

ENDOPHYTES: HIDDEN ALLIES IN PLANT HEALTH AND ECOSYSTEM RESILIENCE

Abstract

Endophytes living inside the tissues of plants, play an important role in determining plant health and ecosystem resilience. It has drawn more and more attention in recent years in light of their mutualistic interactions with their host plants and the larger ecosystem. Endophytes have evolved to intricately interact with their hosts through evolutionary processes, which has benefited both parties in different ways. Endophytes have been discovered in a variety of plant species, including grasses, trees, and crops. These endophytes support a wide range of symbiotic relationships. These connections help plants better absorb nutrients, resist diseases and pests, and are more resilient to abiotic stresses like drought and severe temperatures. Endophytes' ability to modulate plant growth and physiology has shown potential implications in sustainable agriculture, providing an eco-friendly alternative to traditional chemical interventions. Furthermore, their protective mechanisms have proven pivotal in promoting plant health in natural ecosystems, contributing to biodiversity conservation and ecosystem stability. The chapter explored different fascinating studies carried out to identify the mechanisms underlying endophyte-plant interactions. The complexity of these relationships has been revealed through different research into the underlying biochemical pathways and genetic components, opening up new opportunities for biotechnological applications in agriculture and ecological restoration. Also, hidden presence within the green tapestry of nature makes them an indispensable ally, underscoring the profound interdependence that governs life on Earth. Harnessing their potential could usher in a new era of

Authors

Abinash Show

Department of Microbiology
Barrackpore Rastraguru Surendranath
College
Kolkata, India

Sneha Biswas

Department of Microbiology
Barrackpore Rastraguru Surendranath
College
Kolkata, India

Anirban Mandal

Department of Microbiology
Mrinalini Datta Mahavidyapith
Kolkata, India

Arindam Mukherjee*

Department of Botany
Mrinalini Datta Mahavidyapith
Kolkata, India
arindammukherjee6751@gmail.com

sustainable practices, fostering harmony between human activities and the delicate balance of the natural world.

Keywords: Endophytes, Ecosystem, Symbiotic relationships, Endophyte-plant interactions

I. INTRODUCTION

Interactions between plants and microbes offer several benefits, especially for good bacteria. Endophytes, or plant-associated bacteria, are internal inhabitants of plants. They have direct effect over the host plant cells and mediate reactions as a result of interactions without causing harm to the host or evoking severe defense reactions. Numerous studies have shown that endophytic bacteria, also known as plant tissue bacteria, are essential for the growth and fitness of a wide range of monocot and dicot plant species. Endophytes are bacteria and fungi that thrive in seemingly healthy internal plant tissues and are either facultative or obligatory symbiotic microbes. Gram-positive bacteria are recognized to affect plant physiology and development among endophytic microbes. The control of soil-borne diseases, plant growth, symbiotic-mutualistic, commensalistic, and trophobiotic interactions, as well as the support of the host plant's defense against environmental stress (Ryan et al., 2008). The structure of an endophytic community can be influenced by a number of variables, including environmental circumstances, plant-microbe and microbe-microbe interactions, and others (Ryan et al., 2008). By producing phytohormones, low molecular weight compounds, enzymes, antimicrobial substances like antibiotics, and siderophores, several bacterial endophytes have been demonstrated to support plant growth and increase nutrient uptake. Some endophytes have higher pathogen resistance, which makes them perfect candidates for biological control. On Earth, plants play a significant role in the fixation of atmospheric CO₂. Plants can synthesize an almost unlimited variety of carbonaceous molecules and reduce the carbon present in CO₂ thanks to the energy they obtain from solar radiation. This makes plants particularly appealing as nutrient reservoirs for such bacteria because photosynthetic provide as key sources of carbon, nitrogen, and energy for bacteria and other plant-associated heterotrophic microorganisms. Endophytic bacteria perform and exhibit a variety of growth and biocontrol features through different physical, molecular and biochemical pathways. It has been demonstrated that bacterial endophytes inhibit the onset of disease by facilitating the *de novo* synthesis of new chemicals and antifungal metabolites. Different endophytic strains are used for novel compounds isolation and may lead to the discovery of new medications that can effectively treat diseases in people, plants, and animals. Many endophytes have demonstrated a natural potential for xenobiotic degradation or may function as vectors to introduce degradative features, in addition to the creation of new compounds. Endophytes are well known for promoting plant growth by increasing nitrogen fixation or secreting substances resembling plant hormones (Hurek and Reinhold Hurek 2003). They are also known to produce a variety of secondary metabolites with both industrial and medical uses. Furthermore, endophytes' ability to control plant diseases is one of its beneficial traits since, unlike chemical pesticides, they can assist sustainable agriculture and do not harm the environment or have toxic side effects. It is believed that via rhizosphere, endophytic bacteria become colonise in various plant parts/tissues such as roots, stem, leaves, flowers, fruits, and seeds (James et al. 2002). Bacterial endophytes are better protected from abiotic stresses like extreme variations in temperature, pH, nutrient, and water availability as well as biotic stresses like competition than free-living, rhizosphere or phyllosphere microorganisms (Rosenblueth and Martinez-Romero 2006). In addition, endophytic bacteria colonise habitats that are better suited for developing mutualistic partnerships with plants. Endophytic bacteria have primarily been studied after being cultured in lab media, but a more comprehensive plan is emerging that makes use of techniques that do not require the bacteria to be cultured and that analyze sequences from bacterial genes obtained from DNA isolated from inside plant tissues. These

beneficial effects have been the main focus of endophytic bacteria study to comprehend the interactions between bacterial endophytes and their hosts' plants.

II. TYPES OF ENDOPHYTES

Endophytes establish various associations with plants, residing within their tissues as either bacteria (such as actinomycetes or mycoplasma) or fungi. Over 200 genera across 16 bacterial phyla are known to engage with endophytes, with a significant representation from Actinobacteria, Proteobacteria, and Firmicutes. These endophytic bacteria encompass both gram-positive and gram-negative types, including *Achromobacter*, *Acinetobacter*, *Agrobacterium*, *Bacillus*, *Brevibacterium*, *Microbacterium*, *Pseudomonas*, *Xanthomonas* etc. The diversity extends further to bioactive metabolites, many with antimicrobial and anticancer properties. *Streptomyces*, for instance, contributes substantially to this diversity, with 76% of such compounds attributed to this genus.

Actinomycetes, classified within the *Actinobacteria* phylum, are prokaryotic microorganisms that resemble fungi due to their mycelium-like structures and spore formation (Chaudhary et al., 2013; Barka et al., 2016). Historically, they were thought to bridge the gap between fungi and bacteria (Barka et al., 2016), yet their likeness to fungi is only surface-level. While sharing some characteristics with bacteria, actinomycetes exhibit thin cells, a prokaryotic nucleoid-organized chromosome, and a peptidoglycan cell wall. Among endophytes, actinomycetes stand out for producing unique chemical compounds with medicinal significance (Gayathri and Muralikrishnan, 2013; Singh and Dubey, 2015). Many antimicrobial agents are attributed to endophytic actinomycetes, with the genus *Streptomyces* being notably prevalent (Zhao K. et al., 2011; Golinska et al., 2015). *Streptomyces species* have yielded diverse compounds of interest like munumbicins, naphthomycin, clethramycin, coronamycin, edarmycin, saadamycin, and kakadumycins. Other active compounds discovered from actinomycetes include paclitaxel from *Kitasatospora sp.*

Mycoplasma species have also been documented as endophytes in plants. Reports indicate that endophytic mycoplasma species establish a symbiotic relationship with certain red algae, including *Bryopsis pennata*, and *B. hypnoides* (Hollants et al., 2011). However, concrete evidence regarding their applications, extraction sources, or utilization against foodborne diseases or other pathogens remains unverified.

Fungi, as heterotrophic organisms, engage in diverse life cycles that encompass symbiotic associations with various autotrophic organisms (Dayle et al., 2001). Endophytic fungi are categorized into two primary groups based on their phylogeny and life history traits. These groups are clavicipitaceous, which primarily infect specific grasses in cooler regions, and non-clavicipitaceous endophytes, originating from asymptomatic tissues of non-vascular plants, ferns, allies, conifers, and angiosperms. The latter group is confined to the Ascomycota or Basidiomycota categories (Jalgaonwala et al., 2011; Bhardwaj and Agrawal, 2014; Muhilan and Chattopadhyay, 2023).

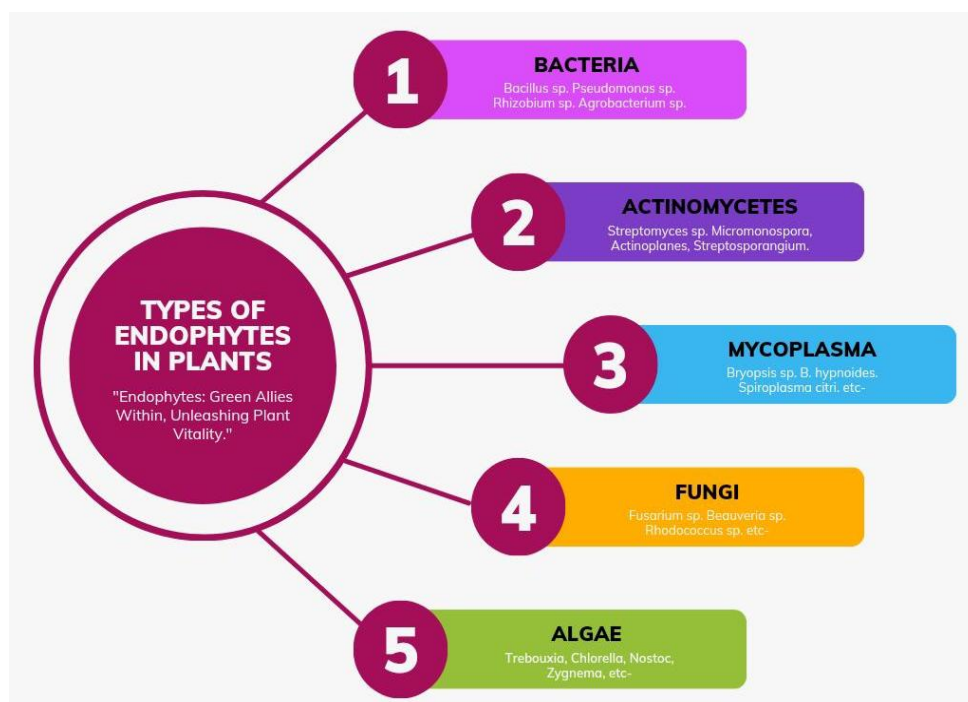


Figure 1: Types of Endophytes Present in Plants

Endophytic fungi contribute significantly to medicine production, yielding widely used antibiotics and anticancer drugs. For instance, Penicillins extracted from *Penicillium* sp. exhibit cytotoxic effects against numerous cell lines. Taxol, isolated from *Taxomyces andreanae*, stands out as an effective anticancer drug derived from endophytic fungi. Various other compounds like clavatul (*Torreya mairei*), sordaricin (*Fusarium spp.*), jesterone (*Pestalotiopsis jesteri*), and javanicin (*Chloridium spp.*) showcase potent antibacterial and antifungal properties against numerous foodborne infectious agents (Jalgaonwala et al., 2011). Furthermore, pestacin, isolated from *P. microspora*, exhibits notable antioxidant characteristics.

