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Endophytic Microbial Community and its Potential Applications: A Review

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ABSTRACT

Endophytes are present in all plant species across the world. They assist their hosts by producing several chemicals/metabolites that provide protection and, ultimately, survival value to their host plants. In various studies, endophytes have been demonstrated to be a new and potential source of novel natural chemicals for application in modern medicine, agriculture, and industry. Endophytes have developed a variety of natural chemicals that include antibacterial, antifungal, antiviral, anticancer, antiparasitic, cytotoxic, antidiabetic, immunosuppressive, antitubercular, anti-inflammatory, and antioxidants. These chemicals are involved in biodegradation and biofertilizers that promote the growth of plants. Screening these endophytic metabolites is regarded as a promising technique to combat drug-resistant human and plant disease strains. In this review, the basic concept of endophytes, the variety of endophytic microbiome, as well as the application of endophytes are presented. This knowledge may be used to extract improved bioactive compounds from endophytes and may serve as a foundation for future research.

Keywords: anticancer, antimicrobial, antioxidant, antiviral, endophytes, medicinal plants

1. INTRODUCTION

Endophytes are bacteria, fungi, and actinomycetes present in plant tissues (roots, stem, and leaves) in natural environment [1]. The word 'endophyte' is derived from the Greek word 'endon' which means 'inside the plant' [2]. They colonize all plants without harming their hosts or causing disease in a symbiotic association that includes mutualism or antagonism [3], either in a localized position or spreading to all parts of the host plant. They live inside the host cell or the intercellular space or vascular system [4]. Endophytes invade a host of naturally occurring wounds during plant growth and epidermal conjunction through the roots, stomata, flowers, and lenticels [2] (Figure 1).

Endophytes maintain their stability in various types of environments by producing a wide range of bioactive compounds. These bioactive compounds exhibit various activities including antimicrobial, nutrient cycling, enhancement of plant growth, biodegradation, bioremediation, antiviral, anticancer, and antitumor activities. Besides these activities, they are also environmentally friendly as compared to synthetic drugs, chemicals, pesticides, and antibiotics [5–9].

Therefore, a better understanding of endophytic microbes is necessary for the discovery of novel endophytes and their

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bioactive metabolites. In light of their importance, this review aims to highlight the recently discovered endophytic microbes along with their potential applications in the future.

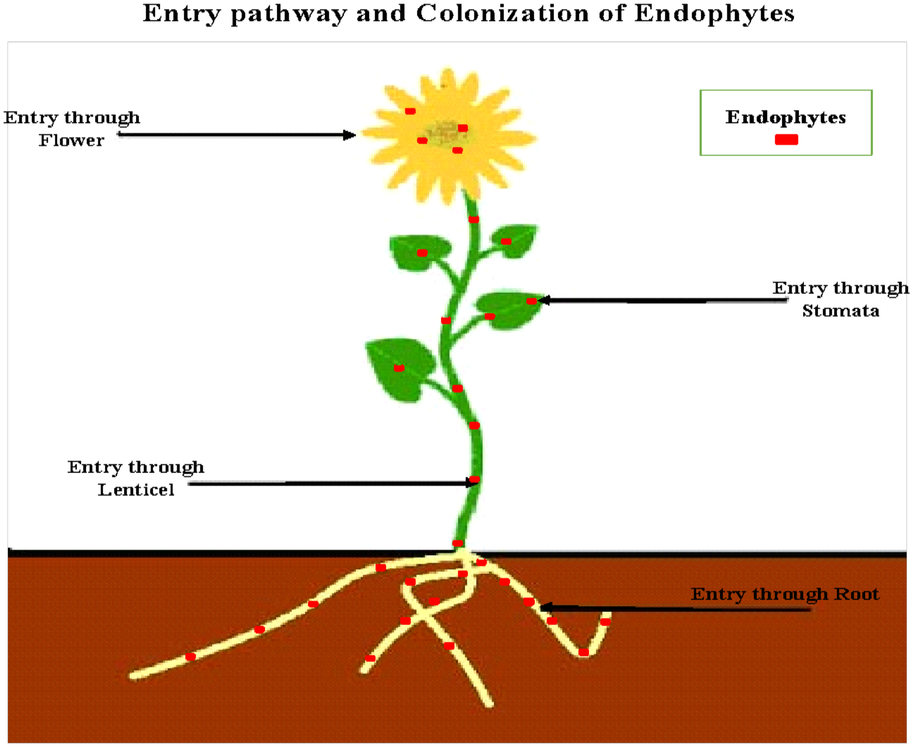

Figure 1. Endophytic Microbes Entry Pathway and Colonization Inside The Host [2].

2. ENDOPHYTIC BACTERIA

Endophytic bacterial microbiota colonizes the host plant in an antagonistic, synergetic, and neutral symbiotic association [10]. From the antagonistic point of view, they protect the plant from diseases. Whereas, in synergetic association, they promote plant growth. The beneficial activities of endophytic bacteria depend upon their location in different parts of the plant body [11]. Bacterial endophytes and their bioactive metabolites have been isolated from different plants in various studies (Table 1). These have the potential for various biological control activities.

