REVIEW

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# Endophytic fungi: their role in plant protection and biological applications

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Endophytic fungi are fungi that inhabit live plant tissues, displaying a diverse range of microbial adaptations that have evolved in such a sequestered habitat. They are a great resource for drug discovery due to their diversity and unique characteristics. These endophytic fungi may provide protection and survival strategies for their host plants by producing a variety of secondary metabolites with a wide range of biological activities, including antimicrobial, anticancer, antiviral, antioxidants, anti-parasitics, immunosuppressants, anti-inflammatories, and biocontrol, having applications in medicine, agriculture, industry, and phytoremediation. In response to endophytic fungal invasion, plants have evolved a variety of beneficial responses over time. As water resources and agricultural lands continue to decrease, and climate change worsens, it is critical to boost agricultural output to feed the world's rising population. Drought, salinity, extreme temperatures, heavy metal toxicity, and oxidative stress are serious abiotic stresses to agriculture and contribute to environmental deterioration. Researchers from all around the world are increasingly interested in bioprospecting endophytic microbial communities as a source of bioactive chemicals for commercial uses. In the medical sciences, biological nanoparticle synthesis has emerged as a viable alternative to chemical nanoparticle production. As a result, "green nanotechnology" emerged as a new field of nanotechnology. For the investigation of endophytic microbial biodiversity, metagenomics approaches and related bioinformatics systems are considered untapped tools. This review mainly focuses on the biology of endophytic fungi and their biological activities on sustainable agriculture.

**Keywords:** Endophytic fungi, antimicrobial, bioprospecting, green nanotechnology, metagenomics.

## INTRODUCTION

Plants harbour a wide diversity of microorganisms such as bacteria, fungi, archaea, algae, and protists both within and outside of their tissues. Plant survival, fitness, biodiversity, and ecosystem function are all influenced by the interactions between these microbes and plants.

The most common symbiotic associations with plants are mycorrhizal and endophytic, and their affiliation aids the plant's growth, development, and disease resistance (Khare *et al.*2018). Saithong *et al.* (2010) define endophytic fungi as those fungi that dwell within photosynthetic plant tissue and create a symbiotic connection, causing no damage to the host plant. The researchers were interested in endophytic fungi after discovering the anticancer medicine taxol from an endophytic fungus, *Taxomyces andrenae* obtained from the Pacific yew tree *Taxus brevifolia*. Endophyte research now focuses on the extraction of bioactive chemicals, the detoxification of xenobiotic contaminants, and the use of endophytes as a biocontrol agent (Choudhary *et al.* 2021).

In terms of structure and function, endophytic fungi might imitate the host plant's metabolite synthesis. Endophytic fungi stimulate the growth of the hosts by triggering the solubilisation of phosphorus, potassium, and zinc. They mobilise the plant nutrients by various mechanisms such as acidification, chelation, exchange reactions, and the release of organic acids. They also protect host plant from pathogens through hyperparasitism, niche exclusion, competition, or antibiosis by producing extracellular exzymes, or by activating plant defences; herbivory; altering plant hormone levels; producing siderophore, ACC deaminase and supplying essential vitamins and tolerance to environmental stress and displays a wide spectrum of biological activities (Yadav *et al.* 2017). Endophytic fungi have a complex nature that has

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yet to be fully understood, thus further study is needed.

The toxification of the environment has increased dramatically as human civilization has progressed. Endophytic fungi isolated from plants grown in contaminated sites with metals such as cadmium, lead, zinc, manganese, and cobalt show metal bioremediation potential by providing various detoxification routes. Endophytic fungi produces important therapeutic agents and chemicals that can be used to treat diseases including cancer, malaria, neurological, cardiovascular, and autoimmune problems (Toghueo, 2020). For many years, several endangered plants have been indiscriminately exploited for the extraction of natural compounds with medical benefits. Endophytic fungi associated with these plants are being studied to address this issue. Endophytic fungi are the least studied and diverse group of fungi that include a wealth of unknown and uncharacterized microorganisms capable of creating new compounds. Endophytic fungi, can be used to synthesise nanoparticles because they produce large amounts of enzymes and are easier to work with in-vitro. Silver nanoparticles stand out among other types of metal nanoparticles because of their unique qualities, such as chemical stability, conductivity, catalytic capabilities, and antibacterial potential throughout a broad range (Diantoro*et al*. 2018). New research trends have shown the biotechnological application of endophytic fungi in the synthesis of biofertilizers and biopesticides, ensuring long-term agricultural sustainability. As a result of abrupt climate change, abiotic stressors are expected to become more common in the coming decades, posing serious concerns for global food security (NouhandAbdel-Azeem, 2020). Despite the fact that endophytic fungi may be cultured under controlled circumstances, commercialization is still hampered by attenuation, shelf life, regulation, and differences between laboratory and field results.

## ISOLATION OF ENDOPHYTIC FUNGI

The endophytic fungi remain hidden within the healthy host tissues, so their symptoms and identifying characteristics, including the reproductive structures, are difficult to visualise. The surface sterilisation procedure affects the isolation and diversity of endophytic fungi from plant parts. Thin and tender leaves require less sterilisation time than thick, hard, and meaty leaves. Fungal species such as *Aspergillus*, *Cladosporium*, and *Penicillium* arise from the plant surface rather than from the inner tissue due to a lack of appropriate surface sterilisation (Hyde andSoytong, 2008). The sampling size has a significant impact on the endophyte species richness, as a small sample size will overlook tiny mycocommunities. Endophytic fungal diversity is also influenced by geographic location, as high diversity is linked to environmental conditions such as temperature and rainfall (Zimmerman and Vitousek, 2012). Endophytic fungi are tissue and organ specific, hence they vary within a particular host's leaves, inflorescence, stem, and roots. Other elements that influence species diversity and richness are canopy levels and the age of the leaf.

## DIVERSITY AND MAJOR GROUPS OF ENDOPHYTIC FUNGI

Endophytic fungi may be found almost everywhere in nature. In the tropics, a single leaf may harbour up to 90 endophytic fungal species, while grassland species can have up to 50 distinct genera (Porras–Alfaro *et al*. 2008). In arctic and boreal environments, endophytic colonisation rates range from 1% to 44%, whereas tropical habitats have colonisation rates of over 90% (Higgins *et al*., 2007). By using molecular methods, most of the endophytic fungi have been identified upto species level.

Ascomycetes, which make up the majority of endophytic fungi, are an ecologically varied group. Sordariomycetes, Dothideomycetes, Eurotiomycetes, and Leotiomycetes are the most common endophytic fungi classes among ascomycetes, with Pleosporales, Xylariales, Hypocreales, Eurotiales, Botryosphaeriales, and Sordariales as significant orders (Wang *et al*. 2016). Dothideomycetes, Sordariomycetes, Leotiomycetes, Chaetothyriomycetidae, and Pezizomycetes were described as prominent classes in boreal, tropical, and arctic hosts, respectively (Rungjindamai*et al*. 2008). Even in polar plants, Ascomycota has been found to be prevalent (Zhang & Yao 2015). Endophytic fungal species have a life cycle that is partially symbiotic and partly saprophytic or latent pathogens, depending on the availability of host tissue or organs (Rashmi *et al*. 2019).

