Research Journal of Pharmacognosy (RJP) 10(4), 2023: 81–94
Received: 1 July 2023
Final revision: 7 Sep 2023
Accepted: 13 Sep 2023
Published online: 17 Sep 2023
DOI: 10.22127/RJP.2023.179187

Review article

The Possible Applications of Endophytic Fungi

Parmida Aleahmad, Leila Ebrahimi*

Department of Entomology and Plant Pathology, College of Agricultural Technology, Faculty of Agriculture & Natural Resources, University of Tehran, Tehran, Iran.

Abstract
Endophytic fungi are microorganisms that colonize plants during their entire, or a significant part of their life cycle without any symptoms, establishing a symbiosis association. They are abundant in plants and have been reported in various tissues, such as roots, stems, leaves, flowers, and fruits. In recent years, research on the beneficial use of endophytic fungi has increased worldwide. These fungi have the ability to protect plants from both biotic and abiotic stresses through different mechanisms. They also improve water and nutritional status leading to increased growth and fitness of host plants. Endophytes are rich sources of bioactive and secondary metabolites, making them promising candidates for the development of compounds with anticancer, antibiotic, antiviral, antidiabetic, and other pharmacological activities. Moreover, they produce various enzymes that hold economic and environmental potential for industrial applications. This study explored the diverse effects of endophytic fungi in agriculture, biofuels, medicine, industry and bioremediation.

Keywords: antagonist; bioremediation; endophytic fungi; medicine; metabolite

Citation: Aleahmad P, Ebrahimi L. The possible applications of endophytic fungi. Res J Pharmacogn. 2023; 10(4): 81–94.

Introduction
Plants host a diverse array of microorganisms, including bacteria, fungi, archaea, algae, and protists, both within and outside their tissues. Through long-term evolution, intricate interactions have developed between these species, resulting in symbiotic relationships [1]. The term "endophytes" refers to microorganisms that reside within plants from the Greek words "*endon-*" meaning within and "*phyton-*" meaning plants. Endophytes are defined as microorganisms that colonize the internal tissues of a host without causing symptoms or apparent harm initially, but may cause disease after a latency period [2].
The colonization of plant tissues by endophytes is not a random occurrence; they have likely adapted to thrive in this niche [3]. While these microorganisms may not remain endophytic throughout their entire life cycle, the term "endophytes" encompasses not only symbiotic species, but also saprophytes and latent pathogens [4]. Within plant systems, endophytes exhibit greater diversity than plant pathogens [5]. Research shows that in natural ecosystems, most, if not all, plants have a symbiotic relationship with fungal endophytes. Fossil records and molecular data indicate that plants have been associated with endophytic fungi for over 400 million years, likely since plants colonized land [6]. Every plant harbors at least one species of endophytic fungi, and many plants, particularly woody plants, may host hundreds or even thousands of different species [7]. Fungal endophytes have been isolated from various plants, including trees, vegetables, fruits, cereal grains, and other crops. They primarily belong to the Ascomycota, with some taxa from the Basidiomycota, Zygomycota, and Oomycota [8].

*Corresponding author: Le_ebrahimi@ut.ac.ir

The composition of endophytic mycobiota in the same plant species is influenced by different biotic and abiotic factors. Biotic factors include plant age, host taxonomy, plant tissue type, intraspecific and interspecific interactions, while abiotic factors comprise collection time (season), geographic factors, climate, soil nutrient availability, and moisture [9].

Endophytic fungi engage in multifaceted interactions with their host, including mutualism, neutralism, commensalism and even antagonism [10]. They play essential roles for their host plants, such as promoting growth and development, increasing biomass, facilitating water and nutrient abortion, enhancing resistance to biotic and abiotic stresses, and promoting the accumulation of secondary metabolites that provide immunity, allelopathic resistance and carbon sequestration [11]. Decades of research have highlighted their ability to produce various metabolites in plants, including bioactive compounds with pharmaceutical, industrial, and agricultural significance [12]. Investigations indicate that endophytic fungi are prolific producers of compounds with practical applications in agrochemicals or medicine, owing to their biological activities such as antiviral, antimicrobial, anticancer, insecticidal, immunosuppressive, and antioxidant properties [13]. This article has discussed some of the diverse functions of endophytic fungi (Table1).

Methods

To gather relevant information, searches were conducted on Google scholar, and Scopus databases covering the period from 2009 to 2023. A combination of the following terms was used either individually or in combination: "endophytes", "antagonist", "industry", "medicine", "metabolite", "bioremediation", and "biofuel". All types of studies, including in vivo, in vitro and clinical trials, were considered in this research.

