Endophytes: An Insight into Plant's Hidden Treasure

ABSTRACT

Endophytes are microorganism colonizing healthy plants tissue without causing any apparent symptoms in the host plant. Bacteria, fungi, actinomycete, virus, archaebacteria and mycoplasma are the common microbes existing as endophytes and found in every plant. Endophytic bacteria have been found in almost each and every plant, where they colonize in the internal tissues of their host plant and forming a range of ~~different~~ mutualistic, symbiotic, commensalistic and trophobiotic relationships. ~~such as~~. Most endophytes appear to originate from the rhizosphere or phyllosphere; however, some may be transmitted through the seed. Endophytes can be a plant growth promoter and also act as a biocontrol agent. Endophytes can also be beneficial to their host plant by producing wide varieties of natural products that could be harnessed for potential use in agriculture, medicine and industrial sector. In recent year's special attention has been given to endophytic microbes because of its ability to produce numbers of interesting and new bioactive secondary metabolites, which are of agricultural, pharmaceutical, and industrial importance. In addition, an endophyte has the potential to remove soil contaminants by enhancing phytoremediation and can also play an important role in soil fertility through nitrogen fixation and phosphate solubilization. There is an increasing interest in developing the potential biotechnological applications of endophytes for improving phytoremediation and the sustainable production of non-food crops for biomass and biofuel production.

Key words: Endophytes, stress, phytostimulation, secondary metabolites

INTRODUCTION

Endophytes are the microorganisms which live inside the plant tissues of leaves, stems and roots which do not have any negative effect on the host plant [1]. All classes of vascular plants and grasses host the endophytic organisms. Organisms such as bacteria, actinomycetes,fungi and mycoplasma are the various plant endophytes. The endophytes are known to exist for more than hundred years. The term endophyte is derived from Greek word endo meaning within and phyte meaning plant. One or more endophytes are harboured by each plant [2]. Endophytes are an outstanding source of secondary metabolites as bioactive antimicrobial natural products. A considerable attention was given to the microorganisms in last 20 years after it was noticed that they have the capacity to protect plants against insect and pest pathogens [1]. The important component in every ecosystem is fungi which involves crucial processes like decomposition, recycling, and transportation of nutrients in different environments. Some bacteria exist as plant endophytes, and indeed in most cases they coexist with endophytic fungi, and their existence has been known for over a hundred years.They influence the physiology, distribution, ecology, and biochemistry of the host plants. Endophytes have been studied extensively for their potential as a novel source of new drugs. Microbes including both bacteria and fungi have become a modern source of medicine that provide effective treatments, such as penicillin from the fungus *Penicillium notatum*, and bacitracin from bacterium *Bacillus subtilis* (please give new references). Endophytes represent a wide variety or huge diversity of microbial adaptations that develop in special and sequestered environments. Their diversity and speciality in habitat make them an exciting field of study in the search for new medicines or novel druglike molecules.

DEFINITION OF ENDOPHYTE

In 1997, Hallman et al., [3] give recent updates from a practical description gave the most common definition of endophytes which stated that endophytes are thosemicrobes that can be isolated from surface sterilized plant tissue or extracted from within the plant which do not visibly harm the host plant. It was suspected that after disinfection of plant surfaces, there was lack of adequate elimination of nucleic acids and hence this definition appeared less suitable for non-cultured species when the molecular detection techniques were introduced in endophyte research.The most endophytes are commonly termed as commensals, with unknown functions in plants, whereas positive (mutualistic) or negative (antagonistic) endophytes show less common effects on plants.

DIVERSITY

The Endophytes have a long history and their diversity among plants is found to be considerably large in number. In ecosystems and plant physiology, diverse endophytic bacteria play an integral role. The bacterial colonization occurs in all plant compartments, generally the intracellular and intercellular spaces of inner tissues. The diversity of endophytic bacteria is mostly based on characterization of endophytic isolates obtained from the initial studies of plant after surface disinfection. The main methods used for the bacterial isolation and also 81 bacterial species forming endophytic associations with plants was characterized by [4]. ~~A list of bacterial endophytes isolated from various plant parts of different agricultural crops was presented from the early reviews by [3].~~ Give a recent list. Different endophytic species mostly depend on plant and bacterial genotype, biotic and abiotic environmental factors. From a large study conducted on bacterial endopyte communities it was revealed that the roots usually contain higher number of species although endophytic bacteria colonize the entire plant. Endophytic species belong to the subgroups α-, β-, and γ-proteobacteria and are closely related to epiphytic species [5]. The most interesting group is the γ-proteobacteria group as it is most diverse and dominant. Reports reveal that most of gram-negative endophytes act as biological control agents and the culturable isolated endophytic bacterial species belong to *Proteobacteria*. Direct amplification of microbial DNA from plant tissue samplesand application of modern bioinformatics tools allows analysis of a bacterial community composition and its phylogenetic structure inside a variety of plant organs or tissues. [6]analysed genomic characteristics of bacterial endophytes that colonize rice roots under field conditions. These authors found that members of γ-proteobacteria dominate the population that comprise mainly Enterobacterrelated endophytes. The endophyte surveys include procedures most commonly based on the surface disinfection of apparently healthy plant tissue samples to kill epiphytic fungi [7]. Subsequently the surface disinfected plant samples are kept in synthetic growth media andisolations can be done after hyphae of the endophyte emerge from the plant tissue and start growing in the agar medium. Some techniques were used which allowed the detection of Non culturable endophytes in plant tissues [8, 9]. Surveys were done before the year 2000 and an average of about 50 endophytic species per plant species were found [10]. Endophyte research began to include molecular methods i.e. rDNA sequencing for the identification of fungi [11, 12], fungal species were identified as per host plant species and substantially an increase in number of species was observed. To identify or to distinguish among sterile cultures genotypic identification methods were used. Endophyte assemblages are composed by rare or singleton species which are isolated only once or very few times, and by dominant or plural species which are frequently isolated from a given host species [13]. Another factor contributing to the large diversity observed in endophytic assemblages is geographical variation, the taxa isolated from the same host species tends to change from one location to another. In a geoclimatic context, endophytic assemblages appear to be richer in tropical than in temperate or cold zones of the world. Plant age also has an effect upon diversity of the endophytes. As time of exposure to endophyte inoculum increases, plants seem to accumulate an increasing number of endophytes in their tissues. This is one of the reasons why older plant parts may harbour more endophytes than younger ones [14].