## PROMOTION OF GROWTH AND FITNESS OF HOST PLANTS BY ENDOPHYTIC FUNGI

Endophytic fungi not only produce hormones, but also boost hormones produced by the host plant, such as indole-3-acetic acid, indole-3-acetonitrile, and cytokinins, which promote host plant growth and fitness. Endophytic fungi that promote plant development are mostly Ascomycota (*Aspergillus, Aureobasidium, Chaetomium, Cladosporium, Colletotrichum, Exophiala, Penicillium, Trichoderma, Fusarium, Gliocladium, Phoma, Phomopsis, Purpureocillium, Talaromyces*), with a few belonging to Basidiomycota (*Limonomyces, Rhodotorula, Rhizoctonia*) and Zygomycota (*Mucor, Rhizopus*) (Cevallos *et al*. 2018). Endophytes have the potential to mobilise insoluble phosphate and provide nitrogen to their host plants by generating ammonia. Agricultural crops with fungal endophytes have been observed to produce higher yields when compared to those without endophytes.

Endophytic fungi, such as *Penicillium chrysogenum* and *Alternaria alternate*, extend the root length of maize plants by producing significant amounts of IAA (Fouda *et al*. 2015). A pestalotin analogue isolated from *Pestalotiopsis microspora* increased the seed germination rate of *Distyliumchinense* due to its strong gibberellin activity (Li *et al*. 2015). Some endophytic fungi isolated from *Cymbidium aloifolium* can produce antibacterial siderophores which also supply iron to the host plant (Chowdappa *et al*. 2020).

## STRESS RESISTANCE OF HOST PLANTS BY ENDOPYTIC FUNGI

Endophytic fungi generate a variety of bioactive chemicals that help host plants survive biotic and abiotic stressors. They also serve as an activator of the host plant's defence mechanism. Several endophytic fungi produce a wide range of antioxidant chemicals that have been shown to improve resistance to abiotic stressors. Pestacin and isopestacin, two powerful antioxidants, have been discovered from the endophytic fungus *Pestalotiopsis microspora* (Xu *et al*. 2010). Environmental stressors, such as heavy metal polluted soil, induce reactive oxygen species (ROS) to develop inside plant tissues, causing oxidative damage to proteins, nucleic acids, and membranes. Since many endophytic fungi have metal sequestration mechanisms, they enable host plants to live in such soil.

## ENDOPHYTIC FUNGI AGAINST BIOTIC STRESSES

Pathogens and herbivores cause major economic losses in agricultural crops. Therefore, endophytic fungi might help with resistance to such biotic pressures. Endophytic fungal species may be useful as biocontrol agents in the development of sustainable agriculture techniques.

### *Increase plant resistance against pathogens by endophytic fungi*

#### By producing antimicrobial compounds

One of the most essential strategies to enhance plant health is to suppress pathogen development. By generating antimicrobial chemicals, endophytic fungi boost the host plant's resistance to infections. Four endophytic fungal isolates from finger millet, belonging to *Aspergillus*, *Penicillium*, *Fusarium*, and *Phoma*, were able to generate anti-Fusarium chemicals (Mousa *et al*. 2015). *Phialocephala sphareoides*, a root endophyte isolated from Norway spruce, produces antifungal compounds that protect the host plant from infections that cause root rot, such as *Heterobasidion parviporum* and *Phytophtora pini* (Terhonen *et al*. 2016).

#### By acting as a component of plant defense

Endophytic fungi also serve in a similar capacity to animal immune cells, acting as mobile pathogen hunters to boost plant immunity. They can operate as a component of plant defence in addition to producing antibacterial compounds. The c-di-GMP-dependent signalling pathway is an essential mechanism for mediating endophytic signalling (Mousa *et al*. 2016).

#### By inducing overproduction of antimicrobial compounds by host plants

Endophytic fungi can cause host plants to produce excessive amounts of antibacterial or immunological chemicals. The endophytic fungus *Trichoderma hamatum* UoM 13 has been shown to increase salicylic acid synthesis and overexpression of defence enzymes and Pathogenesis-related (PR) proteins (Siddaiah*et al*.

2017). *Colletotrichum tropicale*, an endophytic fungus, has been shown to confer resistance to *Theobroma cacao* leaves by triggering activation of host defence genes (Mejia *et al*. 2014).

**By production of extracellular enzymes**

Extracellular enzymes produced by endophytic fungi hydrolyze plant cell walls. Phytopathogens can also be suppressed by these enzymes by destroying their cell walls. Endophytic fungi *Colletotrichum* sp., *Macrophomina phaseolina*, *Nigrospora sphaerica*, and *Fusarium solani* linked with *Catharanthus roseus* reported to generate the enzyme cellulase (Ayob and Simarani, 2016). Forty endophytic fungal isolates from *Ocimum* species were positive for enzyme synthesis, including amylase, protease, and tyrosinase (Pavithra *et al*. 2012). The *Colletotrichum* sp. associated with soybean leaves is an important endophytic fungus capable of producing enzymes during the final stage of leaf production, which participate in plant material degradation (Fernandes *et al*. 2015).

***Increase of plant resistance against herbivores by endophytic fungi***

Plants can be protected from herbivores by endophytic fungi, which produce poisonous substances that prevent the animals from eating them. Due to the generation of bioactive chemicals, the endophytic fungus *Neotyphodium-coenophialum* isolated from *Festuca arundinacea* causes toxicosis in calves that eat the plant (White *et al*. 2002). *Epichloe* is known to generate a number of alkaloids that prevent herbivores from eating the host plant (Brem &Leuchtmann, 2001). *Periglandula*, an endophytic fungal genus isolated from the morning glory family, has also shown to generate ergot alkaloids, making the plant very hazardous to herbivores (Leistner & Steiner, 2018). A recent meta-analysis found that during herbivore stress both hazardous chemical defence mechanisms and plant hormone defence systems were involved (Bastias *et al*. 2017). Even when endophytic fungal alkaloids are absent, the plant can protect itself against herbivore assault and necrotrophic diseases via Jasmonic acid (JA) routes (Zhang *et al*. 2015).

***Endophyte-mediated disease suppression mechanisms***

**Induced resistance**

Induced resistance to diseases may be defined as "the process of active resistance dependent on the host plant's physical or chemical barriers, activated by biotic or abiotic agents". The inducing substance causes the host to produce a translocatable signal, which causes the host to respond in a pathogen-resistant manner in the future. This is a dynamic process in which the inducing chemical triggers variable gene expression, protein synthesis, and particular metabolic changes in response to the plant signal. These alterations in plant metabolism modify the plant's appropriateness as a host, resulting in a lower disease level. Inducing agents can be both biological creatures and chemical molecules, and the host's reaction can be local or systemic.