Results and Discussion

Beneficial aspects of endophytic fungi for host plants

Promotion of fitness and growth of host plants

Endophytic fungi play a crucial role in promoting the fitness and growth of host plants. They have both direct and indirect mechanisms to enhance plant health. Direct mechanisms involve interactions between endophytes and pathogens, where endophytes exhibit antibiosis (inhibition of pathogen growth), secretion of lytic enzyme, production of phytohormones (such as auxin, abscisic acid, and gibberellins), phosphate solubilization, siderophore production (iron-chelating compounds), production of indolic compounds, competition with pathogens, and utilization of 1-aminocyclopropane-1-carboxylate (ACC - a plant growth regulator) [14].

Indirect mechanisms involve endophytes stimulating plant defense responses, including plant resistance, promoting the production of plant secondary metabolites, enhancing plant growth and physiology, and even engaging in hyperparasitism [14].

Endophytes also contribute to nutrient availability for plants and the bio-stimulation of various compounds [15]. They assist in nutrient uptake and utilization by host plants, including organic matter, macronutrients (e.g., nitrogen, phosphorus, potassium, magnesium), and micronutrients (e.g., iron, zinc, copper) [16,17]. Some endophytes are capable of phosphate solubilization, a significant mechanism for plant growth, as demonstrated by studies on endophytic fungi like *Coniochaeta endophytica* A.H. Harrington & A.E. Arnold and *Fusarium lateritium* Nees, Syst. Pilze (Würzburg) [17,18].

Furthermore, endophytic fungi produce plant hormones, including auxin, abscisic acid, and gibberellins (GAs) and etc. [12] which regulate plant growth and development of shoot and root, division and cell elongation, differentiation of vascular tissue, root formation process and responses of tropism. Gibberellins are essential in seed germination, stem elongation, sexual expression, flourishing, fruit formation and senescence [19]. For example, the production of indole acetic acid (IAA), an auxin class hormone, by *Colletotrichum* sp., isolated from *Artemisia annua* L., enhances host plant growth [14]. Studies on *Satureja khuzestanica* Jamzad (SKJ) have shown that endophytic fungi like *Thielavia basicola* (Berk. & Broome) Zopf, *Xenodidymella applanata* (Niessl) Qian Chen & L. Cai and *Chaetosphaeronema achilleae* S.K. Huang & K.D. Hyde have significant effects on plant height, biomass, leaf area and number, and dry weight [20]. Overall, endophytic fungi positively influence plant growth, nutrient uptake, hormone regulation, and defense responses, contributing to the overall fitness of host plants.

Resistance to abiotic stress

Endophytic fungi have a remarkable ability to enhance the resistance of host plants to various abiotic stresses, such as drought, heat, salinity, heavy metals, and mineral deficiency [21]. Endophytic fungi increase the production of phytobeneficial substances like aminocyclopropane-1-carboxylic acid (ACC)-deaminase, auxins, gibberellins, abscisic acid (ABA), siderophores, extracellular polymeric substances, and soil nutrient solubilization, which offer extra arsenal to host plants to counteract different stresses [22].

Drought

Drought is a multifaceted stress that alters the physiological, morphological, biochemical, and molecular traits in plants. Drought stress in plants is characterized by a reduction in photosynthesis ability, a decrement in leaf water potential and turgor pressure, stomatal closure, decrease in cell growth and elongation, and an elevation in activities of reactive oxygen species (ROS) [23]. The positive effects of endophytic fungi on the drought stress tolerance of plants have been observed in various studies. In a study by Morse et al. (2002) [24], the presence of *Neotyphodium* sp., an endophytic fungus, increased the photosynthesis rate and stomatal conductance of *Arizona fescue* Vasey. under water-deficit conditions. Foliar endophytes alter metabolic reactions in the plant through the production of plant hormones, glycosidases, and proteases, resulting in changes in net photosynthesis and stomatal conductance [25]. *Festuca arundinacea* Schreb. inoculated with the *Epichloe* endophytic fungus showed better water status than non-treated plants due to higher proline production in roots and more efficient osmotic adjustment [8]. Abscisic acid (ABA) activates stress-responsive genes and improves the antioxidant system in plants, protecting them against drought-induced oxidative damage. Exogenous application of ABA can enhance drought tolerance in plants [26]. The enhanced drought tolerance of perennial ryegrass in presence of *Epichloë* is a widely recognized example of endophyte-induced drought stress tolerance in hosts [8]. *Piriformospora indica* Sav. Verma, Aj. Varma, Rexer, G. Kost & P. Franken, a root-colonizing endophytic fungus of the Sebacinales order, has shown the capability to induce drought tolerance in *Brassica rapa* subsp. *pekinensis* Linnaeus. (Chinese cabbage) plants [26].