III. DIVERSITY AND DISTRIBUTION OF BACTERIAL ENDOPHYTES

More than 300,000 plant species have one or more endophytes. In plant tissues such as leaves, roots, seeds, stems, fruits, ovules, and tubers, endophytic bacteria have been seen, and they are typically found in intercellular spaces and xylem vessels (Reinhold Hurek and Hurek 1998). Both monocotyledonous and dicotyledonous plants, including herbaceous crop plants like sugar beetroot and maize as well as woody tree species like oak and pear have produced endophytic bacteria. Gram-positive and Gram-negative bacterial species isolated from a variety of host plants are both categorized as bacterial endophytes. Endophytic population diversity varies with bacterial species and host genotypes; it is also influenced by the host's developmental stage and inoculum density. According to reports, endophytes are related with more than 200 genera and 16 phyla of bacterial species, the majority of which being *Actinobacteria*, *Proteobacteria*, and *Firmicutes*. These actinomycetes have historically been thought of as intermediate organisms between fungi and bacteria. Endophytic actinomycetes have the ability to create a wide range of chemical substances with distinctive structures that have significant medical value. Fungi are a heterotrophic group of organisms with a diversity of life cycles that include symbiotic partnerships with a wide range of

autotrophic creatures. On the basis of their phylogeny and lifecycle characteristics, endophytic fungi have been divided into two major categories. These include the non-clavicipitaceous endophytes, which are from asymptomatic tissues of nonvascular plants, ferns and allies, conifers and angiosperms and are restricted to the Ascomycota or Basidiomycota group, as well as the clavicipitaceous endophytes, which infect some grasses restricted to cool regions and infect some grasses that are infected by them. Some of the most widely used antibiotics and anticancer medications are made by endophytic fungus. Numerous cell lines are cytotoxic to penicillanols, which are obtained from *Penicillium* species. The most successful and effective anticancer medicine ever isolated from endophytic fungi is called taxol, which was isolated from *Taxomyces andreanae*.

IV. INTERACTION OF BACTERIAL ENDOPHYTES WITH HOST

The relationship between endophyte and plant is referred to as symbiotic. Colonisation, which is influenced by genotype, growth stage, physiological status, type of plant tissue, agricultural practises, and environmental factors like temperature, water supply, and nutrients, governs the interaction between the host plants and the endophytic community. The glucuronidase reporter system can also be used to see endophytic bacteria colonising internal plant tissues (James et al 2002). The interface between the soil and the roots, known as the rhizosphere, is where the complex interactions between the soil microorganisms and the plant occur (Bulgarelli et al 2012). A variety of microorganisms that may endure in root exudates and compete with one another are found in the rhizosphere. Strains that were equally competitive for colonising the rhizosphere and inside root tissues were discovered by Rosenblueth and Martnez-Romero in 2004. Some bacteria must pass through crevices created at the zone of elongation and differentiation of the root or at the formation of lateral roots in order to colonise the plant. Early endophytic colonisation varied between cultivars in several experiments, but later endophytes were recovered from the various cultivars in about comparable numbers (Pillay and Nowak 1997). According to Araujo et al. (2001), fungal colonisation may influence endophytic bacterial colonisation, or it may be the other way around. *Rhizobium etli* strains differ from one another in their propensity to colonise, and these variations may be due to variations in the genome's composition. Endophytes may actively contribute to colonisation as well. An important step towards endophytic colonisation is the adhesion to plant surfaces, which is accomplished by *Azoarcus sp.* Type IV pili. Additionally suggesting an active host role in the colonisation process, the plant hosts varied in how well the same bacterium could colonise them endophytically. However, phyllosphere bacteria may also be a source of endophytes. Some rhizospheric bacteria can colonise the interior roots and stems, demonstrating that these bacteria constitute a source for endophytes (Germaine et al. 2004). Furthermore, it's possible that communication with the plant root and the following colonisation process are facilitated by bacterial quorum sensing chemicals. Given that some plant extracts have been demonstrated to have quorum quenching properties that could defend them against infections and that some quorum sensing molecules have been demonstrated to directly promote plant growth, plants are likely directly involved in quorum sensing as well (Schikora et al 2016). Additionally, LuxR homologs were discovered in a number of *Populus deltoides* endophytes, which are thought to be involved in reacting to chemicals derived from plants (Schaefer et al 2016). Additionally, this study discovered that several endophyte genomes had quorum sensing gene pairs of the LuxR-LuxI type, highlighting their significance in the endophytic and plant-microbe interactions in great detail (Hartmann et al 2014).

V. BENEFICIAL RELATIONSHIP BETWEEN ENDOPHYTES AND PLANTS

The endophyte and the host plant maintain a symbiotic relationship between them in which both of them become benefited. The host plant offers the microbes safe havens, and they in turn create metabolites that boost nutrient absorption, altering plant development and biomass accumulation. During this association, endophytes may acquire certain genetic information to create particular bioactive compounds comparable to the host plant by horizontal gene transfer. As a result, in this symbiotic relationship, the plants provide nutrients to the microbes and in exchange, the microbes give their potential use in biological control of diseases. Endophytes are distinct from biocontrol strains of rhizosphere bacteria, according to research on the impact of endophytic bacteria on plant development, as they not only promote the growth of plant but also prevent the growth of pathogenic microbes. Endophytic bacteria can control osmotic pressure, stomata function, or plant root development, which will benefit the health of the plants as a whole (Ulrich et al 2008). Therefore, it is necessary to develop economically viable means of using this endophyte trait in a variety of human activities related to plant culture, including food production, forestry, landscaping, and other related activities. Plants use Nitrogen as an essential mineral for survival and growth. Several reports regarding nitrogen fixing bacteria have recently focused on the idea of symbiotic relationships also seen in many non-leguminous plants, like maize, wheat, sugarcane and sorghum (de Carvalho et al 2011). As numerous studies have demonstrated, nitrogen is crucial, particularly for host plants that thrive in soils with low nitrogen levels. Diazotrophic (*Gluconacetobacteria diazotrophicus*) bacteria that fix nitrogen have recently been reported from the sugarcane plants. Since the endophyte can fix nitrogen and multiply, it has been hypothesised that it can meet the host plant's needs for nitrogen (Baldani et al 2014).

In plants, phosphate promotes disease resistance and serves as a precursor for the synthesis of several enzymes used in different physiological processes (Thakur et al 2014). The conversion of an inaccessible and insoluble form of phosphate to an accessible and soluble form is done by the processes of solubilisation and mineralization. The processes are mediated by phosphatases (Bashan et al 2013). Chelators, which are organic acids, are created during the phosphate solubilisation process by phosphate solubilizing bacteria and aid in the removal of metals (Singh et al 2020). The bacteria which solubilize phosphate enhance the functionality, diversity, and ecology of plants in environments by providing them with the essential nutrients. However, as endophytic phosphate solubilizing bacteria are essential for sustainable agriculture and environmental protection, additional study of these organisms is required, from the molecular level through their practical uses. However, as endophytic phosphate solubilizing bacteria are essential for sustainable agriculture and environmental protection, additional study of these organisms is required, from the molecular level through their practical uses. Some endophytic bacteria can solubilize the inaccessible potassium into forms that can be used by the plant. Endophytic bacteria have focussed in agriculture as soil root inoculant due to their ability to penetrate and colonise the interiors of roots (Yuan et al 2015). Endophytic bacteria that solubilize potassium have also been shown to reduce other environmental pressures, like salt stresses, and enhance output in general (Feng et al 2019). Unfortunately, the majority of endophytes that have been isolated and studied were chosen to study other growth promoting features like IAA and nitrogen, omitting the significance of K for plant growth and defence. Zinc is a crucial trace element required by plants and all living

members. So endophytic bacteria which solubilize zinc need increased focus in practical applications and research. Zinc solubilizing bacteria are needed for providing and transforming soil inorganic zinc into a form that host root may reach (Kamran et al 2017). This will ultimately protect our environment by ensuring food and nutrition security.

Plant growth promoting bacteria (PGPB) can help the plant in a variety of ways. Phyto-pathogens counteract several stresses on plants and aid in the restoration of harmed or degraded habitats. Endophytic bacteria are involved in the growth promotion of several plants, like tomato, potato, lettuce, corn, rice, cucumber, and cotton. According to a report 10% of the bacterial isolates found inside tubers of potato were found to encourage host health. Besides a direct method, plant growth enhancement may also result from the endophyte's introduction suppressing a harmful microbiota. Endophytes, on the other hand, provide another option for creating biological control techniques because of the various sites they have colonised. Endophytes have a reputation for causing host plants to become resistant to diseases. They are very much known for encouraging host plant development and growth in a variety of environmental and ecological circumstances.