**Plant resistance induced by endophyte-derived chemicals**

Both pathogen and endophytic fungal stimuli are recognised by the plant, but their defence responses differ. Plants detect some chemicals that are shared by all fungus groups, such as cell wall components, while others, such as proteins, lipids, secondary metabolites, hormone molecules, and volatile compounds, are unique to each species. Pathogen-associated molecular patterns (PAMPs) or microbe-associated molecular patterns (MAMPs) are recognised by plant receptors, which cause PAMP/MAMP-triggered immunity (Nürnberger and Kemmerling, 2009). Fungal cell wall chitin and glucans are significant MAMPs that plant receptors identify. Enzymes released during the infection and colonisation process, such as xylanases, cellulases, and chitinases, are recognised by the host and cause defence responses, either directly or indirectly.

**Hormonal signalling in the development of induced resistance**

'Systemic acquired resistance' (SAR) and 'Induced systemic resistance' (ISR) are the two basic kinds of systemic resistance. The hormone salicylic acid (SA) is significant in SAR, whereas the hormones jasmonic acid (JA) and ethylene (ET) are important in ISR. *Serendipita indica* has been shown to produce resistance in various pathosystems without relying on the JA/ET route (Waller *et al*. 2005), while plant-associated *Trichoderma asperellum* has been shown to trigger resistance in an SA-dependent manner (Yoshioka *et al*. 2012). This demonstrates that hormonal connections are complicated, and that adding endophytic fungi to a plant modifies the entire hormone balance.

### Antibiosis

Antibiosis is defined as the use of endophytic fungi with biocontrol capacity to prevent infections by creating chemical substances. Many endophytic fungi create specialised metabolites and substances that have the potential to impede the growth of other microbes. Several researchers have been attempting to find, isolate, and create commercially viable fungal metabolites to combat phytopathogens. Antimicrobial substances from endophytic fungi, such as alkaloids, flavonoids, peptides, phenols, quinones, steroids, terpenoids, and polyketides, have been discovered in recent investigations (Mousa and Raizada 2013). In certain circumstances, the host and endophyte share sections of a pathway and contribute partially to metabolite synthesis, or one partner drives the metabolism of the other. The endophytic fungus *Neotyphodium lolii* when linked with cold-season grasses, significantly expressed the gene cluster for the alkaloid lolitrem, but produced extremely weakly or at low levels in-vitro (Young *et al*. 2006).

### Mycoparasitism

Mycoparasitism is a phenomenon in which one fungus receives nutrients from another fungus, whether in a biotrophic interaction or necrotrophic contact. Mycoparasitism research is usually carried out in-vitro rather than on plants, and direct interactions between the parasite and the two partners may be examined using contemporary microscope methods. The mycoparasite makes direct contact with the host hyphae, then penetrates inside it, coils around it, and eventually destroys the prey hyphae. Three endophytic fungi isolated from *Phragmites australis* were discovered in the cytoplasm of eight soil-borne pathogens (Cao *et al*. 2009).

### Competition

Endophytic fungi have demonstrated that competition is a key strategy for preventing diseases from colonising the host plant. The removal of some endophytes from mango leaves through fungicide treatment creates space for possible diseases (Mohandoss and Suryanarayanan, 2009). Colonization of oilseed rape roots with the dark-septate endophyte *Heteroconium chaetospira* lowers clubroot symptoms, but the control effect is diminished when pathogen inoculum is increased, indicating that competition is limited in increasing disease load (Lahlali *et al*. 2014). Another study found that applying a foliar combination of isolated endophytes from cacao tree leaves to endophyte-free seedlings decreased disease caused by *Phytophthora* spp. foliage via a competitive mechanism (Arnold *et al*. 2003). Also, endophytic colonisation of tomato and cotton seeds by *Beauveria bassiana* can prevent damping down of seedling diseases caused by *Rhizoctonia solani* and *Pythium myriotylum*, implying space competition (Ownley *et al*.2008).

## ENDOPHYTIC FUNGI AGAINST ABIOTIC STRESSES

Abiotic stress is the most significant source of agricultural loss, accounting for more than half of global crop output. Abiotic stress causes morphological, physiological, biochemical, and molecular changes in plants, all of which have a significant impact on plant development and output. The finding of fossilised fungal hyphae and spores has demonstrated the role of endophytic fungi in the survival of ancient terrestrial plants against abiotic challenges such as drought, salt, metal, UV radiation, and temperature variations (Venugopalan and Srivastava, 2015). Plant resilience to abiotic stressors is enhanced by metabolites and hormones produced by fungal endophytes.

### *Resistance to salinity stress*

More than 45 million hectares of irrigated land have been affected by salt, and 1.5 million hectares are lost to production every year as a result of high saline levels in the soil around the world. Plant development, such as germination, vegetative growth, and reproductive development, has been affected by salinity. Plants are subjected to ion toxicity, osmotic stress, nutritional (N, K, P, Ca, Fe, Zn) deficiencies, and oxidative stress as a result of soil salinity, which inhibits water and mineral uptake (Arif *et al*. 2020). When plants are exposed to salt for an extended period of time, they are subjected to ionic stress, which can result in the premature senescence of adult leaves, reducing the amount of photosynthetic surface available to sustain further development. In barley, salt tolerance is induced by endophytic *Piriformospora indica*, which increases antioxidant levels (Baltruschat *et al*. 2008).

### *Resistance to drought stress*

Drought is a major determinant of agricultural output across the world, and its frequency is predicted to rise each year as climate change worsens the situation. It invariably results in an increase in reactive oxygen species (ROS), which are detrimental to plant health. Endophytic fungi have the potential to improve drought tolerance in plants by producing phytohormones. Abscisic acid (ABA) has been shown to protect plants from oxidative damage by activating stress-sensitive genes and enhancing the antioxidant system of plants (Fatma *et al*. 2013). Exogenous Salicyclic Acid (SA), in addition to ABA, might help to alleviate the deleterious effects of drought stress (Falqueto *et al*. 2017). Drought inhibits photosynthesis and protein synthesis, increases photorespiration, changes cell homeostasis, modifies plant hormone balance, and causes high levels of reactive oxygen species (ROS) in plant cells. Drought stress also reduces nutrient diffusion and mass flow of water-soluble nutrients such as nitrate, sulphate, calcium, magnesium, and silicon (Selvakumar *et al*. 2012).

### *Resistance to heavy metal stress*

Plant endophytic fungi appear to have a high level of metal tolerance and relief capability in polluted soils, according to previous studies. *Exophiala pisciphila*, a root-associated endophytic fungus of *Zea mays* has a high resistance to Cd, resulting in a considerable decrease in Cd phytotoxicity and a significant increase in maize growth (Wang *et al*. 2016). Plant resistance to heavy metal stressors is aided by endophyte phytohormones. IAA supplementation was found to reduce the harmful effects of lead on sunflower development by stimulating root volume, surface area, and diameter (Fässler *et al*. 2010). SA signalling has also been shown to cause a hypersensitive response followed by the creation of "systemic acquired resistance," resulting in the relief of heavy metal stress (Azooz *et al*. 2011).

