophytes are useful regarding environmental aspects. As microbes have the ability to degrade the various hazardous wastes (Figure 4). For example, bioformulation of *Trichoderma* sp. are used for the sustainable agriculture. There are many reports on *Trichoderma* sp., it is an avirulent, antagonist against pathogens as well as provides nutrition to the soil. The promotion of plant growth by endophytes through the production of phytohormones is probably the most recognized method of inducing structural and morphological changes in plants. Because endophytes help in production of phytohormones, endophytes find application in agricultural systems for sustainable agriculture. They improve the growth of plants by triggering systemic acquired response and induced systemic response. They help the plant in production of phytohormones like, jasmonic acid, ethylene, gibberellic acid, auxin, thus plants can improve their growth in normal and stress conditions.

Nitrogen (N_2), Potassium (K), Iron (Fe) and phosphorus (P) are fundamental supplement of nutrition of the plants. The N_2 and P are unit chemicals of the RNA, DNA and proteins. Moreover plants cannot use atmospheric N_2 because they are presented in the complex form. Also plants cannot survive in the deficiency of N_2 therefore require a fixed external supply of nitrogen source. Some endophytes have ability to fix the atmospharic nitrogen and they have potential in agriculture. Biological N_2 fixation has great potential as an alternative to chemical fertilizers. Various endophytes dissolve insoluble phosphate complexes present in rhizosphere and convert them into soluble phosphate for plant nutrition. Some endophytes produce iron-chelating compound, siderophore. Siderophores also specifically help iron-deficient plants to bind nitrogen, since nitrogen-fixing bacteria require Ferric and Molybdenum factors for synthesis and function of nitrogenase. K-solubilizing endophytes convert insoluble potassium into soluble one for plant uptake. There plant growth promoting qualities make endophytes potent alternative as a chemical fertilizer without harm the environment.

Environment safety concern of endophytes

Other than pharmaceutical and agriculture aspects, endophytes play a critical role in the environment safety. Environmental protection and sustainability are considered the highest priority and require great attention worldwide as they are crucial for future development. To ensure sustainability, waste management, the protection of natural resources and biodiversity, and the treatment of pollutants and pollutants are key areas that require priority attention. Today, protecting the environment from degradation is not just about eliminating pollutants and pollutants, but recycling and reusing harmful substances by transforming various waste materials into useful objects in an aesthetic and environmentally friendly way. As humans struggle to find a sustainable way to clean up polluted environments and waste, interest in using different microbes has grown and recently taken priority. With the advent of biotechnology, the potential of microorganisms for specific uses has been the subject of increasing attention and speculation. Microorganisms are unique in nature and often unpredictable. Microorganisms can be used as effective means to solve many environmental problems. The inevitability of the scientific and reliable use of microbes is ominous, and it has dictated an astonishing development of research and innovative tools to provide an effective way to protect our planet and the modern approach to biological waste management and environmental monitoring. There are many literatures for supporting this concept that microbes control pollution by utilizing pollutants as nutrition (Figure 4). Various industrial and household wastes are generated in huge amount in a day although some wastes are recycled but not all the waste treated properly. Some life-threatening pollutants, such as carbon dioxide (CO_2), methane, cynide gases, and radioactive contaminants are produced by various industries and released/ leaked in the environment due to human error and some microbes (for example; Geobacter, *Pseudomonas fluorescens*) utilize these contaminants for their survival but the mechanisms are unknown. Some serious impacts of these contaminants are, CO_2 generated by the different industries and released in the environment that cause lethal impact on the human and animal health along with global warming. Fossil fuels generation is very long process and fuels are used at a large scale in the industries and vehicles. After certain time, it will be difficult to supply fuel because natural sources are running out. Therefore, microbes are the alternative source of fuel requirements because produce biofuels by utilizing paper industrial wastes (cellulose, hemicelluloses and lignin). Plastic are used in the goods packaging (households, agricultural, pharmaceuticals, educational organizations, garments, electronics, and food industries). Excessive use of the plastic leads the soil, water and air pollution. Recycling the complete waste plastics is not possible. People dump plastic in the grounds or water resources and sometimes it is burnt which cause the air pollution. Therefore it is a need to degrade the plastic to reduce the pollution on the earth. Some microorganism shows the biodegradation ability of the plastics. In the Figure 4, it is showing the properties of the microbes to utilize the different waste, such as slaughterhouse waste, textile dyes, nylon, organic waste, heavy metals produced by industries. Other then these uses, microbes are used for management of waste water, arsenic biodegradation, bioremediation and fixation of acid rain (sulphur rain). Finally, it can be concluded that the use of microbes and microbiological technologies are sustainable approach, especially in the field of the environment and other important issues related to the environment.

Figure 4 Representation of various benefits of microbes in field of environment safety. Microbes help in cleaning and detoxify the environment from hazardous waste.