VI. ENDOPHYTES ASSISTED NUTRIENT UPTAKE IN PLANTS

Endophytic bacteria are the helpful microorganisms for plants are found inside plants and which can improve plant growth in different situations. Endophytes cause direct benefit for host plants by controlling phytohormones and enhancing plant nutrient intake linked to growth. Here is a brief explanation of how plants absorb nutrients:

- 1. Colonization:** Endophytes, which are microorganisms like bacteria or fungi, colonize several parts of the host plant, like stems, roots and leaves. They establish a symbiotic relationship, residing within the plant's tissues without causing harm.
- 2. Secretion of Substances:** Endophytes produce substances like enzymes and metabolites that help break down organic compounds in the soil so that nutrients are more readily absorbed by plants. These substances aid in the transformation of complicated nutrients into simpler shapes that plants can absorb.
- 3. Nutrient Mobilization:** Through their enzymatic activities, endophytes help release crucial nutrients, such as phosphorus, nitrogen and micronutrients of organic matter in the soil or from mineral complexes that might otherwise be unavailable to the plant.
- 4. Increased Surface Area:** The presence of endophytes can lead to the formation of structures like mycorrhizae, which are fungal networks that extend the plant's root system. This extended root network increases the plant's capacity to explore a larger soil volume, thereby accessing a wider range of nutrients.
- 5. Increased Nutrient Uptake:** Endophytes can encourage plant root growth, which increases the absorbance of nutrients by plants from the soil. They might also make the nutrient transporters in the roots of the plant more active, which would make it easier for nutrients to be absorbed.

6. **Nutrient Exchange:** In some instances, endophytes absorb nutrients from rhizosphere and trade them with the hosts for other advantageous substances. This reciprocal exchange improves the plant's access to nutrients.
7. **Enhancement of Plant Growth:** Plants may experience greater growth and development as a result of improved nutrient uptake and utilization. Increased biomass, improved root architecture, and generally healthier plant physiology are examples of this.
8. **Stress Tolerance:** Endophytes can also contribute to the plant's stress tolerance, which indirectly aids nutrient uptake. By helping plants withstand environmental stresses like drought or high salinity, endophytes enable plants to continue nutrient uptake even under challenging conditions.

Endophyte-assisted nutrient uptake involves a range of mechanisms that collectively improve the accessibility of essential nutrients in the soil for plants. Through their enzymatic activities, enhanced root growth, and potential nutrient exchange, endophytes play a vital role in enhancing nutrient obtainability, helping to the overall health and vitality of hosts.

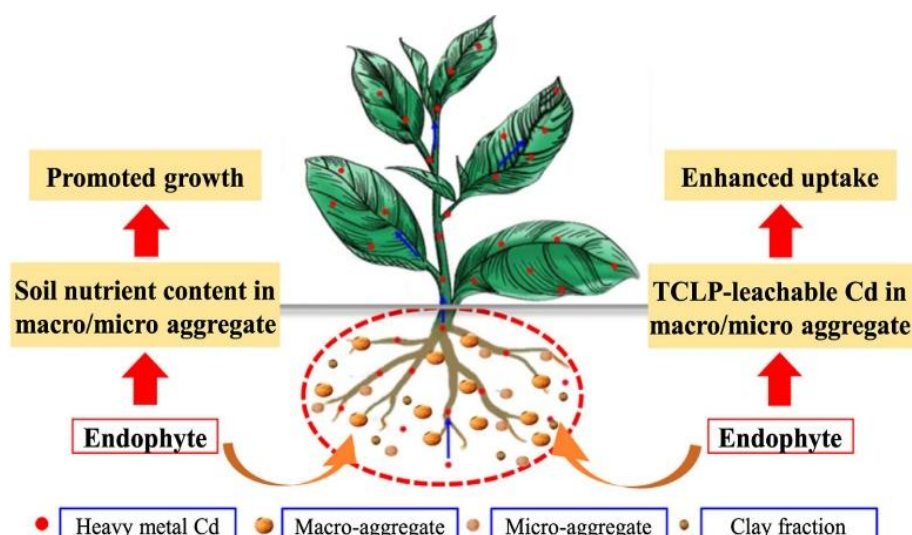


Figure 2: Endophytes Assisted Nutrient uptake Mechanism in Plants

VII. ENDOPHYTIC BIOACTIVE COMPOUNDS

Endophytes are known to synthesize a range of bioactive compounds within a single host or microorganism, offering a valuable resource for drug development against diverse diseases. These compounds hold promising applications across agriculture, food, medicine and cosmetics industries (Strobel and Daisy, 2003; Jalgaonwala et al., 2011; Shukla et al., 2014; Godstime et al., 2014;). These secondary metabolites encompass different functional groups such as benzopyranones, alkaloids, quinones, phenolic acids, flavonoids, terpenoids, steroids, tannins, saponins, xanthenes, tetralones, etc.

The extraction of endophytic metabolites is influenced by various factors including the climatic conditions, geographical location and season of sample collection (Shukla et al.,

2014). Nonetheless, recent years have seen the development of a revolutionary synthetic process, enhancing the feasibility, efficiency, and convenience of extracting from host and other natural sources (Hussain et al., 2012). The production of biologically compounds by microbes is intricately linked to the evolutionary trajectory of host-microorganisms, which might have accumulated genetic blueprint from higher plants. This incorporation allows them to adjust more effectively to the environment of host plants and fulfill functions like protection against insects, pathogen and grazing animals (Strobel, 2003). Some commonly encountered bioactive secondary compounds collected from endophytes are given below in detailed.

Taxol or paclitaxel - a complex diterpene alkaloid, is a promising anticancer agent derived from an endophyte *Metarhizium anisopliae*, commonly found in bark of Taxus tree. This compound stands as one of the most notable advancements in anticancer agents (Zhang et al., 2009; Visalakchi and Muthumary, 2010; Jalgaonwala et al., 2011). Camptothecin, extracted from *Nothapodytes foetida*, has antifungal and cytotoxic properties (Joseph and Priya, 2011; Han and Rahman, 2012). Huperzine A (HupA), originating from *Huperzia serrata*, behaves as a cholinesterase inhibitor (Nair and Padmavathy, 2014). Lignans, like emetics, cathartics and cholagogue from endophytic *Podophyllum hexandrum*, act as reported anticancer agents (Konuklugil, 1995). Resins, including teniposide and etoposide from *P. emodi*, exhibit potent anticancer activity (Konuklugil, 1995). Compounds such as ampicillin, oxacillin, gallic acid, catechin and cefalexin demonstrate bactericidal activities (Akiyama et al., 2001). Terpenoids have antineoplastic, antibacterial and antiviral effects, and also show gastrointestinal stimulation (Jalgaonwala et al., 2011; Godstime et al., 2014). The endophytic fungus *Cytonaema sp.* produces helvolic acid a triterpenoid, known for its potent antibacterial properties (Kumar et al., 2014).

- 1. Antibacterial Properties of Metabolites from Fungal Endophytes:** In recent times, fungi have gained recognition as a valuable source of novel bioactive compounds (Samuel et al., 2011). The groundbreaking discovery of penicillin marked a significant milestone, showcasing its inhibitory effect on Gram-positive bacteria (Demain and Sanchez, 2009). Extracts from *Penicillium citrinum* and *Aspergillus ochraceus* showed broad-spectrum antibacterial function, effectively inhibiting the growth of various microorganisms, notably *Pseudomonas aeruginosa*. Hypericin and its primary precursor Emodin showed antimicrobial efficacy against fungi and bacteria such as *Candida albicans*, *Aspergillus niger*, *Klebsiella pneumoniae*, *Staphylococcus sp.* and *Salmonella enterica*. These effects were observed in an endophytic fungus found in a medicinal plant (Kusari et al., 2012). *Pichia guilliermondii*, endophytically grown in *Paris polyphylla* var. *Yunnanensis*, gives three steroids— ergosta-5,7,22-trienol, 22-dien-3b-ol, 5a,8a-epidioxyergosta-6, ergosta-7,22-dien-3b,5a,6b-triol—and helvolic acid, a triterpenoid. These compounds exhibited potent antibacterial activity against a range of test bacteria (Zhao J. et al., 2010).
- 2. Antiviral Properties of Metabolites from Endophytic Fungi:** Another intriguing dimension involves harnessing secondary metabolites from endophytic fungi to suppress viral growth. While the isolation of antiviral compounds from endophytes remains a work in progress, some promising bioactive agents have already come to light. Given the rise of resistance and multi-resistance against existing medications, coupled with adverse effects and high costs associated with current therapies, the urgency for novel antiviral drugs has

grown. This urgency is further underscored by the HIV/AIDS epidemic and the emergence of AIDS-associated opportunistic infections, including polyoma virus and cytomegalovirus.

Among notable discoveries, Cytonic acid A and B show inhibitory effect on human cytomegalovirus protease. These compounds are extracted from *Cytospora* sp. an endophytic fungus found in *Quercus* sp. (Guo et al., 2008). In another significant finding, Fukami et al. (2000) conducted experiments on the fungus *Trichoderma atroviride* FKI-3849, leading to the identification of two diterpene compounds wickerol A and B as new anti-influenza viral agents having a unique fused 6-5-6-6 ring skeleton. *Pestalotiopsis theae* the fungal strain sourced from an undisclosed tree on Jianfeng Mountain, has yielded pestalothol C. This compound, with anti-HIV properties, has been successfully produced by Chinese researchers (Li et al., 2008).

- 3. Anti-cancer Properties of Metabolites form Endophytic Fungi:** Cancer encompasses a collection of diseases characterized by unchecked cell growth, leading to the loss of properties such as density and anchorage dependence in tumors, contact inhibition, and the inability to undergo apoptosis, thereby impeding organismal survival (Pimentel et al., 2010). Remarkably, endophytic fungal isolates have furnished evidence of yielding anticancer secondary metabolites, offering a prospective avenue for developing novel drugs from various sources, including plants, microorganisms, and marine entities (Firakova et al., 2007).

Endophytes are scrutinized for obtaining bioactive compounds with their potential anticancer activity (Qi et al., 2009). Taxol one of the most important anticancer agent isolated from endophytes. It is an intricately structured diterpenoid, originates from yew species of the *Taxus* genus (Bacon and White, 1994). Taxol and its derivatives incite the polymerization of microtubules during progression of cell division, influencing cellular processes (Tan and Zou, 2001). In China, a potential anti-neoplastic agent Camptothecin isolated from an endophytic fungus in *Camptotheca acuminata* Decne (Wall et al., 1966). This compound serves as a pivotal precursor for the synthesis of topotecan and irinotecan, both recognized anticancer drugs, alongside 10-hydroxycamptothecin (Uma et al., 2008). A mycotoxic compound secalonic acid D, classified as an ergochrome is extracted from an endophytic fungal strain of mangrove plant, exhibits robust anticancer activity (Bills et al., 1996; Qi et al., 2009).