## ENHANCED ACCUMULATION OF BIOACTIVE COMPOUNDS IN HOST PLANTS BY ENDOPHYTIC FUNGI

Many endophytic fungi possess the potential to enhance the accumulation of secondary metabolites from host plants, affecting the amount and quality of pharmaceuticals. Antibacterial, antifungal, immunosuppressive, antiviral, antiparasitic, antioxidant, anticancer, antipyretic, antimalarial, analgesic, or anti-inflammatory bioactivities are typically found in these substances (Singh *et al*. 2021).

### *Bioactive compounds as antibacterial agent*

The emergence of antibiotic resistance, notably the discovery of multiple antibiotic-resistant (MAR) bacteria, has resulted in a decrease in antibiotic action. Antibiotic resistance, according to the World Health Organization (WHO), is one of the most serious risks to human health, posing a significant financial burden on healthcare systems across the world. Endophyte produced antibacterial chemicals have been shown to belong to a variety of structural classes, including alkaloids, peptides, steroids, terpenoids, phenols, quinines, and flavonoids. Secondary metabolites produced by endophytic fungal species such as *Aspergillus niger*, *Curvularia pallescens*, *Guignardia bidwelii*, *Paecilomyces variotii*, and Mycelia sterilia were shown to have antibacterial action against *Staphylococcus aureus*, *Bacillus subtilis*, *Enterococcus faecalis*, *Micrococcus luteus*, *Escherichia coli*, and *Pseudomonas aeruginosa* (Silva *et al*. 2011). The polyketide citrinin generated by the endophytic fungus *Penicillium janthinellum*, isolated from fruits of *Melia azedaracha*, had 100% antibacterial efficacy against *Leishmania* sp. (Momose *et al*. 2000).

### *Bioactive compounds as antifungal agent*

Fungal diseases in the agricultural sector cause crop damage, economic losses, and, eventually, food security and food production. Pathogenic fungi are opportunistic and infect immunocom promised people, putting a strain on the present health-care systems across the world. Mucormycosis, or black fungus infection, has been documented in people who have been infected with the Covid-19 virus in South Asian nations (Rahman *et al*. 2021). Several fungal metabolites, such as

12-hydroxy-13-methoxyverruculogen TR-2, fumitremorgin B, verruculogen, and helvolic acid, as well as others from the endophytic fungus *Aspergillus fumigatus* showed potent antifungal activity against a variety of phytopathogenic fungi (Li *et al*. 2012). The five cadinane sesquiterpenoids isolated from the endophytic fungus *Phomopsis cassiae* derived from *Cassia spectabilis* displayed antifungal activity against *Cladosporium cladosporioides* and *Cladosporium sphaerospermum* (Musiol *et al*. 2006).

***Bioactive compounds as anticancer agent***

As per the report (Bray *et al*. 2018), cancer is the second largest cause of mortality worldwide. Males are more likely to develop lung, prostate, colorectal, stomach, and liver cancer, whereas females are more likely to develop breast, colorectal, lung, cervical, and thyroid cancer. Furthermore, cancer patients frequently encounter negative side effects following treatment procedures, which are also linked with a high level of toxicity. The *Ginkgo biloba* plant's endophyte *Chaetomium globosum* produced three new compounds: azaphilone alkaloids, chaetomugilides A–C, and chaetoviridin E, all of which have strong cytotoxic activity against the human cancer cell line HePG2 (Li *et al*. 2013). The endophytic fungi *Fusarium oxysporum*, *Aspergillus fumigatus*, *Phialocephala fortinii*, and *Trametes hirsute*, as well as various *Trichoderma*, *Penicillium*, and *Phomopsis* species, have been shown to generate podophyllotoxin, which has anticancer properties (Manganyi and Ateba, 2020).

***Bioactive compounds as antioxidant agent***

Free radicals are unstable molecules that naturally form as a result of chemical events like digestion and may initiate chain reactions in the human body, which might lead to cell damage. Numerous studies have shown that oxidative stress causes cellular degeneration, cancer, atherosclerosis, coronary heart disease, diabetes, Alzheimer's disease, hepatic and renal damage, and other neurological illnesses. Antioxidant compounds are used to combat, prevent, and cure illnesses and damages caused by reactive oxygen species (ROS). Several studies have shown that antioxidant activity may be found in compounds such as phenolic acids, phenylpropanoids, and flavonoids, as well as lignin, melanin, and tannins. The medicinal plant *Ginkgo biloba* yielded a total of forty-one bioactive chemicals from the endophyte *Xylaria* sp., which had antibacterial, antioxidant, anti-cardiovascular, anticancer, and antimicrobial effects (Manganyi and Ateba, 2020).

***Bioactive compounds as antiparasitic agent***

Annually, parasite illness affects around 48.4 million people, resulting in one million fatalities. Despite this, there are currently just a few very effective antiparasitic medications on the market, particularly considering the issues of parasite resistance. *Diaporthephaseolorum*, an endophytic fungus found in the roots of *Combretum lanceolatum*, showed anti-parasitic efficacy against *Trypanosoma cruzi*, decreasing amastigotes and trypomastigotes by upto 82 percent (Azevedo *et al*. 2021). Another study found that Oxylipin (9Z,11E)-13-oxooctadeca-9,11-dienoic acid produced from fungal extracts of the endophytic fungus *Penicillium herquei* was effective against *Plasmodium falciparum*, *Trypanosoma brucei*, *Leishmania donovanii*, and *Leishmania* sp. (Hayibor *et al*. 2019).

***Bioactive compounds as potential immunosuppressive drug***

Immunosuppressive medicines, commonly known as anti-rejection drugs, are used to suppress, minimise, or prevent allograft rejection in patients who have had an organ transplant. Immunosuppressive medications' effectiveness is now hampered by a variety of adverse effects, and given their enormous demand, finding safer, more dependable treatments is urgently needed to address these issues. Endophytes have been shown to produce bioactive compounds with immunosuppressive properties in recent investigations. Recent research findings have discovered potent immunosuppressive therapies from fungal endophytes, including sydoxanthone A and B, colutellin A, 13-O-acetylsydowinin B, dibenzofurane, methyl peniphenone, xanthone derivatives, subglutinol A and B, lipopeptide, peniphenone, benzophenone derivatives, (-) mycousnine, polyketide benzannulated spiroketal, polyketide benzannulated spiroketal and cyclosporin A (Adeleke & Babalola, 2021).

***Bioactive compounds as antiviral agent***

Viruses are entity that reproduce exclusively within living cells and are a major source of death and illness in humans across the world. Antiviral medications that are ideal should be effective against the target viral strains while having minimal negative effects on the host cells. The endophytic fungus *Emericella* sp. from the mangrove plant *Aegicera scorniculatum* was discovered to contain isoindolones compounds such as emerimidines A and B, emeriphenolicins A and D, aspernidines A and B, austin, austinol, dehydroaustin, and acetoxydehydroaustin having antiviral properties (Zhang *et al*. 2011). The antiviral chemical Hinnuliquinone, which is a powerful inhibitor of the HIV-1 protease has been reported to be produced by endophytic fungi inhabiting the leaves of *Quercus coccifera* (Singh *et al*. 2004).