Salinity stress

Salinity stress can affect photosynthesis and membrane stability in plants [27]. Excessive sodium leads to the overproduction of ROS, resulting in oxidative damage and disruption of plant physiological and biochemical processes such as water usage efficiency, photosynthesis, and nutrient uptake. This ultimately leads to cellular structure disruption and plant mortality. Endophytes play a role in enhancing salt tolerance in host plants. They can absorb higher concentrations of K^+ and maintain lower Na^+/K^+ ratios in aboveground tissues [8]. Endophytic fungi contribute to salinity tolerance in host plants by promoting higher biomass, modifying root system architecture to regulate salt acquisition and translocation, and facilitating osmoregulation (accumulation of osmolytes such as proline, glycine betaine, sugars, organic acids, polyamines, and amino acids for osmotic adjustment) [28]. The endophytic fungus *Trichoderma atroviride* P. Karst., has been shown to improve germination, seedling establishment, yield, and fruit quality of *Foeniculum vulgare* Mill. (fennel) under salinity stress [29]. *Piriformospora indica*, a root-colonizing endophytic fungus of the Sebacinales order, has been found to induce salt tolerance in barley plants [26]. Three halotolerant endophytic fungi, *Periconia macrospinosa* Lefebvre & Aar.G. Johnson, *Neocamarosporium goegapense* Crous & M.J. Wingf., and *N. chichastianum* Papizadeh, Crous, Shahz. Faz. & Amoozegar, isolated from roots of salt lake plants, have been shown to induce resistance to salinity and drought stress in barley plants [30].

Heavy metals

Heavy metal contamination poses a significant threat to agriculture, crop productivity, and the natural soil microbiota [31]. Trace metals like manganese (Mn), copper (Cu), zinc (Zn), and iron (Fe) are essential for various biological processes in plant life cycles. However, when present in excess, they can become toxic and disrupt plant growth [32]. Plant endophytic fungi have demonstrated remarkable tolerance and the ability to alleviate heavy metal stress in contaminated soils. They produce phytohormones such as indole-3-acetic acid and salicylic acid (SA), which play crucial role in improving plant tolerance to heavy metal stresses [26]. For instance, *Aspergillus welwitschiae* (Bres.) Henn. has been shown to effectively enhance metal stress tolerance in *Glycine max* L. Merrill. (soybean) [31]. The root-associated endophytic fungus *Exophiala pisciphila* McGinnis & Ajello, found in *Zea mays* Linn. (maize), has demonstrated remarkable tolerance to cadmium (Cd), resulting in a significant decrease in Cd induced toxicity and a notable increase in maize growth [26].

Mineral stress

Mineral stress, which refers to inadequate availability of essential nutrients or the toxicity of certain nutrients, is a significant concern in agricultural ecosystems [8]. However, there is evidence to suggest that endophytic fungi can play a role in improving nutrient absorption rates and uptake of essential elements such as calcium (Ca), phosphorus (P), magnesium (Mg), potassium (K), and other microelements [33]. Research has shown that fungal endophytes have the ability to influence root morphology, and architecture, and mycorrhizal colonization, which can ultimately impact nutrient uptake [34]. In addition, studies have indicated that the presence of endophytes has a positive correlation with mycorrhizal fungi, leading to enhanced water and mineral nutrient uptake, including improved availability of phosphorus for plants [35].

Extreme temperatures

Extreme temperatures caused by climate change, including heat and cold stresses, are major concerns for plant scientists worldwide. Both high and low temperature stresses lead to various changes at the molecular, physiological, and cellular levels, resulting in irreversible damage to plant growth and development. These changes include loss of cell membrane fluidity, impairment of photosynthesis, overproduction of ROS, and reduced water absorption [36]. Under temperature stress conditions, the balance between received light and efficient light absorption in leaves during photosynthesis is disrupted, leading to oxidative stress. This oxidative stress is associated with increased electron leakage and the formation of toxic and destructive ROS, which can damage cell membranes, chloroplasts, proteins, and nucleic acids, thereby affecting normal cell metabolism [37]. The enhanced tolerance of host plants to temperature stress can be attributed to various mechanisms, such as the accumulation of fungal bioactive alkaloids (e.g., peramine, ergot alkaloids, indole-diterpenes, lolitrems, and lolines), and reduced ROS production, and promotion of antioxidant enzyme activity in the host plant [8]. In a study by Hamayun et al. (2018) [38], it was found that *Aspergillus japonicas* Saito, isolated from the wild plant *Euphorbia indica* Lam. helps mitigate heat stress in *Glycine max* (soybean) and *Helianthus annuus* Linnaeus. (sunflower) by regulating the activities of abscisic acid, catalase, and ascorbic acid oxidase. Additionally, Li et al. (2021) demonstrated that colonization of *Piriformospora indica* increased the photochemical conversion efficiency and electron transport rate while alleviating damage to the photosynthetic reaction center in *Musa acuminata* Colla (banana) leaves during cold treatment. Furthermore, *P. indica* induced the expression of cold-responsive genes in *M. acuminata* leaves providing a positive response to cold stress [39].