Table 1 Various role of microbes: as an endophyte and as a pathogen. Table is showing that a single microbe behaves as an endophyte and produces secondary metabolites for plant as well as a pathogen which causes disease in plants.

Microbe's name	As Pathogen			As Endophyte		
	Disease name	Host plant	References	Compound name	Host plant	References
Fusarium redolens	Root rot, crown rot and spear rot	Asparagus	**Baayen *et al.*, 2000**	Taxol production	Himalayan yew	**Garyali *et al.*, 2013**
Fusarium solani	Pathogenicity (many disease)	Soyabean and green bean	**Gray *et al.*, 1999**	Camptothecin drug production	Happy tree	**Kusari *et al.*, 2011**
		Shisham	**Rajput *et al.*, 2008**	Tropane production	*Datura metel*	**Naik *et al.*, 2017**
				Camptothecin drug production	*Camptotheca acuminate*	**Ran *et al.*, 2017**
Corynespora cassiicola	Leaf spot	Cotton plant	**Conner *et al.*, 2013**	Camptothecin drug production	*Nothapodytes nimmoniana*	**Murthy *et al.*, 2019**
		Ipomoea batatas (sweet potato)	**Xu *et al.*, 2016**			
		Solanum americanum	**Pereira *et al.*, 2019**			
	Target spot	Tomato	**Schlub *et al.*, 2007**			

Continue Table 1

		Soybean	**Koenning *et al*., 2006**	Decalactone derivatives production (flavor agent)	*Laguncularia racemosa*	**Ebrahim *et al*., 2012**
		Vaccinium corymbosum (blueberry)	**Onofre *et al*., 2016**			
	Rapid leaf fall	Rubber plant	**Chee *et al*., 1988**	Camptothecin drug production	*Nothapodytes nimmoniana*	**Bhalkar *et al*., 2016**
Colletotrichum fructicola	Anthracnose and shoft rot	Avocado	**Fuentes-Aragón *et al*., 2018**	Camptothecin drug production	*Nothapodytes nimmoniana*	**Murthy *et al*., 2019**
Colletotrichum gloeosporioides	Anthracnose disease	Mango	**Kamle *et al*., 2013**	Piperine production	*Piper nigrum*	**Chithra *et al*., 2014**
Pestalotiopsism icrospora	Black spot disease,	*Carya illinoinensis*	**Shi *et al*., 2015**	Taxol production,	*Taxus wallachiana*	**Strobel *et al*., 1996**
	Nut black spot	*Carya illinoinensis*	**Lazarotto *et al*., 2014**	Isopestacin	*Terminalia morobensis*	**Strobel *et al*., 2002**
Fusarium oxysporum	Fusarium wilt disease	*Solanum lycopersicum*	**Srinivas *et al*., 2019**	Vinblastine	*Catharanthus roseus*	**Zhao *et al*., 2000**
	Vascular wilt disease	*Cicerarietinum*	**Upasani *et al*., 2016**	Podophyllotoxin	*Sinopodophyllum*	**Kour *et al*., 2008**
	Panama disease	*Musa* sp. (banana)	**Pegg *et al*., 2019**	Camptothecin drug production	*Nothapodytesnimmoniana*	**Murthy *et al*., 2019**
Alternaria sp.	Leaf spot disease	*Helianthus* sp. (sunflower)	**Khodaei *et al*., 2013**	Vincristine	*Catharanthus roseus*	**Guo *et al*., 1998**
				Paclitaxal (Taxol)	*Salacia oblonga*	**Roopa *et al*., 2015**
Aspergillus niger	Black mold rot disease	*Allium cepa*	**Narayana *et al*., 2007**	Camptothecin drug production	Indian Piper betel	**Aswini and Soundhari, 2018**
	Black rot, Stem end rot and anthracnose disease	*Mangifera indica*	**Prakash and Raoof, 1989**	Gibberellic acid and indole acetic acid	*Cannabis sativa*	**Lubna *et al*., 2018**
	Aspergillus black rot	*Vitis* sp. (grapes)	**Perrone *et al*., 2007**			
	Necrotic leaf spot disease	*Zingiber officinale* (ginger)	**Pawar *et al*., 2008**			
	Tuber rot of yam	*Dioscorea*sp. (yam)	**Awuah and Akrasi, 2007**			

Endophyte as an antagonist for plants

Endophytes also behave as a pathogen for many host plants and causing many plant diseases. *F. oxysporum* is a causal agent of many plant diseases such as wilt disease in tomatoes, vascular wilt disease in chickpea (Figure 5). It can produce secondary metabolites similar to their host plant. Competition is a strong mechanism used by endophytes in preventing pathogens from colonizing the host tissue. Endophytes possess the ability to colonize many plant tissues systemically or locally (**Kumar *et al*., 2020**). For example, they act through colonization and the lurking of nutrients that are available and by occupying the position that is available for pathogens to carry out their activities (**Kumar *et al*., 2020**).