## BIOREMEDIATION BY ENDOPHYTIC FUNGI

Endophytes have been used in a unique way in phytoremediation. Microorganisms have the capacity to bioaccumulate heavy metals and other pollutants from the environment, as well as to improve plant development through pollutant mobilisation and immobilisation. *Penicillium funiculosum*, a fungal endophyte that protects plants from copper stress and promotes plant development, can be employed in bioremediation of pollutants in cultivated areas (Khan and Lee, 2013). Mercury is a toxic metal with an unknown biological role that is extremely mobile and persistent in soil, bioaccumulates and biomagnifies in the food chain, and constitutes a direct threat to human and animal health. Human activities, such as illicit gold mine, have led to the release and buildup of mercury in many ecosystems. High mercury levels have an impact on all phases of plant growth, affecting seed germination and water absorption, reducing biomass, denature proteins, and inhibiting photosynthesis (Patra and Sharma, 2000). In this regard, inoculating plants with mercury-resistant endophytic fungus might be a good way to improve the efficacy of mercury phytoremediation. *Pestalotiopsis microspora*, an endohytic fungus, was shown to be able to grow on the synthetic polymer polyester polyurethane as the only carbon source in both aerobic and anaerobic circumstances, implying that it might be used to cure white plastic pollution (Russell *et al*. 2011).

## BIOPROSPECTING POTENTIAL OF ENDOPHYTIC FUNGI

Bioprospecting is the study of plants, animals, and microbes in order to find active ingredients that may be used in biotechnology. Endophytic fungi are a rich source of bioactive compounds and provide a wide scope of bioprospecting. Aliphatic compounds, phenolic compounds (phenols and phenolic acids, isocoumarin derivatives, lignans, flavonoids, and quinones), alkaloids (indole derivatives, amines, and amides), peptides, polyketides, steroids, and terpenoids (primarily sesquiterpenes, diterpenes, and triterpenes) are some of the substances produced by endophytes that have antagonistic activity. These chemicals exhibit a wide range of biological actions, including antibacterial, antiparasitic, neuroprotective, antioxidant, antidiabetic, immunosuppressive, antiviral, anticarcinogenic, and cytotoxic properties. Extracellular enzymes produced by endophytic fungi are widely utilised in the textile (amylase, cellulase, and oxidoreductase) and detergent (protease, lipase, cellulase, and oxidoreductase) sectors, as well as in food (pectinase, protease, cellulase, and oxidoreductase), paper (xylanase, lipase, and oxidoreductase).

Until recently, crop spraying with a range of synthetic chemical pesticides was the primary method of pest, disease, and weed management. Due to rising agricultural need to support population expansion, this method increased the usage of hazardous and carcinogenic chemicals, potentially jeopardising the plant's and consumer's health. Biological control in agriculture is another use for fungus derived substances which provide a sustainable alternative for chemical control. Several *Trichoderma* species are among the fungal endophyte species that have received the most attention. *Sclerotium sclerotiorum* and *Rhizoctonia solani* hyphae, for example, have been parasitized by *Trichoderma* spp. (Melo & Faull, 2000). Webber was most likely the first to describe utilising an endophytic fungus for biological control. Insect pest controllers such as *Metarhizium anisopliae* and *Beauveria bassiana* are now often utilised in agriculture (Sinia and Guzman-Novoa, 2018).

*Muscodorvitigenus* a fungal endophyte isolated from *Paullinia paullinioides* Radlk. in the Peruvian Amazon, produces naphthalene, an insect repellant (Daisy *et al*. 2002). Iron, silver, copper, zinc, magnesium, and gold nanoparticles have been found to be synthesised by fungal endophyte species. Endophytic fungi-produced iron oxide nanoparticles have been reported to remove colours from wastewater released by the textile and paper industries without damaging the environment (Samsami *et al*. 2020). Gold nanoparticles are non-toxic and have a high absorption property, making them useful in a variety of health-related applications. There has been report on the isolation of *Fusarium solani*, an endophytic fungus, from the plant *Chonemorpha fragrans*, which is exploited for gold nanoparticle production (Claranceet *al*. 2020). Many researchers have claimed that gold nanoparticles are an excellent source of biosensors and an effective cancer-killing agent.

## CONCLUSION

In nature, plants are frequently exposed to many biotic and abiotic stressors at the same time, rather than being subjected to a single factor. An association of endophytic fungi can provide resistance to abiotic stressors, allowing the plant to flourish in regions where it would otherwise be difficult to establish. More research is required to address specific issues related to multiple stresses. The introduction of molecular sequencing techniques has given us insight into endophytic fungal diversity. With the rise of drug-resistant microbes, the need for health services is rapidly increasing, particularly in developing nations. Furthermore, the rising incidence of cancer and other infectious illnesses worsens the situation. The endophytic fungi, which produce a diverse range of secondary bioactive metabolites with unique potential chemicals such as antimicrobials, antioxidants, antivirals, anti-inflammatory, insecticides, nematicides, and others, would provide the best solution.

Endophytic fungi-derived compounds have a wide range of uses, from agriculture to the environment, including bioremediation, biotransformation, biofertilizers, biomedicine, energy, and biocatalysis. The application of endophytic fungi can modify the optimal use of organic and inorganic fertilisers by improving nutrient uptake in plants. Further research towards the use of endophytic fungi in the remediation of contaminated environments is a promising prospect. The development of an appropriate culture method for the long-term synthesis of secondary metabolites would require extensive study of endophytic fungi. Furthermore, researchers from all over the globe are interested in the use of silver nanoparticles in drug delivery systems and diagnostics. This has highlighted the importance of developing safe, dependable, and environmentally acceptable methods for producing silver nanoparticles on a large scale. The bioactive compounds generated by endophytic fungi have strong antifungal action against both human and plant pathogens. Unfortunately, only a limited number of antifungal medicines are presently accessible for the treatment of numerous life-threatening diseases. Approaches such as genome sequencing, next-generation sequencing, metagenomics, comparative genomics, microarray, and metatranscriptomics, as well as quantitative modelling, are crucial for understanding the in-depth interaction between plants and endophytes.

## REFERENCES


Adeleke, B. S.,Babalola, O. O. 2021. Pharmacological Potential of Fungal Endophytes Associated with Medicinal Plants: A Review. *J. Fungi* **7**: 147.

Arif, Y., Singh, P., Siddiqui, H., Bajguz, A.,Hayat, S. 2020. Salinity induced physiological and biochemical changes in plants: An omic approach towards salt stress tolerance. *Plant Physiol.Biochem.***156**: 64-77.

Arnold, A. E.,Herre, E. A. 2003. Canopy cover and leaf age affect colonization by tropical fungal endophytes: ecological pattern and process in Theobroma cacao (Malvaceae). *Mycologia* **5:** 388-398.