Resistance to biotic stress

Endophytic fungi have been widely recognized for their role in assisting host plants in resisting biotic stresses caused by pathogens and pests [26]. These microorganisms can provide benefits by acting as biological control agents and activating the plant's defense response to biotic stresses [3]. One advantage of endophytes over other biocontrol agents is their ability to colonize the internal tissues of plants [14]. The bio-inhibitory action of endophytic fungi occurs through various mechanisms, including hyperparasitism, competition, antibiosis, and induced resistance, which can weaken or eliminate pathogens [40,41]. These mechanisms may vary depending on the specific pathogens and can be employed individually or in combination [3].

Endophytic fungi establish a symbiotic relationship with their host plants, providing protection and enhancing the plant's ability to withstand biotic stresses. This interaction showcases the fascinating and beneficial nature of microorganisms in the plant world.

Antibiotics and secondary metabolites

Antibiotics and secondary metabolites with antimicrobial properties including flavonoids, peptides, quinones, alkaloids, phenols, steroids, terpenoids, and polyketides have been extracted from endophytes [42]. When different microbial species coexist within the same plant, endophytes and the host plant secrete metabolites that inhibit the growth of harmful microorganisms [43]. For example, an endophytic fungus called *Phomopsis cassiae* Sousa da Câmara, isolated from *Cassia spectabilis* (DC.) H. S. Irwin & Barneby, produces active antifungal metabolites such as 3, 11, 12-trihydroxycadalene and cadinane sesquiterpenes which are effective against *Cladosporium sphaerospermum* Penz. And *Cladosporium cladosporioides* (Fresen.) G.A. de Vries [44]. The endophytic fungus *Alternaria* sp., synthesizes a novel alkaloid called altersetin, which exhibits strong inhibition against pathogenic Gram-positive bacteria like *Bacillus subtilis* and *Yarrowia lipolytica* [14]. Volatile organic compounds produced by apple endophytes including *Aureobasidium microstictum* (Bubák) W.B. Cooke, *Coprinopsis atramentaria* (Bull.) Redhead, Vilgalys & Moncalvo, *Chaetomium globosum* Kunze, *Fusarium acuminatum* Ellis & Everh., *Fusarium incarnatum* (Desm.) Sacc., and *Fusarium fujikuroi* Nirenberg effectively prevent the growth of *Venturia inaequalis* (Cooke) G. Winter [18]. In another study, *Ch. Globosum*, *F. acuminatum* and *F. fujikuroi* exhibited more than 90% inhibition of pathogen mycelia growth against *Macrophomina phaseolina* (Tassi) Goid. in volatile compound tests [45]. *Humicola fuscoatra* Traaen, an endophytic fungus isolated from halophytic plants, produces abundant intra- and extracellular metabolites with antifungal, antibacterial and antiproliferative activities against plant pathogens such as *Arthrobotrys conoides* Drechsler, *Pyrenophora graminea* S. Ito & Kurib., *Pyricularia grisea* Cooke ex Sacc., and the bacteria like *Agrobacterium tumefaciens*, *Pseudomonas syringae* and *Xanthomonas oryzae* [46].

Competition

Competition is a powerful mechanism employed by endophytes to prevent pathogens from colonizing the host tissue [47]. Endophytes have the remarkable ability to colonize plant tissues locally or systemically, both intercellularly or intracellularly [48]. By rapidly occupying niches and competing for resources, endophytes effectively remove these resources from the reach of other microorganisms. Competition often occurs in conjunction with other mechanisms [41]. For instance, *Veronaeopsis simplex* (Papendorf) Arzanlou & Crous demonstrates its ability to inhibit *Fusarium oxysporum* sensu Smith & Swingle in *Brassica rapa* subsp. *Pekinensis* (Chinese cabbage) through competition for resources and space [49]. By outcompeting the pathogen, endophytes like *Veronaeopsis simplex* (Papendorf) Arzanlou & Crous. help protect the host plant from colonization and potential damage.

Induced systemic resistance (ISR)