A study conducted by **Baayen *et al*.** in the year **2000** showed two *Fusarium* species, namely *F. oxysporum* f.sp. *asparagi* and *F. proliferatum*. These species were known to be involved in the case of root and crown rot complex of Asparagus. The analysis report of RFLP showed that the rDNA internal transcribed spacer region along with AFLP fingerprinting identified eight strains from asparagus explicitly as *F. redolens*. Out of these, four were tested and found to be pathogenic against asparagus. The study along with the literature reports identify *F. redolens* as a host-specific pathogen involved in root, crown and also spear rot of asparagus, which is classified as *F. redolens* Wollenw. f.sp. *asparagi*. **Mohandoss and Suryanarayanan (2009)**, employed fungicide on the mango leaves moreover they showed elimination of specific endophytes which allowed space for pathogens to proliferate. The mechanism used for competition by most endophytes usually takes place in combination with other mechanisms, instead of acting independently. Since the control method employed by endophytes is often local, they will, however, need to systematically colonize the part of the host where most pathogens may attack. The colonization of the root of oilseed rape with endophyte *Heteroconium chaetospira* could not successfully prevent clubroot symptoms (**Lahlali *et al*. 2014**). The result, therefore, indicates the limitations that may be encountered with competition as a biocontrol method, as it may be inactive when there is a high presence of microorganisms causing disease. The symptoms of Phytophthora sp. were successfully reduced when treated through a foliar application with mixtures of endophytes from leaves of cacao tree leaves, thus showing competition as one mechanism of disease suppression in a plant. However, some of the strains were also observed to produce other active metabolites which are an indication that, competition might not be the only mechanism used in controlling the disease (**Arnold *et al*., 2003**).

Phytotoxins are bioactive compounds isolated from microbes that also plant pathogens. They have been researched for as long as a century and treated as the initiators and virulence factors of infections in predisposed plants. Examples could be the toxins that are host-specific and produced by three separate *Cochliobolus* sp. These caused severe blight infections of crops that are economically important. *Helminthosporium carbonum* produces HC-toxin, which is host specific and causes Northern leaf blight of maize. This inhibits histone deacetylase of maize. *C. heterostrophus* is responsible for Southern Corn Leaf Blight, produces T-toxin. This is considered as one of the vilest plant infections treated as epidemics in modern times. *C. victoriae* produces secondary metabolite, called victorin. This causes a distressing epidemic in Victoria race of oats. This was industrialized by plant breeders, to make oats resistant to the disease crown rust. Therefore, endophytes are introduced to the plant because they produce antibiotics that suppress pathogens**.**

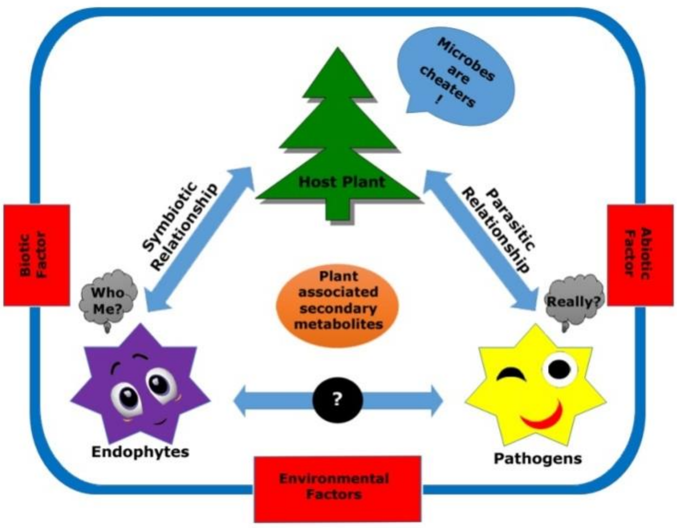

Figure 5 Illustration of plant- microbes (endophytes and pathogens) interaction.

CONCLUSION

The relation between plant and microbes is managed by their virulent and defence genes and surrounding environmental factors. Same microbe shows dual behavior inside plant based on the plant's genes and environment. Endophyte microorganisms are fascinating life forms that survive in a range of host plants. Their access to the complex systems of different plants offers a promising field of research in the fields of microbiology, pharmacology and agricultural sciences. The involvement of different plants as well as molecules of microbial origin is thought to play an important role in the development of symbiotic relationships with different plants. Their entry into plants has been documented to provide different benefits to the host system, including tolerance to a variety of biotic and abiotic stresses and improvements in crop nutrition and productivity. Despite the well-developed immune system of the plant, endophytes have evolved strategies to enter the host system. It has also been suggested that plants have evolved to internalize microorganisms for nutrition and defence. On the other hand, endophytes produce plant secondary metabolites with medicinal values although the exact pathway that leads endophytes to manufacture the bioactive metabolites is still extremely complex. The plant drugs can be product by the microorganisms by genetic engineering and microbiological techniques. Not only for agricultural and medicinal purposes, microbes can be used for environmental safety, biofuel production, and for other industrial purpose.

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