Ayob, F. W.,Simarani, K. 2016. Endophytic filamentous fungi from a *Catharanthus roseus*: Identification and its hydrolytic enzymes. *Saudi Pharmaceut. J.* **24:**273-278.

Azevedo, R. N. D., Ferreira, M. C., Assis, J. C. S. D., Junior, P. A. S., Maia, D. N. B., Almeida Alves, T. M. D., Kohlhoff, M., Zani, C.L., Rosa, L. H. 2021. Bioprospecting of Bioactive Secondary Metabolites of Endophytic Fungi of *Carapichea ipecacuanha* (Rubiaceae), a Neotropical Medicinal Species. In *Neotropical Endophytic Fungi* (Ed. L.H.Rosa) pp. 321-336. Springer, Cham.

Azooz, M. M., Youssef, A. M.,Ahmad, P. 2011. Evaluation of salicylic acid (SA) application on growth, osmotic solutes and antioxidant enzyme activities on broad bean seedlings grown under diluted seawater. *Inter. J. Plant Physiol.Biochem.* **3**: 253-264.

Baltruschat, H., Fodor, J., Harrach, B. D., Niemczyk, E., Barna, B., Gullner, G.,Janeczko, A., Kogel, K.H., Schafer,P., Schwarczinger, I.,Zuccaro, A., Skoczowski, A.2008. Salt tolerance of barley induced by the root endophyte *Piriformospora indica* is associated with a strong increase in antioxidants. *New Phytol.* **180**: 501-510.

Bastias, D. A., Martínez-Ghersa, M. A., Ballaré, C. L., Gundel, P. E. 2017. Epichloë fungal endophytes and plant defenses: not just alkaloids. *Trends in Plant Science*, **22**, 939-948.

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A.,Jemal, A. 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: ACancer J. for Clinicians* **68**: 394-424.

Brem, D., Leuchtmann, A. 2001. *Epichloë* grass endophytes increase herbivore resistance in the woodland grass *Brachypodiumsylvaticum*. *Oecologia* **126**: 522-530.

Cao, R., Liu, X., Gao, K., Mendgen, K., Kang, Z., Gao, J, Dai, Y., Wang, X. 2009. Mycoparasitism of endophytic fungi isolated from reed on soilborne phytopathogenic fungi and production of cell wall-degrading enzymes in vitro. *Current microbiology* **59**: 584-592.

Carroll, F. M. 2017. Sources. In *A Good and Wise Measure* (pp. 411-430). University of Toronto Press.

Cevallos, S., Herrera, P., Sánchez-Rodríguez, A., Declerck, S., Suárez, J. P. 2018. Untangling factors that drive community composition of root associated fungal endophytes of *Neotropical epiphytic* orchids. *Fungal Ecology* **34**: 67-75.

Choudhary, M., Gupta, S., Dhar, M. K., Kaul, S. 2021. Endophytic Fungi-Mediated Biocatalysis and Biotransformations Paving the Way Toward Green Chemistry. *Frontiers in Bioengineering and Biotechnology*, **9**, 419.

Chowdappa, S., Jagannath, S., Konappa, N., Udayashankar, A. C., Jogaiah, S. 2020. Detection and characterization of antibacterial siderophores secreted by endophytic fungi from *Cymbidium aloifolium*. *Biomolecules* **10**: 1412.

Clarance, P., Luvankar, B., Sales, J., Khusro, A., Agastian, P., Tack, J. C., Al Khulaifi, M. M., Al-Shwaiman, H. A., Elgorban, A. M., Syed, A., Kim, H. J. 2020.Green synthesis and characterization of gold nanoparticles using endophytic fungi *Fusarium solani* and its in-vitro anticancer and biomedical applications. *Saudi journal of biological sciences* **27**: 706-712.

Da Rosa, B. V., Kuhn, K. R., Ugalde, G. A., Zabot, G. L., Kuhn, R. C. 2020. Antioxidant compounds extracted from *Diaportheschini* using supercritical CO 2 plus cosolvent. *Bioprocess and biosystems engineering***43**: 133-141.

Daisy, B. H., Strobel, G. A., Castillo, U., Ezra, D., Sears, J., Weaver, D. K., & Runyon, J. B. 2002. Naphthalene, an insect repellent, is produced by *Muscodorvitigenus*, a novel endophytic fungus. *Microbiology* **148**: 3737-3741.

Diantoro, M., Suprayogi, T., Sa'adah, U., Mufti, N., Fuad, A., Hidayat, A., Nur, H. 2018. Modification of electrical properties of silver nanoparticle (pp. 233-248). *Intech Open*.

El Hawary, S. S., Mohammed, R., AbouZid, S. F., Bakeer, W., Ebel, R., Sayed, A. M., Rateb, M. E. 2016. Solamargine production by a fungal endophyte of *Solanum nigrum*. *Journal of applied Microbiology* **120**: 900-911.

Falqueto, A. R., da Silva Júnior, R. A., Gomes, M. T. G., Martins, J. P. R., Silva, D. M., Partelli, F. L. 2017. Effects of drought stress on chlorophyll a fluorescence in two rubber tree clones. *Scientia Horticulturae* **224**: 238-243.

Fässler, E., Evangelou, M. W., Robinson, B. H., Schulin, R. 2010. Effects of indole-3-acetic acid (IAA) on sunflower growth and heavy metal uptake in combination with ethylene diamine disuccinic acid (EDDS). *Chemosphere* **80**: 901-907.

Fatma, M., Khan, M. I. R., Masood, A., Khan, N. A. 2013. Coordinate changes in assimilatory sulfate reduction are correlated to salt tolerance: involvement of phytohormones. *Annual Research & Review in Biology* **3**: 267-295.

Fernandes, E. G., Pereira, O. L., da Silva, C. C., Bento, C. B. P., de Queiroz, M. V. 2015. Diversity of endophytic fungi in *Glycine max*. *Microbiological research* **181**: 84-92.

Fouda, A. H., Hassan, S. E. D., Eid, A. M., Ewais, E. E. D. 2015. Biotechnological applications of fungal endophytes associated with medicinal plant Asclepias sinaica (Bioss.). *Annals of Agricultural Sciences* 60: 95-104.

Gangadevi, V., Muthumary, J. 2009. Taxol production by *Pestalotiopsisterminaliae*, an endophytic fungus of *Terminalia arjuna* (arjun tree). *Biotechnology and applied biochemistry* **52**: 9-15.

Hayibor, K., Kwain, S., Osei, E., Nartey, A.P., Tetevi, G.M., Owusu, K.B.A., Camas, M., Camas, A.S.,Kyeremeh, K. 2019. Ghanaian mangrove wetland endophytic fungus, *Penicillium herquei* strain BRS2A-AR produces (9Z, 11E)-13-oxooctadeca-9, 11-dienoic acid with activity against *Trichomonas mobilensis*. *International Journal of Biological and Chemical Sciences* **13**: 1918-1937.

Higgins, K. L., Arnold, A. E., Miadlikowska, J., Sarvate, S. D., Lutzoni, F. 2007. Phylogenetic relationships, host affinity, and geographic structure of boreal and arctic endophytes from three major plant lineages. Molecular phylogenetics and evolution **42:** 543-555.