Induced systemic resistance is an active process in which specific factors trigger gene expression, protein synthesis, and metabolic changes in the plant. These changes ultimately result in a reduction in disease levels. Resistance-inducing factors can lead to systemic changes in the plan, including the accumulation of compounds such as phytoalexins and defense-related proteins [48]. Endophytes, including non-pathogenic microorganisms, can induce systemic resistance and activate specific genes involved in pathogenesis [14]. Some endophytes possess ability to degrade plant lignin and cellulose, and they can also secrete chitinase which induces the host plant's immune system and decomposes the cell wall structure of phytopathogenic fungi. For example, apple endophytes such as *Acremonium sclerotigenum* (Moreau & R. Moreau ex Valenta) W. Gams, *Aureobasidium microstictum*, *Fusarium lateritium*, and *Coniochaeta endophytica* have been shown to exhibit cellulase activity in vitro [18]. In *Solanum lycopersicum* Linn. (tomato) plants, the endophytic species, *Fusarium solani* (Mart.) Sacc., isolated from tomato roots activated ISR against *Septoria lycopersici* Speg. by activating pathogenesis-related (PR) genes such as PR7 and PR5, which, in turn, led to the production of ethylene and jasmonic acid in the roots [14]. In the case of *Piriformospora indica*, it induces defense responses in *Scrophularia striata* by increasing hydrogen peroxide (H_2O_2), as well as defensive compounds like flavonoids and phenylethanoid glycosides (PhGs) such as echinacoside and acteoside. Moreover, antioxidant enzymes like superoxide dismutase (SOD) and guaiacol peroxidase (POX) are upregulated to regulate the plant's oxidative status [50].

Hyperparasitism

Hyperparasitism is an additional mechanism employed by endophytes to protect their host plants against pathogens. In this process, endophytes directly attack pathogens by twisting and penetrating their hyphae and destroying their cell walls through the production of lyases [14]. For example, *Trichoderma* spp. isolated from Filed as *Citrullus lanatus* (Thunb.) Matsum. & Nakai (watermelon) plants has been found to inhibit pathogens such as *Fusarium oxysporum* f.sp. niveum W.C. Snyder & H.N. Hansen, *F. oxysporum* f.sp. *melonis*, *Monosporascus cannonballus* Pollack & Uecker, *F. solani* and *Macrophomina phaseolina* (Tassi) Goid. They achieve this through the formation of papilla-like structures, appressoria, lysis of pathogen hyphae, and the formation of coil hyphae [51]. *Malus* sp. (Apple) endophytes, such as *Chaetomium globosum* and *Fusarium lateritium,* have demonstrated chitinase activity in vitro. Chitinases are enzymes that degrade chitin, a major component of fungal cell walls, and their activity contributes to the control of fungal pathogens [18].

Biomedical and pharmaceutical industry

Endophytic fungi have received considerable attention from scientists for their natural products following the discovery of positive effect of anticancer drugs (such as taxol) derived from *Taxomyces andreanae* Strobel, A. Stierle, D. Stierle & W.M. Hess in 1990, and the antibiotic penicillin obtained from *Penicillium notatum* Westling, in 1928 [12]. Endophytes are capable of producing a wide range of bioactive metabolites, including phenolic acids, alkaloids, quinones, steroids, saponins, tannins, and terpenoids. This makes them valuable sources of anticancer, antimalarial, antituberculosis, antiviral, antidiabetic, anti-inflammatory, antiarthritis, and immunosuppressive compounds, with potential applications in drug development [14]. The compounds produced by endophytes are generally similar to those produced by their host plants including the cardiotonic digoxin (*Digitalis lanata* Ehrh.), ginkgolides (*Ginkgo biloba* Linnaeus), the antidepressant and antimicrobial hypericin (*Hypericum perforatum* L. var. *ellipticum* Freyn & Sint.), the anticancer pro-drug podophyllo-toxin (*Juniperus communis* L. var. *hemisphaerica* (Presl) Parl.) and the anticancer paclitaxel and its metabolites (*Taxus baccata* L. subsp. *wallichiana* (Zucc.) Pilg.) [43]. For instance, endophytic fungi such as *Penicillium* sp. [52], *Phoma* sp. [53], *Fusarium oxysporum*, *Taxomyces andreanae* [54] and *Fusarium solani* [55] have been reported to possess anticancer properties and secretion of alkaloids. Furthermore, *Penicillium thomii* Maire, an endophytic fungus isolated from *Terminalia chebula* Retz. was found to produce terminatone, which exhibits antioxidant activity [56]. Another example is the production of a sesquiterpene, a potent antioxidant compound, by *Acremonium* sp., an endophytic fungus obtained from the twigs of *Garcinia griffithii* T. Anderson [57]. In a study by Kaur (2018), *Fusarium* sp. and *Alternaria* sp. were identified as alpha-glucosidase inhibitors with potential antidiabetic activity [58]. Most antibiotics derived from endophytic fungi demonstrate strong inhibitory effects against viral growth. For example, *Alternaria tenuissima* (Kunze) Wiltshire, isolated from *Quercus emoryi* Torrey was found to be effective against HIV-1 virus by producing an antiviral compound called Altertoxins [14]. *Gliocladium* sp., an endophytic fungus, exhibited inhibitory activities against *Mycobacterium tuberculosis*, a life-threatening bacterium that commonly affects the lungs, through the production of polyols 3 and 4 compounds, that displayed inhibitory activities against *M. tuberculosis* at a minimum inhibitory concentration [59]. Fusapyrone and deoxyfusapyrone, two alpha-pyrones antifungal compounds isolated from *Fusarium semitectum* Berk. & Ravenel, and derived from *Oryza sativa* L. (rice), demonstrated high potential against mycotoxogenic fungi such as *Aspergillus flavus* Link [60]. Additionally, the endophytic fungus *Paraconiothyrium brasiliense* Verkley, found in *Corylus avellana* L., enhanced the production of paclitaxel in its host plant. Paclitaxel is widely used in chemotherapeutic treatments for various cancers due to its potent biological activity [61]. One well-known example of discovering chemicals derived from endophytic fungi is paclitaxel, also known as Taxol, which is an anticancer drug extracted from *Taxus brevifolia* var. *reptaneta* Spjut, R.W. in a study conducted by Kaul et al. (2012) [62]. Another endophytic fungus, *Alternaria* sp., isolated from *Berkleasmium* sp., was found to produce multiple active substances with cytotoxic, anti-trypanosomiasis and anti-leishmaniasis properties [63]. In a study by Kumari et al. (2021), *Penicillium citrinum* Thom, isolated from *Azadirachta indica* A. Juss., exhibited antimicrobial activity against human pathogenic bacteria (*Staphylococcus aureus*, *Enterococcus* *faecalis*, *Aeromonas hydrophila*) and fungi (*trichophyton mentagrophytes* (C.P. Robin) Sabour.) [64]. Furthermore, *Trichoderma harzianum* Rifai, isolated from *Kadsura angustifolia* A. C. Smith, was shown to produce nigranoic acid, which displays potent antiviral activity inhibiting HIV-1 reverse transcriptase [65]. Khiralla et al. (2020) reported that crude extracts of *Curvularia papendorfii* A, isolated from *Vernonia amygdalina* Delile, exhibited antiviral effects against coronaviruses [66]. Additionally, an endophytic fungus, *Aspergillus nidulans* (Eidam) G. Winter, isolated from *Passiflora incarnate* L., demonstrated antioxidant activity [67]. Lastly, an endophytic *Aspergillus* sp. isolated from *Tabebuia rosea* (Bertol.) Bertero ex DC produced pulchranin, an anticancer compound that effectively inhibited human tumor cells, including liver (Hep-G2) and breast (MCF-7) cell lines [68].