Effect of Climate on Endophytic Population (please remove this paragraph)

Endophytic population varies from species to species and from plants to plants. Within the same species it varies from region to region and also differs with change in climatic conditions within the same region. In 2006, [15] studied the temporal changes in relative frequency of total endophytic fungi. A greater number of genera and species were found in matured leaves of teak and rain tree, they also showed higher colonization frequency in comparison with the young leaves and an increase in the occurrence of leaves during rainy season. Difference in the endophytic population and frequency was studied among sampling dates for all the organs namely, young leaves, petiole, and twigs of *Gingko biloba L*. [16]. These studies proved that in the month of August first occurrence of *Phyllosticta* sp. was seen in both leaves and petioles, in October. A peak in the occurrence was observed and in the month of May there was no occurrence at all. Throughout the growing season, *Phomopsis* sp. was observed in the twigs. Thus, the distribution of the endophytic fungi was organ-specific and it differs from season to seasonas resulted by the studies.

Symbiotic lifestyles

Endophytes show different symbiotic lifestyles. The outcome of a plant endophyte interaction ranges from antagonism to mutualism depending on the species involved. Hence the distinct ranges of plant endophyte interactions are referred as a continuum [17]. Apparently, endophyte surveys use the raw materials obtained from healthy plants, and if sampling is done before the symptoms appear, latent pathogens may be isolated from such plants [18, 19]. However, latent pathogens do not contain an important part of endophyte assemblages; most endophytes do not cause symptoms on plants. For example, 109 different fungal species were identified in *Dactylis glomerata* L, were only 5 species corresponde dto known pathogens of that grass [20]. Most commonly in senescent plant parts some saprophytic fungi are found which have been isolated as endophytes from healthy tissues [21]. Such endophytic species are known as latent saprophytes, these fungi maybe asymptomatic and spatially restricted while their hosts grow, but when the infected host tissue senesces or dies it will grow unrestricted and reproduce. At the other end of the continuum there are endophytes which are beneficial to their hosts, *Neotyphodium* and *Epichloë* species are the best known in this group, these species provide anti herbivore defense, improved nutrient use to their plant hosts as well as drought tolerance [22]. Some other mutualistic species are known that benefit plants by protecting them against pathogens, endophytes such as *Piriformospora indica* Sav. [23], *Acremonium strictum* [24], and some *Stagonospora* species [25] can enhance the growth of their hosts.

Tissue colonization and specificity in endophytic species

Though fungi are eukaryotes and bacteria are prokaryotes, both of them share many characteristics of the plant hosts associations, e.g. bacteria and fungicolonises in the host plant root tissues both intracellular and intercellular.However, theysomewhat differ in their modes of colonisation. Several endophytes usually infect parts of the plant and they are restricted to a small tissue area. This is supported by the fact that often, several endophytic species arerecovered from different fragments of the same plant.Bacteria primarily colonise intercellularly [3], though they have also been found intracellularly. *Epichloe* and *Neotyphodium* species systemically infect the intercellular space of leaves, seeds and reproductive stemsof their host plants. These systemic endophytes can be isolated from multiple fragments of the same plant. They are very often found in the vascular tissues of host plants [26], which is advantageous for distribution. Tissue and organ specificity also occurs, and some endophytes may be found inspecific plant parts such as roots, leaves, or twigs, while others may infect several of these parts [10]. Regarding the specificity shown by endophytes for their host plants, specialists as well as generalists do occur in this group. For example, *Neotyphodium* endophytes are confined to one or two plant species and they have a narrow host range. Other endophytic fungi such as *Alternaria, Penicillium,* or *Piriformosfora* have wide host ranges, encompassing species within different genera or plant families [10, 2]. In fungi asymptomatic colonisation occurs which may be inter- and intra-cellular throughout the root. DSE (Dark Septate Endophytes) which are conidial fungi sometimes colonise the vascular cylinder in asymptomatic interactions, and such pathogens are frequently associated with colonisation. The growth of endophytic fungi within the roots hasbeen found to be frequently extensive as compared to the endophytic growth in the above ground plant organs [17]. Root colonisation can be both inter- and intra-cellular, the hyphae often forming intracellular coils, e.g. DSE [27], the basidiomycete *Piriformospora indica* [28], or *Oidiodendronmaius* and *Heteroconium chaetospira* [29], which can even form characteristic ericoid mycorrhizal infection units. Fungi of the genus *Rhizoctonia* and *Leptodontidium* [30] colonize many orchid roots, systemically and mycoheterotrophically. Any successful endophyte colonization involves a compatible host plant. [31]recently investigated *Azoarcus* sp. strain BH72, which is an obligate nitrogen-fixing endophyte and it expresses nitrogenase (*nif*) genes inside rice roots. The induced plant defence responses may contribute to restricting endophytic colonization in grasses this was suggested by the data.Endophyte colonization has also beenvisualized with the use of the β-glucuronidase (GUS) reporter system. A GUS-marked strain of *Herbaspirillum seropedicae* Z67 was inoculated onto rice seedlings. On coleoptiles, lateral roots, and also at some of the junctions of the main and lateral roots GUS staining was most intense [32]. Hence this study by James et al., [32] showed that endophytes entered the roots through cracks at the point of lateral root emergence. *Herbaspirillum seropedicae* subsequently colonized the root intercellular spaces, cortical cells, aerenchyma, and xylem vessels in leaves and stems with a few penetrating the stele to enter the vascular tissue.