Hyde, K. D.,Soytong, K. 2008. The fungal endophyte dilemma. *Fungal diversity* 33: 163-173.

Khan, A. L., Lee, I. J. 2013. Endophytic *Penicillium funiculosum* LHL06 secretes gibberellin that reprograms *Glycine max* L. growth during copper stress. *BMC plant biology* **13:** 1-14.

Khare, E., Mishra, J., Arora, N. K. 2018. Multifaceted interactions between endophytes and plant: developments and prospects. *Frontiers in microbiology* **9:** 2732.

Lahlali, R., McGregor, L., Song, T., Gossen, B. D., Narisawa, K., & Peng, G. 2014. *Heteroconiumchaetospira* induces resistance to clubroot via upregulation of host genes involved in jasmonic acid, ethylene, and auxin biosynthesis. *PLoS One* **9**: e94144.

Leistner, E., Steiner, U. 2018. The genus *Periglandula* and its symbiotum with morning glory plants (Convolvulaceae). In *Physiology and genetics* (pp. 131-147). Springer, Cham.

Li, F., Sun, Q., Hong, L., Li, L., Wu, Y., Xia, M., Ikejima, T., Peng, Y., Song, S. 2013. Daphnane-type diterpenes with inhibitory activities against human cancer cell lines from Daphne genkwa. *Bioorgan.Med.Chem.Lett.* **23:** 2500-2504.

Li, X. J., Zhang, Q., Zhang, A. L.Gao, J. M. 2012. Metabolites from *Aspergillus fumigatus*, an endophytic fungus associated with *Melia azedarach*, and their antifungal, antifeedant, and toxic activities. *J.Agricult.Food Chem.* **60**: 3424-3431.

Li, X., Guo, Z., Deng, Z., Yang, J.,Zou, K. 2015. A New [alpha]-Pyrone Derivative from Endophytic Fungus *Pestalotiopsis microspora*. *Records of Nat. Prod.* **9**: 503.

Manganyi, M. C.,Ateba, C. N. 2020. Untapped potentials of endophytic fungi: A review of novel bioactive compounds with biological applications. *Microorganisms***8**: 1934.

Mejia, L. C., Herre, E. A., Sparks, J. P., Winter, K., García, M. N., Van Bael, S. A.,Stitt, J., Shi,Z., Zhang,Y., Guiltinan, M.J., Maximova, S. N.2014. Pervasive effects of a dominant foliar endophytic fungus on host genetic and phenotypic expression in a tropical tree. *Front.Microbiol.* **5**: 479.

Melo, I. S. D.,Faull, J. L. 2000. Parasitism of *Rhizoctonia solani* by strains of *Trichoderma* spp. *Scientia Agricola***57**: 55-59.

Mohandoss, J.,Suryanarayanan, T. S. 2009. Effect of fungicide treatment on foliar fungal endophyte diversity in mango. *Sydowia* **61**: 11-24.

Momose, I., Sekizawa, R., Hosokawa, N., Iinuma, H., Maisui, S., Nakamura, H., Naganawa, H., Hamada,M.,Takeuchi, T. 2000. Melleolides K, L and M, new melleolides from *Armillariellamellea*. *J. Antibiot.***53**: 137-143.

Mousa, W. K.,Raizada, M. N. 2013. The diversity of anti-microbial secondary metabolites produced by fungal endophytes: an interdisciplinary perspective. *Front. Microbiol*. **4**: 65.

Mousa, W. K., Schwan, A., Davidson, J., Strange, P., Liu, H., Zhou, T.,Auzanneau, F-I., Raizada, M. N. 2015. An endophytic fungus isolated from finger millet (*Eleusine coracana*) produces anti-fungal natural products. *Front.Microbiol.***6**:1157.

Mousa, W. K., Shearer, C., Limay-Rios, V., Ettinger, C. L., Eisen, J. A.,Raizada, M. N. 2016. Root-hair endophyte stacking in finger millet creates a physicochemical barrier to trap the fungal pathogen *Fusarium graminearum*. *Nature Microbiol.* **1**: 1-12.

Musiol, R., Jampilek, J., Buchta, V., Silva, L., Niedbala, H., Podeszwa, B.,Palka, A., Majerz-Maniecka, K., Oleksyn, B., Polanski, J. 2006. Antifungal properties of new series of quinoline derivatives. *Bioorgan. Med. Chem.***14**: 3592-3598.

Nouh, F. A. A., Abdel-Azeem, A. M. 2020. Role of Fungi in Adaptation of Agricultural Crops to Abiotic Stresses. In:*Agriculturally Important Fungi for Sustainable Agriculture* (Eds. A.N.Yadav, S.Mishra, D. Kour, N.Yadav, A.Kumar) Springer, Cham, pp 55-80.

Nürnberger, T., Kemmerling, B. 2009. Pathogen-associated molecular patterns (PAMP) and PAMP-triggered immunity. *Annu. Plant Rev*. **34**: 16-47.

Ownley, B. H., Griffin, M. R., Klingeman, W. E., Gwinn, K. D., Moulton, J. K.,Pereira, R. M. 2008. *Beauveria bassiana*: endophytic colonization and plant disease control. *J.Inverteb. Pathol.* **98**: 267-270.

Patra, M., Sharma, A. 2000. Mercury toxicity in plants. *The Botan. Rev.***66:** 379-422.

Pavithra, N., Sathish, L.,Ananda, K. 2012. Antimicrobial and enzyme activity of endophytic fungi isolated from Tulsi. *J. Pharmaceut. Biomed. Sci.* **16**: 2014.

Pongcharoen, W., Rukachaisirikul, V., Phongpaichit, S., Rungjindamai, N.,Sakayaroj, J. 2006. Pimarane Diterpene and Cytochalasin Derivatives from the Endophytic Fungus *Eutypellascoparia* PSU-D44. *J.Natur.Prod.* **69**: 856-858.

Porras-Alfaro, A., Herrera, J., Sinsabaugh, R. L., Odenbach, K. J., Lowrey, T.,Natvig, D. O. 2008. Novel root fungal consortium associated with a dominant desert grass. *Appl.Eenviron.Microbiol.* **74**: 2805-2813.

Rahman, F. I., Islam, M. R.,Bhuiyan, M. A. 2021. Mucormycosis or black fungus infection is a new scare in South Asian countries during the COVID 19 pandemic: Associated risk factors and preventive measures. *J. Med.Virol.* **93**:6447-6448

Rashmi, M., Kushveer, J. S., Sarma, V. V. 2019. A worldwide list of endophytic fungi with notes on ecology and diversity. *Mycosphere* **10**: 798-1079.

Rungjindamai, N., Pinruan, U., Choeyklin, R., Hattori, T., Jones, E. B. G. 2008. Molecular characterization of basidiomycetous endophytes isolated from leaves, rachis and petioles of the oil palm, *Elaeisguineensis*, in Thailand. *Fungal Divers*. **33**: 139-161.