Industry

Endophytic fungi are known for their ability to produce a wide variety of secondary metabolites, including alkaloids, phenols and their derivatives, flavonoids, terpenoids, volatile organic compounds (VOC), and various enzymes. This makes them a promising group of microorganisms with potential applications in industrial settings [69,18]. Research also indicates that endophytic fungi can produce a range of hydrolytic enzymes, such as amylase, protease, lipase, cellulase, tannase, and laccase [70]. These microbial enzymes find applications in industries such as cosmetics, biomaterials, leather, detergents, food, energy, fine chemicals, paper and textiles [71]. Certain species of *Colletotrichum*, *Fusarium*, *Phoma*, and *Penicillium*, isolated from *Cymbopogon Citratus* (DC.) Stapf and *Murraya koenigii* (L.) Spreng. have been found to produce asparaginase [72]. Strains of *Amanita muscaria* (L.) Lam., *Boletus luridus* Schaeff., *Hydnum rufescens* Sensu Auct., and *Lactarius acerrimus* Britzelm., isolated from *Sarcoscypha austriaca* (Beck ex Sacc.) Boud., have been reported to produce protease [73]. *Cladosporium cladosporioides*, *Colletotrichum crassipes* (Speg.) Arx, *Curvularia brachyspora* Boedijn, and *Drechslera hawaiiensis* Bugnic. ex Subram. & B.L. Jain, isolated from *Adhatoda vasica* (Nees.), *Coleus aromaticus* Benth., *Costus igneus* N.E.Br. and *Lawsonia inermis* L., respectively, are capable of producing amylase, laccase, and lipase [74]. *Acremonium curvulum* W. Gams, *Aspergillus niger* Tiegh., *Cochliobolus lunatus* R.R. Nelson & F.A. Haasis and *Gibberella baccata* (Wallr.) Sacc., isolated from *Bauhinia forficate* Link, have been found to produce lipase and xylanase [75]. *Alternaria alternata* (Fr.) Keissl. and *Penicillium chrysogenum* Thom, isolated from *Asclepias sinaica* (Boiss.) Muschl., are known cellulase producers [76]. *Talaromyces emersonii* Stolk and *Nigrospora sphaerica* (Sacc.) E.W. Mason, have been reported as pectinase producers [70].