3. ENDOPHYTIC FUNGI

Endophytic fungi have been found in a variety of tissues, including leaves, flowers, fruits, roots, and stems in symbiotic associations [28]. The metabolites isolated from these fungi have agricultural, pharmaceutical, and biotechnological applications. Various studies have reported high antibacterial, antifungal, antiviral, antioxidant, anticancer, and other activities of fungal endophytes presented below in Table 2.

Table 1. Endophytic Bacterial Strains, Their Hosts, Site of Isolation, and Biocontrol/Activity

Endophytic Bacterial Strains	Metabolites/Compounds	Host Plant	Biocontrol / Activity	Site of Isolation	References
Bacillus velezensis Bvel1	Iturin A2, Surfactin C13 and C15, Oxydifficidin, Bacillibactin, L-dihydroanticapsin, and Azelaic acid	Olive Tree	Activity against post-harvest fungal pathogens, including bunch rot disease in grape berries	Roots	Nifakos et al. [12]
Serratia marcescens MOSEL-w2	Cotinine (alkylpyrrolidine), L-tryptophan, L-lysine, L-Dopa, and L-ornithine.	*Cannabis sativa*	*Phytophthora parasitica*	Rhizosphere	Iqrar et al. [13]
Pseudomonas protegens Sneb1997, *Serratia plymuthica* Sneb2001	Not indicated	Soybean and Peanut	Not indicated	Not indicated	Zhao et al. [14]
Paenibacillus sp.Xy-2 KP715166	2(1H)-pyrazinone	*Houttuynia cordata*	Cytotoxic activity of compound 1 against HL-60 (human promyelocytic leukemia cells)	Not indicated	Mahdi et al. [15]
Serratia rubidaea ED1	Not indicated	*Chenopodium quinoa*	Plant growth-promoting (PGP) and phosphate solubilizing	Roots	Mahdi et al. [15]
Pseudomonas mendocina DSM 50017T *Erwinia amylovora* CFBP 1232T *Acinetobacter baumannii* B389 *Bacillus pumilus* DSM 1794 *Microbacterium liquefaciens* HKI 11374 *Xanthomonas codiaei* DSM 18812TB *Citrobacter freundii* 22054_1 *Flavobacterium hibernum* DSM 12611T *Pantoea agglomerans* DSM 8570 *Microbacterium liquefaciens* DSM 20638T *Bacillus licheniformis* DSM 13T *Pseudomonas aeruginosa* 8147_2	Indole acetic acid (IAA), Siderophore, Urease, and Catalase	*Brassica napus*	Siderophore production (SP), Phosphate solubilization (PS), and antifungal activity (AFA) against *Leptosphaeria maculans*	Roots, Stems, and Leaves	Lipková et al. [16]
Kocuria rhizophila 14asp	AAC De-aminase,	Not indicated	Enhancing plant growth	Not indicated	Khan et al. [17]

Endophytic Bacterial Strains	Metabolites/Compounds	Host Plant	Biocontrol / Activity	Site of Isolation	References
	Superoxide dismutase (SOD), Peroxidase (POD), and Catalase (CAT)				
Burkholderia seminalis Strain 869T2	Indole Acetic Acid (IAA), Siderophore Synthesis	*Chrysopogon zizanioides*	Plant growth-promoting	Roots	Hwang et al. [18]
Bacillus velezensis YB-130	Lanthipeptide	Wheat	Antifungal	Spikes	Xu et al. [19]
Bacillus velezensis KN12, *Bacillus amyloliquefaciens* DL1, *Bacillus velezensis* DS29, *Bacillus subtilis* BH15, *Bacillus subtilis* V1.21, and *Bacillus cereus* CS30	Chitinase, Proteases, Glucanase, Pregn-4-ene-3, 20-dione, 17-hydroxy-6-methyl-, bis (O-methyloxime, disulfide, methyl 1-(methylthio) propyl, Propanoic acid, 2-methyl-, decyl ester, Benzofuranyl derivatives, Propanethioic acid, S-pentyl ester, Metronidazole-OH, and Sulfadiazine	*Piper nigrum* L.	Antifungal and plant growth-promoting	Root	Nguyen et al. [20]
Pseudomonas brassicacearum CDVBN10	Siderophores, Solubilizes P, Synthesizes cellulose	*Brassica napus* cv rescator	Plant growth-promoting	Roots	Jiménez-Gómez et al. [21]
Bacillus subtilis 6Sm	Siderophore synthesis, Indole acetic acid (IAA) and Abscisic acid (ABA), Proteases	*Zea mays*	Plant growth-promoting and antifungal	Stems	Jiménez-Gómez et al. [21]
Streptomyces sp. SH-1.2-R-15	Chartreusin	*Dendrobium officinale*	Antibacterial and anticancer activity	Root, Leaf, and Stem	Zhao et al. [22]
Pantoea ananatis VERA8	Five indole derivatives, 1H-indol-7-ol (1), Tryptophol (2), 3-Indolepropionic acid (3), Tryptophan (4), 3,3-di(1H-indol-3-yl)propane-1,2-diol (5), and two diketopiperazines, cyclo(L-Pro-L-Tyr) (6), cyclo[L-(4-hydroxyprolinyl)-L-leucine (7) along with one dihydrocinnamic acid (8)	*Baccharoides anthelmintica*	Effects on melanin synthesis in murine B16 cells towards for vitiligo treatment	Roots	Rustama et al. [23]