Transmission and acquisition of endophytes

Endophytes transmission may occur both horizontally and vertically. Horizontal transmission occurs when the inoculum is transported to another plant and when the endophytes infect the seed progeny of an infected plant vertical transmission occurs. Horizontal transmission is the predominant mechanism of dispersion among endophytic species. Some studies reveal that plant seedlings and seeds are virtually free of endophyte. And as the leaves or seeds grow older the incidence of fungal endophytes increases [9, 14]. This type of process must be driven by horizontal transmission. There is a paradox related to the understanding ofthe mechanisms of horizontal transmission of endophytes: for horizontal transmission occurs, endophytic inoculum is produced and dispersed. But then in an asymptomatic host, where and when is the inoculum produced? In the case of latent saprophytes, when infected host tissue dies the inoculum which infects new hosts can be produced. The endophytes found in healthy tissues aresaprophytes which produce fructifications in dead plant parts [20]. From this point of view, leaf litter may be an important source of endophytic inoculum. In other situations, inoculum can also be produced in an inconspicuous way in infected hosts. For example, in *Epichlo0ë* endophyte which infect grasses a microscopic layer of hyphae and conidia is formedon the surface of their leaves. It is assumed that this inoculum might horizontally infect new hosts [33]. Phytophagous insects may also take part in the spread of endophytes, since spores of some fungal species are resistant to gut digestion, and are present in their faecal pellets. Vertically transmitted endophytes are discovered by means of studying seed transmitted fungi, and such studies are scarce [9]. Vertical transmission to host progeny occurs by means of seed infection in *Neotyphodium* endophytes and some *Epichloë* species. Approx 100% of the seeds containing fungal mycelium are produced by an infected plant near the embryo and in the aleurone layer. These seeds give rise to asymptomatic infected plants. Therefore, these endophytic speciesare vertically transmitted in a fashion similar to a maternally inherited character [22]. Because of this, the incidence of these endophytes is very high in natural populations of their hosts [34].

Applications of Endophytes

Role of endophytes in adaptation of agricultural crops to abiotic and biotic environmental stress: Climate change become apparent mainly in the form of rising temperatures, dry spells, abrupt changes in the weather (such as flash droughts), intense rainfall, and uneven distribution [35]. The effects of climate change vary depending on the location [36]. The global distribution of plants and plant phenology are changing as a result of all these deviations from a formerly more stable climate, especially the rise in temperature [37, 38]. This also greatly increases the threats to the survival of natural ecosystems [39]. In light of this dire situation, plant-associated microbes seem like a viable ally for contemporary agriculture in the fight against climate change. Temperature seems to be a key factor influencing changes in endophyte presence in plant tissues [40]. However, it has been shown that heat has no effect on the endophyte infection frequency of *N. coenophialum* of its host, the tall fescue *S. phoenix*. Furthermore, warmingincreased the amounts of proline by 28% but had no effect on ergovaline or ADF [41]. It is commonly known that endophytic fungi give their host plants a competitive edge by strengthening their resilience to environmental stressors [42]. Furthermore, some endophytes can enhance plant growth during drought stress exposure [43, 44]. Through increased tiller and entire plant survival, endophyte infection provided population stability in tall fescue under drought stress [45]. Such endophytes have been demonstrated to promote drought recovery (physiological and biochemical adaptations), drought avoidance (morphological adaptations), and drought tolerance (adaptations) in infected grasses reviewed in [46]. When there is little water available, *Neotyphodium* sp. and *Arizona fescue* (*Festuca arizonica* Vasey) produce more leaf area per total plant biomass and less thick leaves, which are associated with higher net absorption rates [47]. This could partially elucidate the mechanisms underlying endophytic fungal drought resistance. In the case of *Acremonium coenophialum* Morgan-Jones and Gams associated with tall fescue (*Festuca arundinacea* Shreb), endophyte-mediated adaptation to drought stress was explained as an avoidance mechanism; the endophyte had minimal effect on plant water soluble mineral and sugar concentrations and no effect on leaf osmotic potential [48]. The symbiotic relationship between endophytic fungi and their hosts may be influenced by environmental factors from the plants' original home. The effects of the fungal endophyte *Neotyphodium* sp. on plant growth and seed yield were examined in this manner for three genotypes of *L. perenne* L. that were obtained from various natural settings. The endophyte infection in the genotype that was taken from a dry environment decreased plant growth when there was a sufficient quantity of water, but it promoted regrowth when there was a drought. Endophyte infection markedly accelerated the establishment of reproductive tillers and seed production in the genotype from a seasonally wet or dry location (effects related with adaptation to drought). Conversely, when endophyte infection was present, the genotype originating from a moist site demonstrated increased sensitivity to drought stress [43]. Under drought stress conditions, harbouring endophytes may have a metabolic cost for some genotypes of host plants [49]. The mechanisms responsible for drought stress tolerance can be explained by enhanced osmotic adjustment in the meristematic and growth zone, which helps to protect the apical meristem and enables tiller survival [50]. As shown with the model of *Pirifomospora indica* and *Arabidopsis thaliana*, upregulation of several genes providing drought resistance may also be implicated [51]. In the event of an extreme drought, plants may benefit greatly from the use of fungus endophytes. But, as previously mentioned, certain issues can arise, such as when particular endophytes infect grass. However, in the event of climate change, other plant-associated microorganisms may also be influenced, in addition to fungal endophytes and their interactions with their host plants.