- 4. Antifungal Properties of Metabolites form Endophytic Fungi:** Endophytic fungi offer a diverse array of antifungal metabolites, pivotal in combating numerous disease-causing fungi. Fusapyrone and deoxyfusapyrone - two important alpha pyrones compounds, isolated from *Fusarium semitectum* identified by Altomare et al. (2000), are antifungal. These compounds demonstrated substantial efficacy against pathogenic and toxin producing filamentous fungi, like *Alternaria alternata*, *Botrytis cinerea*, *Aspergillus flavus*, *Phoma tracheiphila*, *Cladosporium cucumerinum* and *Penicillium verrucosum*.

Pathogenic fungi like *Cryptococcus neoformans*, *Candida albicans* and *Aspergillus fumigatus* pose health threats to humans. Broad spectrum antifungal polyene compounds like amphotericin B, nystatin, and natamycin produced by *Streptomyces* sp. exhibit inhibitory effects for various fungi, such as *Aspergillus* sp. And *Candida* sp.

(Gupte et al., 2002; Hay, 2003; Iznaga et al., 2004; Gohel et al., 2006). Recent work by Wu et al. (2015) led to the isolation of two novel cytotoxic and antifungal components, namely (4S,6S)-6-[(1S,2R)-1,2-dihydroxybutyl]-4-hydroxy-4-methoxytetrahydro-2H-pyran-2-one and (6S,2E)-6-hydroxy-3-methoxy-5-oxodec-2-enoic acid as well as three other compounds, LL-P880, Ergosta-5,7,22-trien-3b-ol and LL-P880 as secondary metabolites from *Dendrobium officinale*. This investigation highlighted the remarkable antifungal prowess of these compounds, effective against *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Trichophyton rubrum* and *Candida albicans*.

- 5. Anti-diabetic Properties of Metabolites form Endophytic Fungi:** Common diabetes i.e. Diabetes mellitus (DM), is a prevalent disorder marked by impaired insulin secretion and action, originating from beta cell dysfunction in the liver. The resultant insulin deficiency leads to elevated blood sugar levels (hyperglycemia), adversely affecting carbohydrate, protein and fat metabolism. Diabetes related complications like retinopathy, nephropathy, neuropathy, cardiovascular issues and ulceration further compound the complexities of this condition. This extensive range of diabetes encompasses heterogeneous diseases (Bastaki, 2005), prompting the development of numerous medications and drugs from diverse biological sources for its management. Endophytic microorganisms, sharing the capability to synthesize bioactive compounds with their hosts, offer a potential avenue for sourcing anti-diabetic materials (Dompeipen et al., 2011).

Acarbose, an α -glucosidase inhibitor of endophytic fungal origin, stands out as widespread oral agents employed to mitigate postprandial control of glucose (Hanefeld and Schaper, 2007). Alongside these, various natural products from micro-organisms and medicinal plants show promise as α -glucosidase inhibitor (Suthindhiran et al., 2009; Elya et al., 2012). Similarly, Ramadanis et al. (2012) embarked on isolating and characterizing α -glucosidase as anti-diabetic bioactive compounds from endophytic fungi found in *Swietenia macrophylla* seeds. In the African forest, *Pseudomassaria* sp. Yielded a non-peptide fungal metabolite with insulin-like properties. This compound remains intact through the elementary canal and can be administered orally. Remarkably, it demonstrated significant decrease in blood glucose in a two-mouse model, signaling potential advancements in diabetes treatment.

- 6. Antioxidant Properties of Metabolites form Endophytic Fungi:** Endophytic fungi assume a crucial role in generating valuable antioxidant bioactive compounds. Scientists investigated thirty-nine fungi edophytically found in five Thai medicinal plants, observing their production of phenolic compounds. These phenolic compounds, renowned for their potent antioxidant properties and robust reducing capabilities, play a pivotal role. Among the fungi examined, *Eupenicillium shearii* CMU18 exhibited the highest phenolic compound content, along with notable ABTS+ radical scavenging ability, exceptional reduction potential, and a capacity to inhibit lipid peroxidation in liver tissue of rat.

Additionally, *Paraconiothyrium spp.*, found in the leaves of *Rheedia brasiliensis*, exhibited commendable antioxidant attributes. The crude extract from *Paraconiothyrium spp.* displayed the capacity to curtail cell growth of immortalized human keratinocytes while also exhibiting efficacy against psoriasis through the reduction of free radicals.

7. Insecticidal Properties of Metabolites form Endophytic Fungi: Endophytic fungi produce different insecticidal compounds that play a pivotal role in making host plant resistant against a range of insect pests responsible for causing severe damage to crops. As for example, *Nodulisporis* sp. an endophytic fungus in *Bonita daphnoides*, synthesizes indole diterpenes and nodulisporic acid. These compounds show crucial insecticidal properties, particularly against blowfly caterpillars (Demain, 2000). Similarly, *Muscodar vitigenus*, isolated from *Paullina paullinioides*, yields naphthalene, which serves as a potent insect repellent. From the endophytic fungus *Gaultheria procumbens*, two novel biopesticide compounds—5-hydroxy-2-(1-oxo-5-methyl-4-hexenyl) benzofuran and 5-hydroxy-2-(1-hydroxy-5-methyl-4-hexenyl) benzofuran —have been searched which are with high level of toxicity against spruce budworm and its larvae (Findlay et al., 1997). Daisy et al., 2002 reported that *M. vitigenus* exhibited insect inhibitory qualities as well as repelled wheat stem sawfly.

Other studies have unveiled *Claviceps chaetomium* and *Claviceps purpure* obtained from *Achnatherum inebrians*, show their insecticidal efficacy against cotton aphids in China (Zhang et al., 2010). Prior research identified *Neotyphodium* sp. an endophytic fungus which produced a paxiline analogous element and N-formilonine within the host *Echinopogon ovatus*. These bioactive metabolites demonstrated repellent effects against *Listronotus bonariensis* and other insects. *Fusarium oxysporum* endophytic fungi offer protection against root knot disease of tomato caused by *Meloidogyne incognata* (Hallman and Sikora, 1994), while endophytic fungi from Central American banana plants regulate *Rhadopholus similis* the burrowing nematode (Pocasangre et al., 2000). Terpenes compounds isolated from *Copaifera* sp. exhibited antiparasitic and synergistic activity in vitro (Izumi et al., 2012). In yet another instance, insecticidal compounds Azadirachtins A and B, isolated from an endophytic fungus *Penicillium (Eupenicillium) parvum* within the host plant neem (*Azadirachta indica*), demonstrated significant insecticidal effects (Kusari et al., 2012).

Table 1: List of some Endophytic Bacteria Isolated, Identified, and assessed with their role in Plant Health and Biocontrol Effects

Role	Bacteria
Nitrogen Fixation	<i>Herbiconiux solani</i> SS3, <i>Pseudomonas</i> sp., <i>Rhizobium herbae</i> SR2r., <i>Flavobacterium aquidurensense</i> SN2r, <i>Paenibacillus polymyxa</i> P2b-2R,
Phosphorous solubilization	<i>Burkholderia</i> sp., <i>Pseudomonas</i> sp., <i>Paraburkholderia</i> , <i>Novosphingobium</i> , <i>Ochrobactrum</i> , <i>Paenibacillus polymyxa</i> ,
Zinc solubilization	<i>Arthrobacter</i> sp., <i>Bacillus</i> spp., <i>Pseudomonas</i> spp., <i>Klebsiella</i> spp.
Potassium solubilization	<i>Bacillus</i> sp., <i>Paenibacillus polymyxa</i> , <i>Alcaligenes</i> spp., <i>Burkholderia</i> sp. FDN2-1, <i>Enterobacter</i> spp.
Hormones: indole-3-acetic acid, jasmonic acid & salicylic acid	<i>Enterobacter</i> sp., <i>Klebsiella</i> sp., <i>Bacillus</i> sp. PVL1, <i>Bacillus amyloliquefaciens</i> RWL-1; <i>Bacillus</i> sp. DLMB, <i>Bacillus</i> sp. MBL_B17, <i>Leifsonia xyli</i> SE134, <i>Bacillus subtilis</i> MBL_B13, <i>Bacillus subtilis</i> LK14,
Antibiotics: Bacillomycin	<i>Bacillus subtilis</i> CPA-8, <i>Bacillus subtilis</i> fmbj, <i>Bacillus</i>

2,4-diacetylphloroglucinol	<i>subtilis AU195</i>
Volatile organic compounds: 2,3-butanediol, acetoin, 2-hexanone,	<i>Enterobacter TR1, Bacillus amyloлицefaciens ALB629 and UFLA285, Bacillus spp. Bacillus Velenzensis DSN012, Bacillus Velenzensis 5YN8</i>

Table 2: Endophytic Source of Bioactive Compounds and their Application against Pathogenic Microbes

Endophytes found in	Bioactive compounds	Active against pathogen	Mode of transmission
<i>Chloridium sp.</i>	Javanicin	<i>Pseudomonas sp.</i>	Surgical instruments or Contaminated water
<i>Streptomyces coelicolor, Boesenbergia rotunda</i>	Munumbicins	<i>Escherichia coli</i>	Raw or pasteurized milk, ground meats,
<i>Cryptosporopsis quercina</i>	Saadamycin	<i>Campylobacter jejuni</i>	Uncooked or raw poultry and milk
<i>Cladosporium sp.</i>	Cardiac glycosides, phenolic compounds	<i>Klebsiella pneumoniae</i>	Aerosols and contaminated water
<i>Diaporthe helianthi</i>	Fabatin, tyrosol	<i>Enterococcus hirae</i>	Via nosocomial infection of hospitalized patients
<i>Cytonaema sp.</i>	Cytonic acids A and B	<i>Hepatitis virus, Human cytomegalo virus</i>	Berries, shellfish or contaminated water
<i>Nigrospora sp.</i>	Saadamycin	<i>Fusarium oxysporum</i>	Cereals, maize and groundnuts
<i>Fusarium proliferatum</i>	Beauvericin	<i>Clostridium botulinum</i>	Poorly processed, canned food
<i>Diaporthe helianth, Hypericum perforatum</i>	emodin, Hypericin, tyrosol	<i>Salmonella sp</i>	Eggs, meat, and untreated tree nuts
<i>Saccharothrix mutabilis</i>	Capreomycin	<i>Mycoplasma (TB)</i>	Eggs, uncooked meat, or poultry
<i>Phomopsis sp.</i>	Munumbicins	<i>Aspergillus niger</i>	Cereals maize, tree nuts and groundnuts
<i>Kennedia nigricans, Streptomyces sp.</i>	Munumbicins	<i>Vibrio cholerae</i>	Raw or poorly rcooked shellfish

VIII. PLANTS IMMUNITY BY ENDOPHYTES

Endophytes perform a vital role in enhancing the immunity of plants through their intricate interactions within the plant's tissues. These microorganisms, including fungi and bacteria, establish a symbiotic association with the host plant, residing within its various parts such as stems, leaves and roots. This partnership often yields a myriad of benefits for the plant concerned. The synthesis of secondary metabolites with antibacterial characteristics by endophytes is one of the main ways they support plant immunity. By preventing the growth and reproduction of possible infections, these substances serve as a first line of defense. Endophytes can successfully stop the invasion of harmful bacteria by doing this, which could otherwise result in diseases that are bad for the health of the plant. Moreover, endophytes can stimulate the defense mechanisms of plant. They can induce the production of phytohormones and other signaling molecules that trigger induced systemic resistance (ISR) or systemic acquired resistance (SAR). SAR involves the activation of defense responses throughout the entire plant, while ISR involves the systemic response initiated by localized infection. Both mechanisms bolster the plant's ability to fend off pathogens upon subsequent attacks.