Russell, J. R., Huang, J., Anand, P., Kucera, K., Sandoval, A. G., Dantzler, K. W., Hickman,D.,Jee, J., Kimovec, F.M., Koppstein, D., Marks, D.H., Mittermiller, P.A., Núñez, S.J., Santiago, M., Townes, M.A., Vishnevetsky, M., Williams, N.E., Vargas, M.P.N., Lori-Ann Boulanger, L-A., Carol Bascom-Slack, C., Strobel, S.A., 2011. Biodegradation of polyester polyurethane by endophytic fungi. *Appl.Environ.Microbiol.* **77**: 6076-6084.

Saithong, P., Panthavee, W., Stonsaovapak, S.,Li, C. 2010. Isolation and primary identification of endophytic fungi from *Cephalotaxusmannii* trees. *Maejo Inter. J. Sci.Technol.* **4**: 446-453.

Samsami, S., Mohamadizaniani, M., Sarrafzadeh, M. H., Rene, E. R., Firoozbahr, M. 2020. Recent advances in the treatment of dye-containing wastewater from textile industries: Overview and perspectives. *Process Safety Environ.Protect.***143**: 138-163.

Selvakumar, G., Panneerselvam, P., &Ganeshamurthy, A. N. 2012. Bacterial mediated alleviation of abiotic stress in crops. In:*Bacteria in Agrobiology: Stress Management* (Ed.D.K.Maheshwari ) pp. 205-224, Springer, Berlin, Heidelberg.

Siddaiah, C. N., Satyanarayana, N. R., Mudili, V., Gupta, V. K., Gurunathan, S., Rangappa, S., Huntrika, S.S., Srivastava, R. K. 2017. Elicitation of resistance and associated defense responses in *Trichoderma hamatum* induced protection against pearl millet downy mildew pathogen. *Scient. Rep.* **7**:43991.

Singh, A., Singh, D. K., Kharwar, R. N., White, J. F.,Gond, S. K. 2021. Fungal endophytes as efficient sources of plant-derived bioactive compounds and their prospective applications in natural product drug discovery: Insights, avenues, and challenges. *Microorganisms* **9**: 197.

Singh, S. B., Ondeyka, J. G., Tsipouras, N., Ruby, C., Sardana, V., Schulman, M., Sanchez, M., Pelaez, F., Mark W Stahlhut, M.W., Munshi,S., Olsen, D.B., Lingham, R. B. 2004. Hinnuliquinone, a C2-symmetric dimeric non-peptide fungal metabolite inhibitor of HIV-1 protease. *Biochem.Biophysic.Res.Commun.***324**: 108-113.

Sinia, A., Guzman-Novoa, E. 2018. Evaluation of the entomopathogenic fungi *Beauveria bassiana* GHA and *Metarhiziumanisopliae* UAMH 9198 alone or in combination with thymol for the control of Varroa destructor in honey bee (*Apis mellifera*) colonies. *J.Apicult. Res.* **57**: 308-316.

Sun, X., Ding, Q., Hyde, K. D.,Guo, L. D. 2012. Community structure and preference of endophytic fungi of three woody plants in a mixed forest. *Fung.Ecol.***5**: 624-632.

Terhonen, E., Sipari, N., Asiegbu, F. O. 2016. Inhibition of phytopathogens by fungal root endophytes of Norway spruce. *Biol. Cont.* **99**: 53-63.

Toghueo, R. M. K. 2020. Bioprospecting endophytic fungi from *Fusarium* genus as sources of bioactive metabolites. *Mycology***11**: 1-21.

Venugopalan, A., Srivastava, S. 2015. Endophytes as in vitro production platforms of high value plant secondary metabolites. *Biotechnol.Adv.***33**: 873-887.

Waller, F., Achatz, B., Baltruschat, H., Fodor, J., Becker, K., Fischer, M., Heier, T., Hückelhoven, R., Neumann, C., Wettstein, D. V., Franken, P.,Kogel, K. H. 2005. The endophytic fungus *Piriformospora indica* reprograms barley to salt-stress tolerance, disease resistance, and higher yield. *Proc. Nat. Acad. Sci.***102**: 13386–13391.

Wang, J. L., Li, T., Liu, G. Y., Smith, J. M., Zhao, Z. W. 2016. Unraveling the role of dark septate endophyte (DSE) colonizing maize (*Zea mays*) under cadmium stress: physiological, cytological and genic aspects. *Scient.Rep.* **6**: 1-12.

White Jr, J. F., Belanger Faith., Meyer William, Sullivan, R. F., Bischoff, J. F., Lewis, E. A. 2002. Minireview article: Clavicipitalean Fungal Epibionts and Endophytes-Development of Symbiotic Interactions with Plants. *Symbiosis* **33**: 201.

Xu, J., Ebada, S. S., Proksch, P. 2010. Pestalotiopsis a highly creative genus: chemistry and bioactivity of secondary metabolites. *Fung. Divers.* **44**: 15-31.

Yadav, A.N., Verma, P., Kour, D., Rana, K.L., Kumar, V., Singh, B., Chauahan, V.S., Sugitha, T., Saxena, A.K., Dhaliwal, H.S. 2017. Plant microbiomes and its beneficial multifunctional plant growth promoting attributes. *Int. J. Environ. Sci. Nat.Resour.***3**: 1-8.

Yoshioka, Y., Ichikawa, H., Naznin, H. A., Kogure, A., Hyakumachi, M. 2012. Systemic resistance induced in *Arabidopsis thaliana* by *Trichoderma asperellum* SKT 1, a microbial pesticide of seedborne diseases of rice. *Pest Manag.Sci.* **68**: 60-66.

Young, C.A., Felitti, S., Shields, K., Spangenberg, G., Johnson, R.D., Bryan, G.T., Saikia, S. and Scott, B. 2006. A complex gene cluster for indole-diterpene biosynthesis in the grass endophyte *Neotyphodiumlolii*. *Fung. Genet. Biol.* **43**: 679-693.

Zhang, G., Sun, S., Zhu, T., Lin, Z., Gu, J., Li, D.,Gu, Q. 2011. Antiviral isoindolone derivatives from an endophytic fungus *Emericella* sp. associated with *Aegicerascorniculatum*. *Phytochemistry* **72**: 1436-1442.

Zhang, S., Li, X., Sun, Z., Shao, S., Hu, L., Ye, M., Zhou, Y., Xia, X., Yu, J. Shi, K. 2015. Antagonism between phytohormone signalling underlies the variation in disease susceptibility of tomato plants under elevated $CO_2$. *J. Exp. Bot.* **66**: 1951-1963.

Zhang, T., Yao, Y. F. 2015. Endophytic fungal communities associated with vascular plants in the high arctic zone are highly diverse and host-plant specific. *PLoS One* **10**: e0130051.

Zimmerman, N. B., Vitousek, P. M. 2012. Fungal endophyte communities reflect environmental structuring across a Hawaiian landscape. *Proc. Nat. Acad. Sci.* **109**: 13022-13027.