Crops can be significantly impacted when heat and salinity stress occur at the same time. In soybean (*Glycine max* L.) plants, the endophytic fungus *Trichoderma virens* SB10 inoculation and Glycine Betaine (GB) treatments resulted in a considerable tolerance against these two stresses. *T. virens* SB10 increased the synthesis of gibberellins, IAA, and SA in the presence of GB. Proline buildup and Na+ uptake was also reduced while macronutrient (N, Ca, and K) absorption increased as a result of the fungus and GB co-treatment. A high K+/Na+ ratio was maintained as a result of effects on the expression of the two primary genes involved in salt tolerance, GmHKT1 and GmSOS1[52]. Due to the upregulation of Ascorbate Peroxidases (APX), Superoxide Dismutases (SOD), Peroxidases (POD), and decreased Glutathione (GSH) enzymes, treated plants showed faster growth rates and an increase in antioxidant activities. The plant microbiome can help shield plants from drought and excessive salinity, according to multiple findings [53, 54, 55]. The endophytic fungus *Piriformospora indica* increases the expression of genes by raising the levels of auxin, ABA (abscissic acid), SA, and cytokinin implicated in the drought stress response of maize hosts [56]. Additionally, it has been demonstrated that *Trichoderma harzianum* increases rice's resistance to drought by influencing the expression of the genes for SOD, DBP, aquaporin, and dehydrin [57]. The alteration in the metabolism of soluble sugars and amino acids, symbiotic partnerships between plants and endophytic fungus like *Piriformospora indica* might improve the ability of plants to respond to drought stress. For example, it was discovered that *P. indica* enhances barley's (*Hordeum vulgare* L.) ability to adapt to drought stress [58]. Reduced effects of salinity were observed in soybeans inoculated in salinized conditions with the endophytic fungus *Porostereum spadiceum* AGH786. By activating genes for ion transporters, ROS scavenging, and the production and signalling of phytohormones like auxin, JA, and ethylene (ET), endophytic microbes can reduce the oxidative stress caused by salt in plants[59]. Seed bio-priming is a cutting-edge helpful method that uses biostimulating substances like growth-promoting microbes to enhance the physiological processes of seeds and increase their resistance to stress[60]. *Paecilomyces lilacinus* KUCC-244 and *Trichoderma hamatum* Th-16, two salt-tolerant endophytic fungus, were employed to bio-prime the seeds of wheat and mung beans (*Vigna radiata* L.). The findings demonstrated that under very salinity circumstances, both endophytes, especially *T. hamatum* Th-16, enhanced the growth and chlorophyll content of wheat and mung bean plants. Additionally, the primed plants showed improved photosynthetic characteristics and elevated antioxidant enzyme activities[61].

The endophytic fungus *Epichloegansuensis* has been shown to have protective effects against cold stress. During the germination of Drunken horse grass (*Achnatherum inebrians*) seeds, it increases the biosynthesis of alkaloids and unsaturated fatty acids, which in turn increases tolerance to cold stress. Additionally, it was noted that certain genes linked to cold stress in grapevine were upregulated by the endophytic rhizobacterium *Parabulkholderia phytofirmans* PsJN [62, 63]. Endophytic bacteria have showed several beneficial effects on their host plant. Plant growth is promoted through improved nutrient acquisition, including nitrogen fixation [64] and production of plant growth enhancing substances such as cytokinins and indole acetic acid [65]. The adaptation to environmental abiotic or biotic stress can be enhanced by modulating the plant metabolism and phytohormone signalling by the endophytic bacteria, since endophytic bacteria have the advantage of being relatively protected from the harsh environment of the soil under drought, high salt or other stress conditions therefore, they show a special interest for improved crop adaptation [66]. It was seen that this endophyte enhances cold tolerance of grapevine plants by altering the photosynthetic activity of bacterial endophyte *Burkholderia phytofirmans* PsJN and also the metabolism of carbohydrates involved in cold stress tolerance [67]. The bacterium present in the plant promotes acclimation to chilling temperatures that result in increased photosynthetic activity, lower cell damage, and accumulation of cold-stress-related metabolites like starch, proline, and phenolic compounds. In wheat plants grown under reduced irrigation conditions a similar positive effect of the bacterium on metabolic balance and reduced effect of drought stress was shown. Retention of higher concentrations of glycine betain-like compounds are induced by endophytic bacteria *Pseudomonas pseudoalcaligenes* which leads to improved tolerance for salinity stress in rice [68]. Cohen *et al.*, [69] presented accumulation of the abscisic acid produced by endophytic *Azospirillum*s pp. mitigated the water stress tolerance in maize plants and the plant growth promoting hormones such as indole acetic acid and gibberellins further enhanced the effect. For plant growth and development abscisic acid is the critical phytohormone and its level showa riseunder stress condition.

Phytostimulation: Basically 16 essential elements are required by the plants such as C, H, N, O, and P and 11 more. These essential elements enhance the growth and development of the plant in chemical form, which they obtain from soil, water, atmosphere, and organic matter. Endophytes also play an important roleuptake of these nutrients. They elicit different modes of action in tall fescue adaptation to Phosphorus deficiency [70] and induce increased uptake of Nitrogen[71]. A wide range of phytohormones are produced by endophytic bacteria such as auxins, cytokinins, and gibberellic acids. An endophytic bacterium named *Burkholderia vietnamiensis* is isolated from the wild cottonwood (*Populus trichocarpa*), it produces indole acetic acid, which helps in promoting the plant growth [72]. This was confirmed when a comparison was made between plants without inoculation and plants inoculated with *Burkholderia vietnamiensis* on nitrogen free media, where the inoculated plants gained more dry weight and more nitrogen content. *Cladosporium sphaerospermum*a fungus was isolated from the roots of Glycine max (L) Merr. which showed the presence of higher amounts of bioactive compounds GA3, GA4, and GA7, and further induced maximum plant growth in soybean as well as in rice varieties[73].

Pigment Production: From endophytic fungus belonging to *Penicillium* sp. An orange pigment was isolated and identified as quercetin glycoside and this was the first report on quercetin glycoside produced by an endophytic fungi. Endophytic fungus strain named SX01 obtained from the twigs of Ginkgo biloba L, also identified as *Penicillium purpurogenum*, and was able to produce abundant soluble red pigments which could be used as natural food colorant [71]. Isolated from the *Monodictys castaneae* an endophytic fungus was found to inhibit few human pathogenic bacteria *Salmonella typhi, Staphylococcus aureus, Vibrio cholerae, Klebsiella pneumonia* and also proved to be more active than streptomycin [72].

Enzyme Production: Certain soil microbes produce various commercially important enzymes. Endophytic fungi such as *Fusarium lateritium, Penicillium aurantiogriseum, Acremonium terricola, Cladosporium cladosporioides, Cladosporium sphaerospermum,* *Aspergillus japonicas, Phomopsis archeri, Nigrospora sphaerica, Penicillium glandicola, Pestalotiopsisguepinii, Phomatropica, Monodictyscastaneae, Tetraploaaristata,* and *Xylaria* sp. have indicated their potential for the production of pectinases, cellulases, xylanases and proteases enzyme involving biotechnological processes. *Acremonium zeae*, an endophyte isolated from maize produces hemicellulase enzyme [73] which may be suitable for the bioconversion of lignocellulosic biomass into fermentable sugars.