Plant Protection Mechanism by Endophytes: Endophytes shield plants by producing compounds that thwart pathogens, triggering immune responses, forming physical barriers, and bolstering stress tolerance. These microorganisms also compete for nutrients, induce systemic resistance, and in some cases, directly attack pathogens, enhancing plant protection. Through a variety of ways, endophytes protect plants, and there are primarily two types.

1. Direct Mechanism

- **Antibiosis:** Endophytes produce bioactive chemicals that are hazardous to prospective pathogens as part of their antibiosis mechanism. These substances act as a barrier for plants, inhibiting the growth, development, and survival of dangerous microorganisms. Through this method, harmful organisms are kept from colonizing plant tissues and causing disease. Endophytes successfully ward off diseases by releasing these bioactive compounds, which supports the plant's general health and vitality.
- **Lytic Enzyme Secretion:** The lytic enzyme secretion mechanism of endophytes contributes to plant protection through various ways: pathogen disruption, biofilm penetrating, nutrient release, induced defense responses, direct antagonism, and detoxification.
- **Phytohormone Production:** The phytohormone production mechanism of endophytes contributes to plant protection in the following ways: enhanced defense responses, induced systemic resistance, systemic acquired resistance, cross-talk and balance, regulation of plant growth and development.
- **Phosphate Solubilization:** The phosphate solubilization mechanism of endophytes improves nutrient uptake, root development, stress tolerance, and defense responses in plants. These combined effects provide the overall health and resilience of the plant, ultimately protecting it from potential threats like pathogens.

- **Siderophores Production:** Siderophores, which are molecule-producing endophytes, bind to iron ions in the soil, increasing their availability for uptake by plants. Iron is a critical component for plant growth and defense, therefore understanding this is important. Endophytes increase the accessibility of iron for plants by chelating it. This improved nutrition delivery encourages healthier plant growth and development, which in turn helps the plant resist infections. Endophytes' synthesis of siderophores may reduce possible pathogens' access to iron. Siderophores competition makes the environment unfavorable for pathogenic bacteria because iron is also necessary for their growth.

2. Indirect Mechanism

- **Induction of Resistance in Plant:** Induction of plant resistance refers to the process by which plants are primed to enhance their defense mechanisms in response to certain stimuli. This heightened state of readiness makes the plant more resistant to pathogens and other environmental stressors. Several key points characterize the induction of plant resistance are primed defense mechanism, SAR, hormonal signaling, environmental adaptation, natural and synthetic elicitors.
- **Simulation of Secondary Metabolites in Plant:** Simulation of secondary metabolites of plant involves the creation of models or systems to replicate the production and accumulation of these specialized compounds within plants. Secondary metabolites in plant are organic compounds which are not positively involved in essential growth processes but often serve various roles, such as defense against herbivores, attraction of pollinators, and response to environmental stress.
- **Promotion of Growth and Physiology in Plant:** Endophytes have the capacity to influence the growth and physiology of host plants significantly through their interactions with the host plants. Here are some ways that endophytes might improve plant physiology and growth: nutrient uptake and solubilization, nitrogen production, hormone production, root development, symbiotic nitrogen fixation.
- **Hyper-parasitism and Predation:** Hyper-parasitism and predation involving endophytes are interactions where these microorganisms engage in relationships with other microbes or organisms. Hyper-parasitism occurs when an organism (in this case, an endophyte) parasitizes another parasitic organism. Endophytes can act as hyper-parasites by targeting other microorganisms, such as fungi or bacteria that are already parasitizing plants. The endophytes establish themselves within these parasitic organisms, influencing their behavior, growth, or pathogenicity. Predation involves an organism (endophyte) consuming another organism (e.g., a pathogen) for nourishment. Some endophytes have been found to exhibit predatory behavior by attacking pathogens or other microorganisms within the plant's environment. This can contribute to disease suppression by reducing the population of harmful pathogens.
- **Indolic Compound Production:** The synthesis of indolic compounds by endophytes exemplifies the intricate chemical dialogues that occur within the plant microbiome. These compounds have far-reaching effects on plant growth, development, defense,

and stress tolerance, making them valuable tools for enhancing agricultural practices and sustainable crop production.

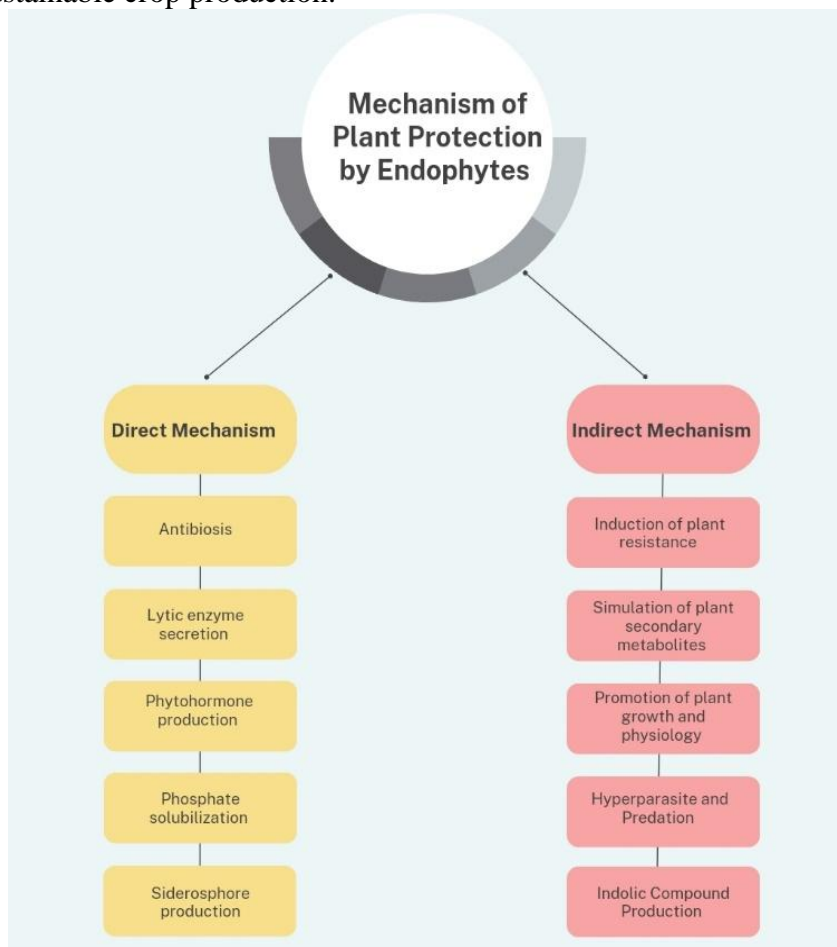


Figure 3: Plant Protection Mechanism by Endophytes

IX. ENDOPHYTES AND PLANT RELATIONSHIP

Fossilized plant tissues from various parts have yielded compelling evidence for the relationships between plants and endophytes. The close and enduring bond between plants and microbes is evident through genetic exchanges that facilitate the transfer of information between both organisms.

Information exchanges contribute to better survival in both adverse and favorable conditions, enhancing the closeness of the plant-endophyte association for heightened adaptation. The evolutionary bond between endophytic fungi and plants might facilitate improved adaptation, aided by endophytes secreting protective chemical compounds against pathogens and insects (Strobel, 2003; Kusari and Spiteller, 2012). Consequently, endophytic fungi synthesize diverse bioactive compounds, to contribute to their host plants. Coevolution between plants and endophytes suggests the potential for endophytes to generate secondary bioactive metabolites, supporting the chemical defense of plants (Carroll, 1988; Li et al., 2008). This, in turn, bestows growth, protection and survival benefits to their host, granting access to isolating and characterizing substances of substantial industrial potential, spanning agriculture and medicine (Strobel, 2003).

In its early stages, the endophytic fungus *Piriformospora indica* was harnessed for producing pyriform chlamydo spores. *P. indica* exhibits a remarkable ability to establish root colonization in plants, augmenting their growth and development (Verma et al., 1998; Rai et al., 2001). In several aspects, *P. indica* shares similarities with arbuscular mycorrhizal fungi (AM) (Rai and Verma, 2005; Deshmukh et al., 2006). This fungus also demonstrates multifunctionality, serving as a biofertilizer, bioprotector, growth regulator, and contributor to drought tolerance (Sun et al., 2010). Notably, *P. indica* contributes to phosphate transportation from fungus to plant, facilitated by a phosphate transporter gene (PiPT). This revelation deepens the understanding of phosphate transfer mechanisms in host plants.