Biofuel

Fossil fuels are non-renewable resources, so there is a growing focus on finding environmentally-friendly, readily available and clean alternatives [77]. Biodiesel, a natural renewable alternative, is gaining attention due to its lower toxicity, emissions, and better biodegradability compared to traditional fuels [78]. Biodiesel is composed of fatty acid methyl or ethyl esters that can be derived from biomass [79]. Microbial lipids, particularly those produced by oleaginous fungi, are emerging as a promising alternative for biodiesel production. This approach avoids the need for extensive land cultivation, reduces raw material costs, and minimizes competition with food production [80]. Some fungal species, known as oleaginous fungi, have the ability to accumulate significant amounts of intracellular lipids [81]. For example, endophytic fungi such as *Lasiodiplodia exigua* Linald., Deidda & A.J.L. Phillips, *Phomopsis* sp., and *Pestalotiopsis microspore* (Speg.) Bat. & Peres, isolated from biodiesel fresh plants like *Sapindus mukorossi* var. *carinatus* Radlk., *Jatropha curcas* L., *Cascabela thevetia* (L.) Lippold, *Mesua ferrea* L., *Terminalia bellerica* Roxb., *Pongamia pinnata* (L.) Pierre, and *Ricinus communis* L., have been identified as biofuel “minifactories” due to their high lipid content [80].

Textile industry

The textile industry generates effluents that contain toxic dye components consisting of organic compounds and heavy metals. These spent dyes are non-biodegradable and pose a significant threat to the environment [82]. Due to their complex molecular structures, conventional biological treatment methods like activated sludge process, electrochemical treatment, chemical coagulation, chemical oxidation, and carbon absorption have limited success in degrading and removing these dyes [83]. However, certain fungal enzymes have shown the potential for decolorizing dyes by breaking them down and altering their structure [84]. For instance, *Penicillium megasporum* Orpurt & Fennell, isolated from *Cupressus torulosa* D. Don, has been found to produce laccase, an enzyme used for the decolorization of synthetic textile dyes such as congo red, orange G, and rhodamine B [83].

Bioremediation

Bioremediation is a process that involves using plants, microorganisms, and enzymes to detoxify contaminants in soils and other environments [85]. Certain endophytic fungi exhibit resistance to metals like zinc, cadmium, manganese, chromium, cobalt, and lead. They can also induce tolerance in host plants growing in contaminated sites, making these microorganisms valuable tools for metal remediation or assisting in phytoremediation processes [86]. For example, the endophyteic fungus *Drechslera* sp., isolated from *Neurachne alopecuroidea* R. Br., has shown the ability to degrade methyl tertiary-butyl ether (MtBE), a common gasoline additive [87]. In a study by Pietro-Souza et al. 2020, *Aspergillus* sp., *Curvularia geniculata* (Tracy & Earle) Boedijn, and *Westerdykella* sp., isolated from the root systems of *Aeschynomene fluminensis* Vell. var. *tuberculata* (Griseb.) Rudd and *Polygonum acuminatum* Kunth, were successful in removing mercury [87].

Table 1. Various beneficial aspects of endophytic fungi

Benefits	Mechanism	Endophyte fungi	Host plant	Ref.
Promotion growth of host plants	1.Direct mechanism: • Antibiosis lytic enzyme secretion • Phytohormone production • Phosphate solubilization • Siderophore production • Indolic compound production • Competition • 1-Aminocyclopropane-1-carboxylate utilization 2.Indirect mechanism: • Induction of plant resistance • Stimulation of plant secondary metabolites • Promotion of plant growth and physiology • Hyperparasitism 3.Increasing the uptake and supply of organic matters, macronutrients and micronutrients 4. Phosphate solubilization 5.Producing varieties of plant hormones	*Coniochaeta endophytica* and *Fusarium lateritium*	*Malus* sp.	[18]
		Thielavia basicola, Xenodidymella applanata and Chaetosphaeronema achilleae	*Satureja khuzestanica*	[20]
		Colletotrichum sp.	*Artemisia annua*	[14]
Resistance to abiotic stress in host plants	Increase the production of phytobeneficial substances in host plants	*Neotyphodium* sp.	*Arizona fescue*	[24]
		Epichloe	*Festuca arundinacea*	[8]
		Piriformospora indica	*Brassica rapa* subsp. *Pekinensis*	[26]
		Trichoderma atroviride	*Foeniculum vulgare*	[29]
		Periconia macrospinosa, Neocamarosporium goegapense, N. chichastianum	*Salt lake plants*	[30]
		Aspergillus welwitschiae	*Glycine max*	[31]
		Exophiala pisciphila	*Zea mays*	[26]
		Aspergillus japonicus	*Euphorbia indica*	[38]
		P. indica	*Banana leaves*	[39]
Resistance to biotic stress in host plants	1. Hyperparasitism 2. Competition 3. Antibiosis 4. Induced resistance	*Aureobasidium microstictum, Coprinopsis atramentaria, Chaetomium globosum,*	*Malus* sp.	[18], [45]