Phytoremediation: Phytoremediation refers to cleaning up a place mediating plants and microbes. This in situ, solar-powered remediation technique has a cheap cost and great public acceptance because it involves little disturbance of the environment and little upkeep. One of the main issues impeding the use of medicinal plants as raw materials is heavy metal toxicity. Typically, plants absorb heavy metals from the soil, which can have an impact on the health of the plants as a whole as well as their capacity to create significant secondary metabolites [74]. Their presence frequently causes non-tolerant plants to lose their enzyme activity, which is the foundation for the synthesis of secondary metabolites. Plants that are exposed to heavy metal toxicity produce higher ROS [75]. Even while ROS are typical byproducts of metabolism, certain circumstances might cause an excessive amount of ROS to be formed, surpassing the body's defense mechanisms, which can cause oxidative stress in plants and ultimately lead to cell death [76].While ROS can lead to an increase in the production of secondary metabolites, an excess of ROS can have a negative effect on the production of secondary metabolites by causing damage to primary metabolites, which are the building blocks of secondary metabolites, such as proteins, lipids, and nucleic acid compounds [76]. Conversely, endophytes have been shown to help plants get rid of reactive oxygen species (ROS) by scavenging active oxygen systems, which are usually activated when plants are under stress [75]. Through a number of processes, such as transformation, chelation, solubilization, and precipitation, endophytes restrict the uptake of hazardous heavy metals by plants and/or render them immobile [77, 78]. For example, they absorb these hazardous heavy metals into their cell walls through a process known as biosorption, which entails a variety of processes such as ion exchange, electrostatic interaction, precipitation, and redox reaction [79].

By generating volatile organic compounds (VOCs) including terpenoids and phenylpropanoids, endophytes also shield medicinal plants against heavy metals[80]. Additionally, endophytes generate a variety of useful hydrolytic enzymes that have the ability to sequester a wide range of organic and inorganic substances [81, 82]. Numerous microorganisms have been shown to convert hazardous heavy metals into less toxic forms by degrading and immobilizing them [79, 83]. Thus, it has been shown that microbial enzymes possess exceptional, distinctive qualities that many chemical catalysts might lack. Endophytes support medicinal plants by enhancing immunological function and physiological responses [84]. For instance, endophytic 1-aminocyclopropane-1-carboxylic acid deaminase (ACC) enhances plant growth and development while countering the inhibitory effects of ethylene, thereby helping plants to tolerate stress conditions [75, 85]. Finally, the root is thought to be the primary entrance point for heavy metals, despite the fact that they can enter through other plant sections as well. In the remediation of heavy metals and other harmful chemicals, fungi have been shown to be the most prevalent. By thickening their cell walls and increasing their surface area, the hyphae of fungal microorganism's aid in the amelioration of heavy metals and improve the absorption of those toxic elements into their cell wall [86, 87]. Additionally, endophytic cell walls produce polysaccharides such amino, carboxyl, and hydroxyl groups. These compounds increase the binding sites with positive metal compounds, acting as a barrier to metal ions [75].

Endophytes are saprobic decomposers: Several recent studies have explored relationships between endophytes and their role as saprobes [21]. The evidence is circumstantial; however, it seems likely that some (or many) saprobes are derived from endophytes [88]. If the hypothesis that the saprobes are derived from endophytes is correct then, it is more likely that they would be host or tissue specific. Endophytes may have developed intimate relationships with their hosts during evolution and may be host or even tissue specific [89]. Several studies provide evidence to support the hypothesis that saprobe host specificity in plants is dependent on internal endophytes, while reports are available that host components may regulate the endophytes [90]. Whatever the reason it is clear that many endophytes in wood and leaves are host, or host family specific [91] and that this specificity must depend on factors such as initial endophyte colonization or substances within leaves and wood.

As plant litter decomposers, endophytes offer a crucial ecosystem service[92]. However, a number of studies have demonstrated that the involvement of endophytes as saprobic decomposers is largely circumstantial [88]. Within the host plants, the endophytic and saprophytic life cycles of plant endophytes would alternate. Endophytes either turn into saprobes when their host tissues die off or when their plants reach senescence. On aged plant portions, a few fungal endophytic species, including Anthostomella, Arecomyces, Arecophila, Capsulospora, and Linocarpon, have been noted to turn saprophytic [89]. The main agents in the breakdown of plant litter are endophytic fungal communities. This is an extremely intricate process that involves multiple fungal taxa that undergo significant changes over time [93]. It has been revealed that the foliar or above-ground plant endophytes play a major role in the decomposition of litter [94, 95]. Plant components, lignin content, and other resistant substances combined to form AUR (acid unhydrolyzable residue) impede the breakdown of plant litter. The production of ligninolytic enzymes by ligninolytic endophytes, which may be found in both grasses and trees, offers a possible solution for completing the challenging process of decomposing litter [96].

The final transition to alternative fuel supplies has been signalled by rising energy usage and quickly depleting fossil fuel reserves. Numerous endophytic bacteria that can directly produce biofuels or have the ability to degrade various carbon sources with the help of enzymes have been identified in recent investigations, making them valuable for the generation of biofuels. For instance, it has been reported that the endophytic fungus *Gliocladium roseum* produces a blend of volatile hydrocarbons collectively referred to as myco-diesel [97]. According to [98], xylariaceous fungus that produce large quantities of methyl esters (91%) are thought to be a promising source of biofuel. Other fungal genera known to produce hydrolytic enzymes that can break down sugarcane biomass in order to produce bioethanol are the fungal endophytes *Aspergillus niger* DR02, *Trichoderma atroviride* DR17, *Alternaria* sp. DR45, *Annulohypoxylonstigyum* DR47, and *Talaromyces wortmannii* DR49 [99]. It was discovered that *Bacillus subtilis*, an oleaginous endophytic bacterium with high lipid synthesis, was a good fit for the manufacture of biodiesel [100]. The production of lignocellulolytic enzymes by the endophytic bacteria *Pantoeaananatis* Sd-1 can also be used to produce bioethanol from lignocellulosic biomass [101].