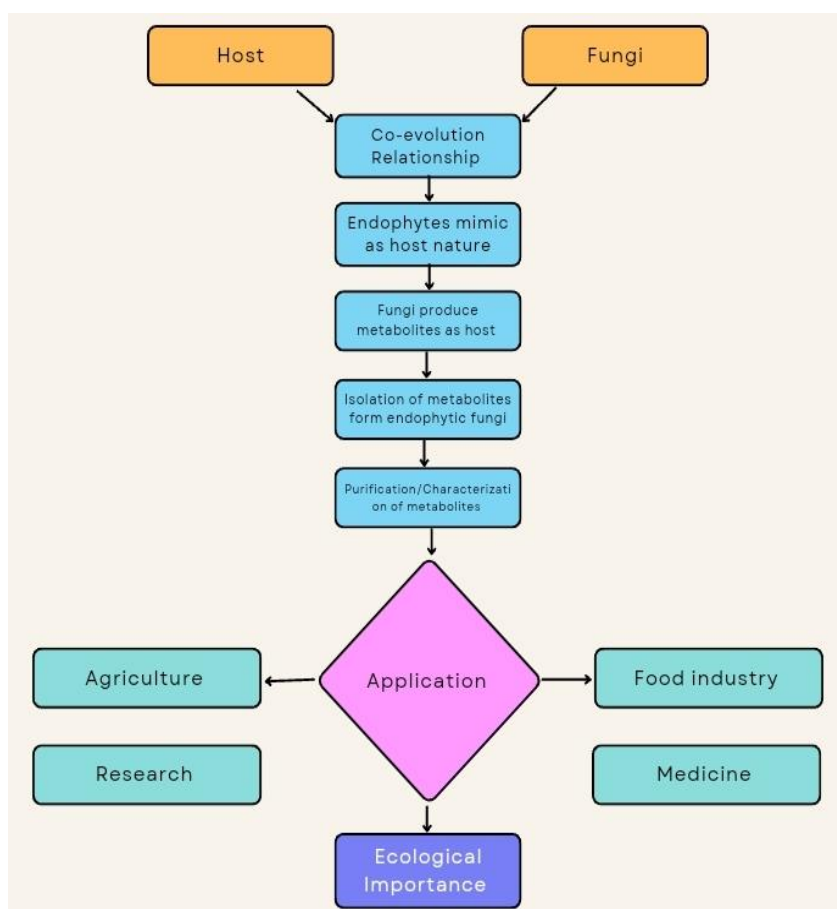


Figure 4: Host-Endophytes Interaction and their Application

X. ENDOPHYTIC BACTERIA IN PHYTOREMEDIATION

Because of their toxicity, hydrophobicity and propensity to linger in the environment for an extended length of time, organic compounds discharged into the environment through numerous anthropogenic activities pose a severe threat to the ecosystem. The presence of various organic compounds in soil, such as hydrocarbons, polychlorinated biphenyls, polyaromatic hydrocarbons, phenols, toluene, chlorophenols, trinitrotoluene, herbicides, benzene and pesticides even at very low concentrations inhibits metabolic activities and growth of soil accompanying microbes (Oleszczuk, 2006, Porteous Moore et al., 2006). In addition, organic chemicals can come in the food chain and, because of the toxicity, they can

create cancer and mutagenicity in both people and animals. As a result, one of the key problems in the sphere of engineering and environmental sciences is the removal of these organic compounds from water and soil. An economical, effective, and eco-friendly technology for 21st century is phytoremediation, or to clean up polluted water and soil with the help of plants. Additionally, plants employed for phytoremediation could be used to produce biomass or biofuels as well as store carbon. When microorganisms and plants work together, the plant gives the related rhizosphere and endophytic bacteria a habitat and nutrition. By decomposing the contaminant, the bacteria help the plant increase its ability to withstand stress, grow better, and purify its surroundings. These interactions were extensively investigated and employed to improve plant development, soil fertility and phytoremediation of polluted water and soil. Plants and endophytes have complex and diverse interactions with one another. While endophytic bacteria colonise inside of plants without making their host plants pathogenic, *Rhizobacteria* colonise the area immediately around the roots of plants. Since many endophytic bacteria have close ties to plants and are important plant growth promoters, they have also attracted a lot of interest. Endophytic bacteria with metabolic and pollutant degradation pathways can reduce volatile organic compound evapotranspiration as well as phytotoxicity. Additionally endophytic bacteria having growth enhancing properties may help plants adapt to and thrive in contaminated soil. Various endophytic bacteria have recently been separated from various hosts, and many of these have demonstrated actions that both degrade pollutants and promote plant growth. So, endophytic bacteria are very capable for some phytoremediation approaches due to their plant growth promoting and pollutant degrading capabilities (Khan et al., 2013). It is still understated how crucial plant-endophyte synergisms are for removing pollutants from water and soil. Though the role of bacterial endophyte to increase the phytoremediation of soil contaminated by heavy metal has been reviewed in various recent review articles, the role of endophytic bacteria for the enhancement of the phytoremediation of organic pollutants has largely been unmentioned. It has been suggested that endophytic bacteria may improve three specific aspects of remediation of organic pollutants: (a) plant growth and biomass production; (b) the bioavailability of organic pollutants; and (c) the population size and activity of native bacteria which degrade organic pollutants by horizontal gene transfer. Additionally, increased plant biomass output can lower the proportion of organic pollutants to plant tissue, reducing plant stress. The capability of genetically altered endophytic bacteria, horizontal gene transfer, and meta-genomic research can enhance plant endophyte association for the cleaning up of contaminated water and soil will be highlighted in the last section.

XI. FUTURE PROSPECTS

The future prospects of endophytes are promising and hold significant potential across various fields. Researchers and scientists have recognized the value of these hidden allies, and ongoing studies are paving the way for their practical applications. Endophytes offer a natural and eco-friendly approach to increase crop production and protect hosts from pests and diseases. By reducing the need for chemical pesticides and fertilizers, endophytes can contribute to sustainable agricultural practices, promoting environmentally friendly farming methods. Endophytes have the potential to assist plants in adjusting to shifting environmental conditions as climate change continues to have an impact on global ecosystems. Their capacity to increase plant resistance to stress, such as drought, may be significant in reducing the influence of climatic variance on agricultural productivity. The distinct biochemical characteristics and genetic diversity of Endophytes provide novel opportunities for

biotechnological development. They might be employed in the creation of brand-new bioactive substances, biopesticides, and biofertilizers, advancing medical science, agriculture, and environmental management. In degraded ecosystems, introducing beneficial endophytes can aid in the restoration process. They can help establish and support native plant populations, promoting biodiversity and ecosystem stability. Some endophytes have shown potential in producing bioactive compounds with pharmaceutical properties. Research on endophyte-derived compounds may help to the detection of new medicines and therapies for human and animal health. Understanding endophyte-plant interactions can help researchers better understand the complex world of plant microbiomes. Understanding these connections can help us better understand the intricate microbial populations that affect plant health and ecosystem dynamics. Certain endophytes have demonstrated the capacity to improve plant biomass and bioenergy production. By improving the productivity and growth of bioenergy crops, they can contribute to renewable energy solutions. To ensure the safe and sustainable use of endophytes, it is essential to take into account potential obstacles including regulatory clearances, scalability, and potential ecological implications as research in this area progresses. Despite these difficulties, the continuous study and use of endophytes hold considerable potential for improving agriculture, environmental protection, and people's quality of life in the years to come.

XII. CONCLUSION

Endophyte realm is an exciting and growing area of research that offers great potential in many areas. The relationship between the host plants and its endophyte highlights a dynamic evolutionary process in which the endophyte inhabits the plant tissues and often uses its chemical arsenal to support various aspects of the plant's growth, health and defense. Endophytes have the capacity to support plant health by stimulating growth, increasing nutrient uptake, improving abiotic stress tolerance and providing protection against a variety of pathogens. Endophytes, which come from bacteria, fungi and other families, produce a variety of bioactive metabolites that show anti-viral, anti-bacterial, anti-cancer and anti-fungal activity. These endophyte compounds, derived from endophyte's rich biochemical repertoire, hold great promise in pharmaceutical applications as well as bioremediations and agricultural strategies for sustainable crop production. In a world where innovation and green solutions are in high demand, endophytes provide an opportunity to explore the potential of nature's invisible allies. The ability of endophytes to form complex biochemical networks within a plant's physiology is an illustration of the beauty and intricacy of nature. As science continues to unravel the mysteries of these microcosm environments, endophytes will play an important role in solving some of humanity's greatest challenges, bridging the gap between the microscopic and macroscopic realms, and potentially pushing the boundaries of sustainable development.

REFERENCES

- [1] Akiyama, H., Fujii, K., Yamasaki, O., Oono, T., and Iwatsuki, K. (2001). Antibacterial action of several tannins against *Staphylococcus aureus*. *J. Antimicrob. Chemother.* 48, 487–491. doi: 10.1093/jac/48.4.487.
- [2] Altomare C, Perrone G, Zonno MC, Evidente A, Pengue R, Fanti F, Polonelli L (2000) Biological characterization of fusapyrone and deoxyfusapyrone, two bioactive secondary metabolites of *Fusarium semitectum*. *Nat Prod.* 2000 Aug;63(8):1131-5.
- [3] Araujo, W. L., H. O. Saridakis, P. A. V. Barroso, C. I. Aguilar-Vildoso, and J. L. Azevedo. 2001. Variability and interactions between endophytic bacteria and fungi isolated from leaf tissues of citrus rootstocks. *Can. J. Microbiol.* 47:229–236.