Table 1. Continued

Benefits	Mechanism	Endophyte fungi	Host plant	Ref.
		Fusarium acuminatum, Fusarium incarnatum, Fusarium fujikuroi		
		Phomopsis cassiae	*Cassia spectabilis*	[44]
		Humicola fuscoatra	*Halophytic plants*	[46]
		Veronaeopsis simplex	*Brassica rapa* subsp. *Pekinensis*	[49]
		Fusarium solani	*Solanum lycopersicum*	[14]
		Trichoderma spp.	*Citrullus lanatus*	[51]
Biomedical and pharmaceutical industry	Producing many bioactive metabolites such as phenolic acids, alkaloids, quinones, steroids, saponins, tannins, and terpenoids	*Aspergillus sp*	*Tabebuia rosea*	[68]
		Penicillium thomii	*Terminalia chebula*	[56]
		Acremonium sp.	*Garcinia griffithii*	[57]
		Alternaria tenuissima	*Quercus emoryi*	[14]
		Fusarium semitectum	*Oryza sativa*	[60]
		Paraconiothyrium Brasiliense	*Corylus avellana*	[61]
		Alternaria sp.	*Berkleasmium* sp	[63]
		Penicillium citrinum	*Azadirachta indica*	[64]
		Trichoderma harzianum	*Kadsura angustifolia*	[65]
		Curvularia papendorfii	*vernonia amygdalina*	[66]
		Aspergillus nidulans	*Passiflora incarnate*	[67]
Industry	Producing a variety of secondary metabolites such as alkaloids, phenols and its derivatives, flavonoids, terpenoids, volatile organic compounds (VOC), and different enzymes	*Colletrotrichum, Fusarium, Phoma, Penicillium*	*Cymbopogon Citratus* and *Murraya koenigii*	[72]
		Alternaria alternata, Penicillium chrysogenum,	*Asclepias sinaica*	[76]
		Amanita muscaria, Boletus luridus, Hydnum rufescens, Lactarius acerrimus	*Sarcoscypha austriaca*	[73]
		Cladosporium cladosporioides, Colletotrichum crassipes, Curvularia brachyspora, Drechslera hawaiiensis	*Adhatoda vasica, Coleus aromaticus, Costus igneus, Lawsonia inermisare*	[74]
		Acremonium curvulum, Aspergillus niger, Cochliobolus lunatus, Gibberella baccata	*Bauhinia forficate*	[75]
Biofuel	Accumulating remarkable amounts of intracellular lipids	*Lasiodiplodia exigua, Phomopsis* sp., *Pestalotiopsis microspore*	*Sapindus mukorossi, Jatropha curcas, Cascabela thevetia, Mesua ferrea, Terminalia bellerica, Pongamia pinnata, Ricinus communis*	[80]
Textile industry	Producing enzymes with the ability of decolorization of dyes by degradation and altering their structure	*Penicillium megasporum*	*Cupressus torulosa*	[83]
Bioremediation	• Resistance to some metals • Inducing tolerance in their host plants in contaminated sites	*Drechslera* sp.	*Neurachne alopecuroidea*	[87]
		Aspergillus sp., *Curvularia geniculate, Westerdykella* sp.	*Aeschynomene fluminensis* and *Polygonum acuminatum*	[86]

Conclusion

In recent years, there has been a growing focus on endophytes, particularly endophytic fungi, due to their significant potential as microbial sources for various applications. They have emerged as valuable resources in agriculture, industry, medicine, and bioremediation. Endophytic fungi offer opportunities for biocontrol in agriculture, aiding in pest and disease management while promoting sustainable farming practices. They also produce diverse secondary metabolites that have bioactive properties, making them valuable for natural product development. In industry, endophytic fungi show promise in enzyme and biofuel production, with applications in cosmetics, food, textiles, and detergents.

Additionally, they possess medicinal potential, producing bioactive compounds with antimicrobial, anti-inflammatory, and anticancer properties, which can lead to the discovery of novel therapeutic agents. In bioremediation, endophytic fungi play a crucial role in detoxifying contaminants in the environment, particularly their ability to tolerate heavy metals and degrade pollutants. Understanding and tracking microbial flora, including endophytic fungi, allows for a better understanding of ecological dynamics. The study of endophytes, especially endophytic fungi, holds great promise and presents exciting opportunities for advancements in various fields. Continued research will contribute to the development of innovative solutions for contemporary challenges.

Acknowledgments
None.

Author contributions
Parmida Aleahmad was involved in literature searching, and writing the manuscript draft; Leila Ebrahimi contributed in developing the idea, revising, editing, and final approval.

Declaration of interest
The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

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Abbreviations

ACC: 1-aminocyclopropane-1- carboxylate; IAA: indole acetic acid; GA: gibberellin; ABA: abscisic acid; ROS: reactive oxygen species; SA: salicylic acid; PhG: phenylethanoid glycoside; SOD: superoxide dismutase; POX: guaiacol peroxidase; VOC: volatile organic compound