Hormonema sp. CECT-13,092, a novel endophytic ascomycete from the Eucalyptus tree, has been shown to have the ability to enhance lignocellulosic biorefinery processes such enzymatic saccharification, biopulping, and biobleaching. This fungus has demonstrated the first-ever bio-bleaching activity as well as the highest delignification activity of 26.7%, increasing sugar yields by an astounding 8 times[102]. Additionally, [103]reported that five new laccase-producing fungal endophytes *Neofusicoccum luteum*, *Ulocladium* sp., *Pringsheimiasmilacis*, *Hormonema* sp., and *Neofusicoccum austral*were effectively used as a pre-treatment to improve saccharification and biopulping of *Eucalyptus globulus* wood. In addition, two endophytic fungi, *Ulocladium*sp. and *Hormonema* sp., have been used to pre-treat olive tree pruning. It has been observed that their use, combined with a mild acid pre-treatment, enhances enzymatic hydrolysis by 12% [104].

Endophytes as producer of Antibiotics: Antibiotics are defined as low-molecular-weight organic natural products made by microbes that are active at low concentration against other microbes. Products obtained naturally from endophytic microbes inhibit or kill a wide variety of harmful disease-causing agents which include fungi, bacteria, viruses, and protozoans. Endophytes isolated from the plants are known for their antimicrobial activity. They help to prevent the growth of microbial pathogens in plants. Endophytes isolated from medicinal plants showed bioactivity for broad spectrum of pathogenic microbes [105]. The bioactivity of the endophytic microorganisms was assayed by [106] such as *Colletotrichum truncatum, Alternaria tenuissima, Thielaviasub thermophila, Dothideomycetes* sp., *Alternaria* sp., *Chaetomium* sp., and *Nigrospora oryzae* isolated from the medicinal plant. *Tylophora indica* against *Sclerotinia sclerotiorum* and *Fusarium oxysporum* which were found to inhibit their growth.Endophytic fungi produce several classes of antimicrobial compounds, such as terpenoids, peptides, alkaloids, phenyl propanoids, polyketides, and aliphatic compounds [107]. The ability of the endophytes to produce host-based secondary metabolites shows that there is possibility of the existence of several complex cross-talks between the endophytes and host plant at the genetic level. The evolutionary studies and the inability of endophytes to produce secondary metabolites in subculturing (either due to loss of extra-chromosomal material acquired from the host plant or silencing of genes in the absence of host) supports the possibility of host-based secondary metabolites production [108].

Bioactive compounds and natural products from endophytes: Antioxidant metabolites are often produced by endophytic fungi. Pestacin and Isopestacin were isolated from *Pestalotiopsis microspora* from plant *Terminalia morobensis,* native of the Papua New Guinea [109]. Approximately half of the deaths worldwide are caused due to Infectious and parasitic diseases [110]. For drug discovery natural sources have been proven as the best source even though it is the generation of nano to pico drugs. Medicinal plants and theendophytes obtained from them are an important source of valuable bioactive compounds and secondary metabolites that contribute to more than 80% of the natural drugs available in the market [111]. For antiarthritic, antimicrobial, anticancer, antidiabetic, anti-insect, and immunosuppressant activities an excellent source of drug is obtained in the form of novel secondary metabolites from Endophytic microorganisms as they are the storehouse of secondary metabolites. A number of bioactive metabolites have been reported to produce from endophytes in a single plant or microbe which served as an excellent source of drugs for treatment against various diseases and with potential applications in medicine, cosmetics, food and agriculture industries [112, 113]. These secondary metabolites were categorized into various functional groups, alkaloids, benzopyranones, chinones, phenolic acids, flavonoids, saponins, tannins, quinones, steroids, terpenoids, tetralones, polyketones, xanthones, and many others [112, 114, 115]. Various factors affect the Extraction of metabolites from endophytes, like the season inwhich sample is collected, climatic condition and geographical [113]. During the past few years, a revolutionary synthetic process developed has made extraction from plants and other natural sources more feasible, efficient and convenient [116]. The evolution of the host microorganisms has led to a direct association of the endophytes that producebioactive substances, which may include genetic information from higher plants, it allows them to better adapt to the host plant and perform particular functions, such as protection against different types of pathogens, insects, and grazing animals [109]. Some of the commonly occurring secondary bioactive compounds from endophytes include : Taxol, the world’s first billion dollar anticancer drug it consist of a highly functionalized diterpenoid and famous anticancer agent that is found in each of the world's yew tree species (*Taxus sp*) Taxol (paclitaxol), was produced by the endophyte *Metarhizium anisopliae* which is found in the bark of *Taxus* tree, it contains a complex diterpene alkaloid which is one of the most promising anticancer agents developed or synthesized to date [117, 118] Camptothecin, from *Nothapodytes foetida* is known to have cytotoxic and antifungal properties [114]. Huperzine A (HupA), from *Huperzia serrata*, can act as a cholinesterase inhibitor [119] Lignans, such as cathartics, emetics and cholagogue, isolated from endophytic *Podophyllum hexandrum*, are reported to act as anticancer agents [120]. Plants show a Diversity of endophytic fungi residing within they represent a rich resource of bioactive natural products which are capable to exploit the pharmaceutical and agricultural field [121]. Fungal metabolites from endophytes greatly affect the biology of predators. Herbivores [122]. Until 2003 approximately 4,000 biologically active secondary metabolites have been described [123]. The so called "creative fungi" produces most of these metabolites and they include species of *Acremonium, Aspergillus, Fusarium* and *Penicillium*, but researches on endophytes ability to produce novel metabolites were few [121] isolated around 6500 endophytic fungi and tested their biological potential. 135 secondary metabolites were subjected and it was found that 51% of bioactive compounds (38% for soil isolates) isolated from endophytic fungi were new natural products. These workers concluded that endophytic fungi are a good source of novel compounds and that "screening is not a random walk through a forest". The major query of how microbial endophytes gain access to their host plants has also been the subject of study. Most mycorrhizal fungal endophytes and bacterial endophytes from the soil gain access through the roots; but bacterial endophytes are not thought to invade plant tissue directly; instead, they generally tend to enter the plant through natural openings or wounds.