- [4] Bacon, C.W., and White, J.F. (1994). *Microbial Endophytes* (New York: Marcel Dekker Inc.).
- [5] Baldani JI, Reis VM, Videira SS, et al. (2014) The art of isolating nitrogen-fixing bacteria from Non-leguminous plants using N-free semi-solid media: a practical guide for microbiologists. *Plant Soil* 384: 413–431. <https://doi.org/10.1007/s11104-014-2186-6>.
- [6] Barka, E. A., Vatsa, P., Sanchez, L., Gaveau-Vaillant, N., Jacquard, C., Klenk, H. P., et al. (2016). Taxonomy, physiology, and natural products of Actinobacteria. *Microbiol. Mol. Biol. Rev.* 80, 1–43. doi: 10.1128/MMBR.00019-15.
- [7] Bashan Y, Kamnev AA, de-Bashan LE (2013) A proposal for isolating and testing phosphate Solubilizing bacteria that enhance plant growth. *Biol Fertil Soils* 49: 1–2. <https://doi.org/10.1007/s00374-012-0756-4>
- [8] Bastaki S. Diabetes mellitus and its treatment. *International Journal of Diabetes and Metabolism* (2005) 13 (3): 111–134. <https://doi.org/10.1159/000497580>
- [9] Bhardwaj A., Agrawal P. (2014). A review fungal endophytes: as a store house of bioactive compound. *World J. Pharm. Pharm. Sci.* 3 228–237. [Google Scholar]
- [10] Bills GF, R. A. Giacobbe, S. H. Lee, F. Pelaez and J. S. Tkacz, Tremorgenic mycotoxins, paspalitrem A and C from a tropical *Phomopsis*. *Mycol. Res.*, 1992, 96, 977.
- [11] Carroll, G. (1988) Fungal endophytes in stems and leaves: from latent pathogen to
- [12] mutualistic symbiont. *Ecology*, 69: 2-9.
- [13] Chaudhary, H. S., Soni, B., Shrivastava, A. R., and Shrivastava, S. (2013) Diversity and versatility of actinomycetes and its role in antibiotic production. *Int. J. Pharm. Sci.* 3, S83–S94.
- [14] Daisy, B., Strobel, G., Ezra, D., Castillo, U., Baird, G., Hess, W.M. (2002) *Muscodor vitigenus anam*. Sp. Nov., an endophyte from *Paullinia paullinioides*. *Mycotaxon.* 84:39- 50.
- [15] Dayle, E. S., Polans, N. O., Paul, D. S., and Melvin, R. D. (2001). Angiosperm DNA contamination by endophytic fungi: detection and methods of avoidance. *Plant Mol. Biol. Rep.* 19, 249–260. doi: 10.1007/BF02772897.
- [16] De Carvalho, T. L. G., Ferreira, P. C. G., & Hemerly, A. S. (2011). *Sugarcane Genetic Controls Involved in the Association with Beneficial Endophytic Nitrogen Fixing Bacteria*. *Tropical Plant Biology*, 4(1), 31–41. doi:10.1007/s12042-011-9069-2
- [17] Demain, A.L. (2000) Microbial natural products: a past with a future, p. 3-16. In S. K. Wrigley, M. A. Hayes, R. Thomas, E. J. T. Chrystal, and N. Nicholson (ed.), *Biodiversity: new leads for pharmaceutical and agrochemical industries*. The Royal Society of Chemistry, Cambridge, United Kingdom.
- [18] Demain A L and Sanchez S. Microbial drug discovery: 80 years of progress. *The Journal of Antibiotics* (2009) 62, 5–16.
- [19] Deshmukh, S., Huckelhoven, R., Schafer, P., Imani, J., Sharma, M., Weiss, M., ... Kogel, K.-H. (2006). *The root endophytic fungus Piriformospora indica requires host cell death for proliferation during mutualistic symbiosis with barley*. *Proceedings of the National Academy of Sciences*, 103(49), 18450–18457. doi:10.1073/pnas.0605697103
- [20] Domperipen E. J, Srikanth Y, Suharso WP, Herry C (2011) Potential Endophytic Microbes Selection for Antidiabetic Bioactive Compounds Production. *Asian Journal of Biochemistry* 6(6):465-471 DOI:10.3923/ajb.2011.465.471
- [21] Elya, B., Basah, K., Mun'im, A., Yuliastuti, W., Bangun, A., & Septiana, E. K. (2012). *Screening of α-Glucosidase Inhibitory Activity from Some Plants of Apocynaceae, Clusiaceae, Euphorbiaceae, and Rubiaceae*. *Journal of Biomedicine and Biotechnology*, 2012, 1–6. doi:10.1155/2012/281078
- [22] Feng K, Cai Z, Ding T, et al. (2019) Effects of potassium-solubilizing and photosynthetic bacteria on tolerance to salt stress in maize. *J Appl Microbiol* 126: 1530–1540. <https://doi.org/10.1111/jam.14220>
- [23] Firakova S. H., Sturdikova M., Můčková M. (2007) Bioactive secondary metabolites produced by microorganisms associated with plants. *Biologia* 62(3):251-257.
- [24] Gayathri P. and Muralikrishnan V.(2003) Isolation and characterization of Endophytic Actinomycetes from mangrove plant for antimicrobial activity. *Int.J. Curr. Microbiol. App. Sci.* 2(11): 78-89.
- [25] Germaine K, Keogh E, Borremans B et al. (2004) Colonisation of poplar trees by gfp expressing bacterial endophytes. *FEMS Microbiol Ecol* 48: 109–118.
- [26] Godstime, O. C., Enwa, F. O., Augustina, J. O., and Christopher, E. O. (2014). Mechanisms of antimicrobial actions of phytochemicals against enteric pathogens – a review. *J. Pharm. Chem. Biol. Sci.* 2, 77–85.
- [27] Gohel V., Singh A., Vimal M., Ashwini P., Chhatpar H. S. (2006) Bio-prospecting and antifungal potential of chitinolytic microorganisms. *Afr. J Biotechnol.* 5:54-72.
- [28] Golinska, P., Wypij, M., Agarkar, G., Rathod, D., Dahm, H., and Rai, M. (2015). Endophytic actinobacteria of medicinal plants: diversity and bioactivity. *Antonie Van Leeuwenhoek* 108, 267–289. doi: 10.1007/s10482-015-0502-7.

- [29] Guo, B., Dai, J., Ng, S., Huang, Y., Leong, C., Ong, W., Carte, B.K. 2000. Cytonic acids. A and B, novel tridepside inhibitors of hCMV protease from the endophytic fungus *Cytonaema* species. *J. Nat. Prod.* 63:602-604.
- [30] Broad-spectrum antifungal activity against various fungi, such as *Aspergillus* sp. And *Candida* sp. (Hay, 2003; Gupte et al., 2002; Iznaga et al., 2004;
- [31] Hallmann, J.; Sikora, R.A. 1994: Influence of *Fusarium oxysporum*, a mutualistic fungal endophyte, on *Meloidogyne incognita* infection of tomato - *Zeitschrift für Pflanzenkrankheiten und Pflanzenschutz* 101(5): 475-481
- [32] Han, T., and Rahman, K. (2012). Alkaloids produced by endophytic fungi: a review. *Nat. Prod. Commun.* 7, 963–968.
- [33] Hanefeld M & Schaper F. The Role of Alpha-Glucosidase Inhibitors (Acarbose). *Pharmacotherapy of Diabetes: New Developments* pp 143–152.
- [34] Hartmann, A., Rothballer, M., Hense, B. A., and Schröder, P. (2014). Bacterial quorum sensing compounds are important modulators of microbe-plant interactions. *Front. Plant Sci.* 5:131. doi: 10.3389/fpls.2014.00131
- [35] Hay R. Antifungal drugs. In: Katsambas A, Lotti T, editors. *European Handbook of Dermatological Treatments*. Berlin, Germany: Springer; 2003. pp. 700–710. [Google Scholar]
- [36] Hollants, J., Leroux, O., Leliaert, F., Decleyre, H., De Clerck, O., and Willems, A. (2011). Who is in there? Exploration of endophytic bacteria within the siphonous green seaweed *Bryopsis* (Bryopsidales, Chlorophyta). *PLoS ONE* 6:e26458. doi: 10.1371/journal.pone.0026458.
- [37] Hussain, M. S., Fareed, S., Ansari, S., Rahman, M. A., Ahmad, I. Z., and Saeed, M. (2012). Current approaches toward production of secondary plant metabolites. *J. Pharm. Bioallied Sci.* 4, 10–20. doi: 10.4103/0975-7406.92725.
- [38] Hurek T & Reinhold-Hurek B (2003) *Azoarcus* sp. Strain BH72 as a model for nitrogen-fixing grass endophytes. *J Biotech* 106: 169–178.
- [39] Iznaga, Y., Lemus, M., González, L., Garmendía, L., Nadal, L., & Vallín, C. (2004). *Antifungal activity of actinomycetes from cuban soils. Phytotherapy Research*, 18(6), 494–496. doi:10.1002/ptr.1466
- [40] Izumi, E., Ueda-Nakamura, T., Veiga V.F., Jr., Pinto, A.C., Nakamura, C.V. (2012) Terpenes from *Copaifera* demonstrated in vitro antiparasitic and synergic activity. *J. Med. Chem.* 55, 2994–3001.
- [41] Jalgaonwala, R. E., Mohite, B. V., and Mahajan, R. T. (2011). Natural products from plant associated endophytic fungi. *J. Microbiol. Biotechnol. Res.* 1, 21–32.
- [42] James E. K., Gyaneshwar P., Mathan N., Barraquio W. L., Reddy P. M., Iannetta P. P., Olivares F. L. & Ladha J. K. (2002) Infection and colonization of rice seedlings by the plant growth-promoting bacterium *Herbaspirillum seropedicae* Z67. *Mol Plant Microbe Interact* 15: 894–906.
- [43] Joseph, B., and Priya, R. M. (2011). Bioactive compounds from endophytes and their potential in pharmaceutical effect: a review. *Am. J. Biochem. Mol. Bio.* 1, 291–309. doi: 10.3923/ajbmb.2011.291.309.
- [44] Kamran S., Shahid I., Baig D. N., et al. (2017) Contribution of zinc solubilizing bacteria in growth promotion and zinc content of wheat. *Front Microbiol* 8: 2593. <https://doi.org/10.3389/fmicb.2017.02593>.
- [45] Khan, A. L., Hussain, J., Al-Harrasi, A., Al-Rawahi, A., & Lee, I.-J. (2013). *Endophytic fungi: resource for gibberellins and crop abiotic stress resistance. Critical Reviews in Biotechnology*, 35(1), 62–74. doi:10.3109/07388551.2013.800018
- [46] Konuklugil, B. (1995). The importance of Aryltetralin (*Podophyllum*) lignans and their distribution in the plant kingdom. *Ankara Univ. Eczacilik Fak. Derg.* 24, 109–125. doi: 10.1501/Eczfak_0000000159.
- [47] Kumar, S., Aharwal, R. P., Shukla, H., Rajak, R. C., and Sandhu, S. S. (2014). Endophytic fungi: as a source of antimicrobials bioactive compounds. *World J. Pharm. Pharm. Sci.* 3, 1179–1197.
- [48] Kusari, S., Verma, V.C., Lamshoeft, M., Spitteller, M. An endophytic fungus from *Azadirachta indica* A. Juss. that produces azadirachtin. (2012) *World J. Microbiol. Biotechnol.* 28, 1287–1294.
- [49] Li E, L. Jiang, L. Guo, H. Zhang, and Y. Che, (2008) “Pestalochlorides A-C, antifungal metabolites from the plant endophytic fungus *Pestalotiopsis adusta*,” *Bioorganic and Medicinal Chemistry*, vol. 16, no. 17, pp. 7894–7899.
- [50] Y.R. Li, Y.R., Q.H. Liu, H.X. Wang, T.B. Ng (2008) A novel lectin with potent antitumor, mitogenic and HIV-1 reverse transcriptase inhibitory activities from the edible mushroom *Pleurotus citrinopileatus*. *Biochim. Biophys. Acta*, 1780, pp. 51-57.
- [51] Mónica Rosenblueth, Esperanza Martínez-Romero (2004) *Rhizobium etli* maize populations and their competitiveness for root colonization. *Arch Microbiol* 2004 May;181(5):337-44
- [52] Moore, F. P., Barac, T., Borremans, B., Oeyen, L., Vangronsveld, J., van der Lelie, D., Moore, E. R. B. (2006). *Endophytic bacterial diversity in poplar trees growing on a BTEX-contaminated site: The*

- characterisation of isolates with potential to enhance phytoremediation. Systematic and Applied Microbiology*, 29(7), 539–556. doi:10.1016/j.syapm.2005.11.012
- [53] Muhilan B.M., Chattopadhyay I. (2023). Endophytes and their bioactive metabolite's role against various MDR microbes causing diseases in humans", Elsevier BV, in *Endophytic Association: What, Why and How*; Edi by Shah and Deka, pp135-158.
- [54] Nair D. N., and Padmavathy, S. (2014) Impact of endophytic Microorganisms on plants, environment and humans. *Sci. World. J.* (Article ID 250693): 1- 11.
- [55] Oleszczuk, P. (2006). *Persistence of polycyclic aromatic hydrocarbons (PAHs) in sewage sludge-amended soil. Chemosphere*, 65(9), 1616–1626. doi:10.1016/j.chemosphere. 2006.03.007
- [56] Pillay, V. J., and J. Nowak. (1997) Inoculum density, temperature and genotype effects on in vitro growth promotion and epiphytic and endophytic colonization of tomato (*Lycopersicon esculentum* L.) seedlings inoculated with a pseudomonad bacterium. *Can. J. Microbiol.* 43:354–361.
- [57] Pimentel, M. R., Molina, G., Dionisio, A. P., Maróstica, M. R., and Pastore, G. M. (2011). Use of endophytes to obtain bioactive compounds and their application in biotransformation process. *Biotechnol. Res. Int.*576286. doi: 10.4061/2011/576286.
- [58] Pocasangre, L., Sikora, R.A., Vilich, V. and Schuster, R-P. (2000) Survey of banana endophytic fungi from Central America and screening for biological control of *Radopholus similis*. *Acta Horticulturae* 531, 283–289.
- [59] Rai, M., & Varma, A. (2005). *Arbuscular mycorrhiza-like biotechnological potential of Piriformospora indica, which promotes the growth of Adhatoda vasica Nees. Electronic Journal of Biotechnology*, 8(1). doi:10.2225/vol8-issue1-fulltext-5
- [60] Rai M., Acharya D., Singh A., Varma A. (2001) Positive growth responses of the medicinal plants *Spilanthes calva* and *Withania somnifera* to inoculation by *Piriformospora indica* in a field trial *Mycorrhiza*, 11, pp. 123-128
- [61] Reinhold-Hurek B, Hurek T. (1998) Interactions of gramineous plants with *Azoarcus* spp. and other diazotrophs: identification, localization and perspectives to study their function. *Crit Rev Plant Sci.* 17:29-54.
- [62] Rosenblueth M. & Martinez-Romero E. (2006) Bacterial endophytes and their interactions with hosts. *Mol Plant Microbe Interact* 19: 827–837.
- [63] Ryan, R.P., Germaine, K., Franks, A., Ryan, D.J., and Dowling, D.N., (2008) Bacterial endophytes: recent developments and applications *FEMS Microbiol. Letts.*, vol. 278 No. 1, pp. 1–9.
- [64] Samuel, P., Prince, L. and Prabakaran, P. (2011). Antibacterial activity of marine derived fungi collected from South East Coast of Tamil Nadu, India. *J Microbiol Biotech Res.* 1, 86-94.
- [65] Schaefer, A. L., Oda, Y., Coutinho, B. G., Pelletier, D. A., Weiburg, J., Venturi, V., et al. (2016). A LuxR homolog in a cottonwood tree endophyte that activates gene expression in response to a plant signal or specific peptides. *mBio* 7: e01101-16. doi: 10.1128/mBio.01101-16
- [66] Schikora, A., Schenk, S. T., & Hartmann, A. (2016). *Beneficial effects of bacteria-plant communication based on quorum sensing molecules of the N -acyl homoserine lactone group. Plant Molecular Biology*, 90(6), 605–612. doi:10.1007/s11103-016-0457-8
- [67] Shukla, S. T., Habbu, P. V., Kulkarni, V. H., Jagadish, K. S., Pandey, A. R., and Sutariya, V. N. (2014). Endophytic microbes: a novel source for biologically/pharmacologically active secondary metabolites. *Asian J. Pharmacol. Toxicol.* 2, 1–16.
- [68] Singh R., Dubey A. K. (2015) Endophytic Actinomycetes as Emerging Source for Therapeutic Compounds. *Indo Global Journal of Pharmaceutical Sciences*, 5(2): 106-116.
- [69] Singh Y. D., Singh M. C. (2020) Biotechnological aspects of mangrove microorganisms. In: *Biotechnological Utilization of Mangrove Resources*, 381–398.
- [70] Strobel, G. and Daisy, B., (2003) Bioprospecting for microbial endophytes and their natural products. *Microbiol. Mol. Biol. Rev.*, vol. 67, no. 4, pp. 491–502.
- [71] Sun C., Johnson J. M., Cai D. G., Sherameti I., Oelmüller R., Lou B. G., (2010) *Piriformospora indica* confers drought tolerance in Chinese cabbage leaves by stimulating antioxidant enzymes, the expression of drought-related genes and the plastid-localized CAS protein *J. Plant Physiol.*, 167, pp. 1009-1017
- [72] Suthindhiran K. and Kannabiran K. (2009) Cytotoxic and Antimicrobial Potential of Actinomycete Species *Saccharopolyspora salina* VITSDK4 Isolated from the Bay of Bengal Coast of India. *American Journal of Infectious Diseases* 5 (2): 90-98, 2009 ISSN 1553-6203
- [73] Tan, R. X., & Zou, W. X. (2001). *Endophytes: a rich source of functional metabolites (1987 to 2000). Natural Product Reports*, 18(4), 448–459. doi:10.1039/b100918o.

- [74] Thakur D, Kaushal R, Shyam V (2014) Phosphate solubilising microorganisms: role in phosphorus nutrition of crop plants-a review. *Agric Rev* 35: 159. <https://doi.org/10.5958/0976-0741.2014.00903.9>
- [75] Ulrich K., Ulrich A., Ewald D. (2008) Diversity of endophytic bacterial communities in poplar grown under field conditions. *FEMS Microbiol Ecol.* 63: 169-80.
- [76] Uma S. R., Ramesha B. T., Ravikanth G., Rajesh P. G., Vasudeva R., and Ganeshiah K. N. (2008) "Chemical profiling of *N. nimmoniana* for camptothecin, an important anticancer alkaloid: towards the development of a sustainable production system," in *Bioactive Molecules and Medicinal Plants*, K. G. Ramawat and J. Merillion, Eds., pp. 198–210, Springer, Berlin, Germany.
- [77] Verma S., Varma A., Rexer K.H., Hassel A., Kost G., Sarbhoy A., Bisen P., Bütehorn B., Franken P. (1998) *Piriformospora indica* gen. et sp. nov., a new root-colonizing fungus *Mycologia*, 90, pp. 896-903
- [78] Visalakchi, S., and Muthumary, J. (2010). Taxol (anticancer drug) producing endophytic fungi: an overview. *Int. J. Pharma Bio. Sci.* 1, 1–9.
- [79] Wall M.E., M. C. Wani, C. E. Cook, K. H. Palmer, A. T. McPhail, and G. A. Sim, (1966) "Plant antitumor agents. I. The isolation and structure of camptothecin, a novel alkaloidal leukemia and tumor inhibitor from *Camptotheca acuminata*," *Journal of the American Chemical Society*, vol. 88, no. 16, pp. 3888–3890.
- [80] Wu, T.; Cheng, D.; He, M.; Pan, S.; Yao, X.; Xu, X. (2014) Antifungal action and inhibitory mechanism of polymethoxylated flavones from *Citrus reticulata* Blanco peel against *Aspergillus niger*. *Food Control*, 35, 354–359. [Google Scholar] [CrossRef]
- [81] Yu H, L. Zhang, L. Li et al. (2010) "Recent developments and future prospects of antimicrobial metabolites produced by endophytes," *Microbiological Research*, vol. 165, no. 6, pp.437–449.
- [82] Yuan Z.S., Liu .F, Zhang G.F. (2015) Characteristics and biodiversity of endophytic phosphorus and potassium solubilizing bacteria in moso bamboo (*Phyllostachys edulis*). *Acta Biol Hung* 66:449–459. <https://doi.org/10.1556/018.66.2015.4.9>
- [83] Zhang, J. Y., Tao, L. Y., Liang, Y. J., Yan, Y. Y., Dai, C. L., Xia, X. K., et al. (2009). Secalonic acid D induced leukemia cell apoptosis and cell cycle arrest of G1 with involvement of GSK-3 β / β -catenin/c-Myc pathway. *Cell Cycle*, 8(15), 2444–2450.
- [84] Zhao, J., Mou, Y., Shan, T., Li, Y., Zhou, L., Wang, M., & Wang, J. (2010). *Antimicrobial Metabolites from the Endophytic Fungus Pichia guilliermondii Isolated from Paris polyphylla var. yunnanensis*. *Molecules*, 15(11), 7961–7970. doi:10.3390/molecules 15117961
- [85] Zhao, K., Penttinen, P., Guan, T., Xiao, J., Chen, Q., Xu, J., et al. (2011). The diversity and antimicrobial activity of endophytic actinomycetes isolated from medicinal plants in Panxi Plateau China. *Current Microbiology*, 62(1), 182–190.