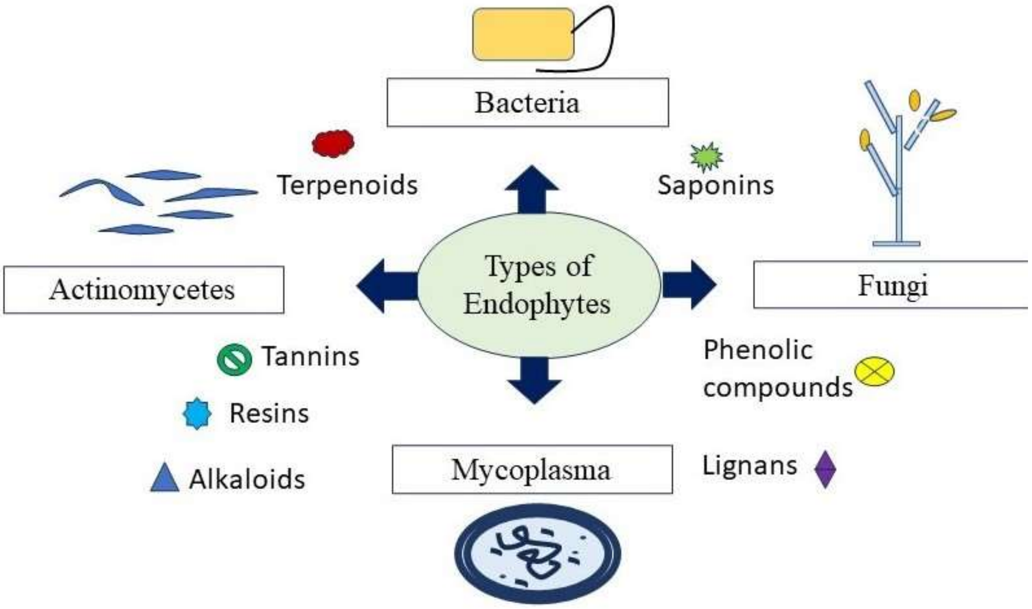

Fig 1: Different types of endophytes and the bioactive compounds produced

Endophytes as nanoparticle biosynthesizers: Biosynthesis of nanoparticles have emerged as a budding frontier technology owing to its versatile functions, potential bioactivity, non-pathogenic nature, and enormous therapeutic applicability of these particles [124]. For the synthesis of both silver and gold nanoparticles, a variety of endophytes have been exploited

[125, 126]. With their antibacterial, antifungal, antioxidant, antimicrobial, antidiabetic, anticancer, and photocatalytic degradation properties, these biosynthesized nanoparticles have a plethora of potential uses in nano medicine [127]. Owing to the special optical, electrical, and magnetic qualities, silver nanoparticles are particularly useful in bio-labeling, antibacterial agents, catalysts, and sensors. According to reports [128, 129], silver nanoparticles synthesized using endophytic bacteria, such as *Bacillus cereus*, *Bordetella* sp., and *Pseudomonas veronii* isolated from the host plants *Adhatodabeddomei*, *Piper nigrum*, and *Annona squamosa*, respectively, exhibit antibacterial activity. Additionally, fungi endophytes have been employed in the manufacturing of nanoparticles. For example, *Aspergillus clavatus* from *Azadirachta indica*, *Alternari*a sp. from *Raphanus sativus*, *Setosphaeria* sp. from *Solanum nigrum*, and *Phomopsis helianthi* from *Nyctanthesarbor-tristis* have all been used to synthesize silver nanoparticles, which have been found to have significant antimicrobial and antifungal potential [130, 131, 132]. Additionally, endophytic fungal nanoparticles are essential for the biological control of plant diseases.

Endophytes as biological control agents: As the evidences reveal the endophytes play a role in the outcome of plant pathogen interactions which lead to disease has been increased in recent years. A diverse mechanism has been observed by which they may counteract pathogen development. Some endophytic species may induce plant defense mechanisms which counteract pathogen attack, some endophytes have competition for resources and plant space between incoming pathogens and resident endophytes, some of them produce antibiotic substances which inhibit pathogen growth and some parasites of plant pathogens are known to behave as endophytes

Interactions with plant pathogenic fungi

There are many endophytic species which produce antibiotic substances [17]. The growth of several plant pathogenic fungi species can be inhibited by endophyte cultures produced from liquid extracts [133, 134]. If such compounds were produced by endophytes present inside the plants, this could constitute a defense mechanism against the fungal pathogens. Several experiments were performed where plants were inoculation with endophytes as well as after the application of endophytic culture filtrates plant protection against pathogenic fungi was observed. This suggests that the endophyte may produce an antifungal compound that induces plant defense mechanisms in the plant. Such a case occurred when the fungi *Chaetomium* and *Phoma*, endophytes of wheat were inoculated in plants, reduced severity of foliar disease was observed which was caused by *Puccinia* and *Pyrenophora*spp., the same protective effect was observed when only endophytic culture filtrates were applied to the plants [135]. The endophytes may restrict the entry of other fungi by producing zones of inhibition. Endophyte infection alters plant biochemistry in such a way that defense mechanisms against pathogens are induced. *Piriformospora indica* Sav. [136] is a root endophyte with a wide host range, including several species of cereals and *Arabidopsis*. When barley plant was inoculated with this endophyte it showed resistance towards vascular *Fusarium culmorum*as well as a leaf pathogen *Blumeria graminis*, an increase in yield and salt stress tolerance was also observed [23]. The protection against the leaf pathogen appears to be mediated by a mechanism of induced resistance, because in the plantsinoculated by pathogen there is a defense response which involves the death of the host cells. An endophyte named *Acremonium strictum* W. Gams has been frequently isolated from *Dactylis glomerata* L. and other grasses [20] and the study by [137] conclude that this fungus is a mycoparasite of *Helminthosporium solani* Durieu and Mont., which is a potato pathogen. Cultivars of several turfgrass species infected by *Neotyphodium* and *Epichloe* endophytes are commercially available. Since cultivars infected from*Neotyphodium* and *Epichloe* show an increased resistance to herbivores, plant pathogens, the use of such symbiotic cultivars resulted in a reduced use of insecticides and fungicides in lawns. The outcome of some pathogen attacks might be dependent on the endophytic mycobiota associated to a host plant.

Mechanisms of insect control displayed by endophytic fungi

Since the pioneer works in the field, the capacity of endophytic fungus to repel insects, induce weight loss, growth and development reduction and even to increase pest death rate, was correlated with toxin production. In several cases, it was shown that the mode of action of certain fungi was based on the capability to render the plant unpalatable to several types of pests like aphids, grasshoppers, beetles, etc [138]. Bacon *et al.,* [139] established for the first time a correlation between an endophytic fungi, *Epichloëtyphina* and the toxicity of its host, *F. arundinacea,* to herbivorous domestic mammals. It is now a fact that several toxins are produced by endophytic fungi and that these substances confer host protection against different herbivorous. The review of [140] in which the most important toxins found in *L. perenne*, like ergot alkaloids of two types, ergopeptine and clavine and neurotoxines called lolitrems are described. In opposition to the ergot toxins that are isolated directly from the endophytic fungi, the neurotoxins produced by endophytes like *A. lolii* are only percursors of toxins like, for example, paxiline. It is not known if the precursor is converted in lolitrems by the plant or if the fungus is not capable of synthesizing it in pure culture but is able to do so while inside the plant. In 1986, Miller [141] showed that the protection of Canadian fir that against the spruce budworms resulted from the production of toxic secondary metabolites by endophytic fungi. In 1988, Prestidge and Gallagher [142] established a relationship between the presence of the fungus *A. lolii* in *Lolium perenne* and the growth, survival and feeding behaviour of *Listronotus bonariensis* larvae. In this case, the reduction in insect attacks towards infected plants was due to a strong toxin, lolitrem B, also toxic to mammals. This toxin, once added to insect diets, reduced insect growth and survival. Its assimilation occurs by ingestion but not by absorption through the insect integument. In certain cases, the production of toxin by the endophytic fungi was a plausible explanation for interactions resulting in natural insect control. Clark et al. [143] showed in *Abies balsamea* and red spruce *Picea rubens,* that from 900 samples of fungal isolates, five produced toxic substances and three of those produced powerful toxins that, once extracted and given to insects, caused death and decreased development rate of *C. fumiferana*. Many other cases of insect control involving toxins produced by endophytic microorganisms can be found in the literature. Siegel et al. [144] verified the presence of the alkaloids N-formil, N-acetilloline, peramine, lolitrem B and, ergovaline during plant attack by aphids. Several grasses infected with *Acremonium* spp. and *E. typhina* were analysed. These fungi, generally produce alkaloids, mainly peramine and ergovaline. Peramine, lolitrem B and ergovaline were found in *Lolium* and *Festuca* infected with *A. coenophialum* and *A. lolii* and in *Festuca longiflora* infected with *E. typhina*. Individuals of *Rhopalosiphumpadi* and *Schizaphis graminum* did not survive in grasses containing the alkaloid loline. On the other hand, ergovaline did not affect both insect species. Surveys have been carried out aiming to the discovery of toxins useful to insect control. Two active toxins against the Spruce budworm *C. fumiferana* were found in an unidentified endophytic fungus infecting the wintergreen *Gaultheria procumbent* [145]. Alkaloids from *N. lolii* and *L. perenne* are capable of altering insect behaviour. Several of these alkaloids were added to the diet of adult individuals of the Coleoptera *Heteronychusaratur*. Ergovine showed moderate effects whereas ergotamine, ergovaline from the ergot-type alkaloid family seem to be responsible for the plant resistance [146]. The majority of works related to toxin production was performed in grasses. However, Calhoun et al. [147], for the first time, identified toxic products synthesized by endophytic fungi in woody plants and that were able to modify growth and death rates in larvae of the spruce budworm *C. fumiferana* feeding on balsam fir. The endophytes in this case were identified as *Phyllosticta* and *Hormonemadematioides* and the toxic compounds were mainly heptelidic acid and rugulosine.

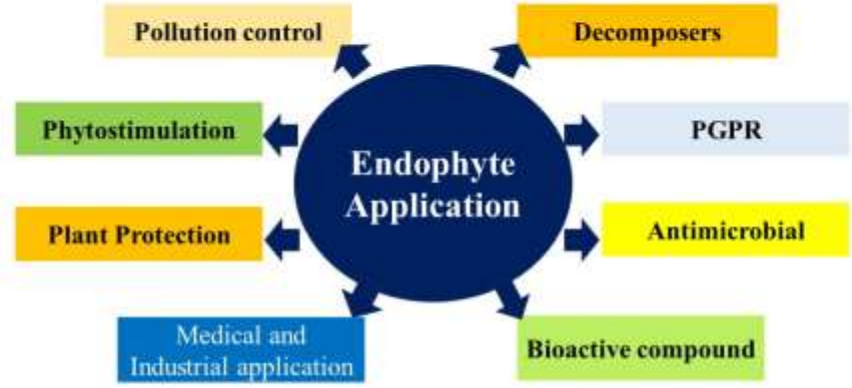

Fig: Application of endophytes in various fields

Conclusion and Future Prospect

Exploitation of endophyte - plant interactions can result in the promotion of plant health and can play a significant role in low-input sustainable agricultural applications. Endophytes appear to have the potential to produce a wide range of metabolites and bioactive compounds with the significant biological activity for applications in industry, crop protection, pharnaceuticals and environmental recovery. One promising area of research for future studies is developing endophytes to promote the sustainable production of biomass and bioenergy crops in conjunction with phytoremediation of soil contamination. One of the major problems facing in future of endophyte biology is the rapidly diminishing forests, which hold the greatest possible resources for acquiring novel endophytic microbes and their products. Endophytes have all been used to synthesize silver nanoparticles, which have been found to have significant antimicrobial and antifungal potential. Additionally, endophytic fungal and bacterial nanoparticles can be an essential future tools for the biological control of plant diseases. Thus, when a plant species disappears, so too does its entire suite of associated endophytes. So, there is a need to immediate preservation of biodiversity and make national collections of microbes that live in those areas.

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