Endophytic Bacterial Strains	Metabolites/Compounds	Host Plant	Biocontrol / Activity	Site of Isolation	References
Bacillus velezensis strain OEE1	Cellulase, Pectinase, and Amylase	Olive Tree	Antifungal and biofertilizer	Not indicated	Cheffi et al. [24]
Bacillus atrophaeus XEGI50	Not indicated	*Glycyrrhiza uralensis*	Antimicrobial	Not indicated	Mohamad et al. [25]
Stenotrophomonas maltophila H8 (*Xanthomonadales: Xanthomonadaceae*), *Pseudomonas aeruginosa* H40 (*Pseudomonadales: Pseudomonadaceae*) and *Bacillus subtilis* H18 (*Bacillales: Bacillaceae*)	Peroxidase, Polyphenol oxidase, and Catalase	Not indicated	Activity against fungal phytopathogen	Not indicated	Selim et al. [26]
Pseudomonas stutzeri KJ437485	Phenol, 3, 5-bis (1, 1-dimethylethyl)	*Ulva reticulate*	Antibacterial activity	Not indicated	Dhanya et al. [27]

Table 2. Endophytic Fungal Strains, Their Hosts, Site of Isolation, and Biocontrol/Activity

Endophytic Fungal Strains	Metabolites / Compounds	Host Plant	Biocontrol / Activity	Site of Isolation	References
Penicillium sp. CAM64	Penialidin A-C, Citromycetin, p-hydroxyphenylglyoxalaldoxime, and Refelfin A	*Garcinia nobilis*	Anticancer and Antibacterial	Leaves	Jouda et al. [29]
Aspergillus sp. MN148642	Arugosin C, Ergosterol, Iso-emericellin, Sterigmatocystin, Dihydrosterigmatocystin, Versicolorin B, and Diorcinol	*Tecoma stans* (L.)	Anticancer and Antimicrobial	Leaves	Elsayed et al. [30]
Curvularia sp. G6-32	Asperpentyn	*Sapindus saponaria* L.	Antioxidant and Anticholinesterase	Not indicated	Polli et al. [31]
Nigrospora oryzae MH071153 *Alternaria alternata* MH071155 *Aspergillus terreus* MH071154	Saponins	Brahmi	Plant growth-promoting	Leaves	Soni et al. [32]
Botryosphaeria fabicerciana MGN23-3	Mellein and β-orcinaldehyde	*Morus nigra*	Antibacterial and Antioxidant	Leaves	Silva et al. [33]

Endophytic Fungal Strains	Metabolites / Compounds	Host Plant	Biocontrol / Activity	Site of Isolation	References
Drechslera sp. strain 678	monocerin and Alkynyl	*Neurachne alopecuroidea*	Antifungal and Bioremediation	Roots	D'Errico et al. [34]
Aspergillus awamori	IAA, Phenols and Sugars	*Withenia somnifer*	IAA production	Not indicated	Mehmood et al. [35]
Fusarium oxysporum GG008	5-hydroxymethylfurfural(HMF) and Octa decanoic acid	*Sceletium tortuosum* L	Antibacterial	Not indicated	Manganyi et al. [36]
Pleosporales sp. SK7	Abscisic acid-type sesquiterpene, and One asterric acid derivative	*Kandelia candel*	Antibacterial, Antioxidant, and Cytotoxic	Leaves	Wen et al. [37]
Alternaria sp. MHE 68	Linoleic acid, Octa decadienoic acid, and Cyclo de casiloxane	*Pelargonium sidoides* DC	Antibacterial	Leave and Roots	Manganyi et al. [38]
Aspergillus aculeatus F027	Di keto piperazine cyclo-(L-Phe-N-ethyl-L-Glu), along with two known diketopiperazines cyclo-(L-Pro-L-Leu) and cyclo-(L-Pro-L-Phe)	*Ophiopogon japonicus* (Linn. f.)	Antibacterial	Leaves	Ma et al. [39]
Arthrinium sp. MFLUCC16-1053	Not indicated	*Zingiber cassumunar*	Antibacterial	Leaves	Pansanit et al. [40]
Aspergillus niger CSR3	Phosphate solubilization, Indole acetic acid (IAA), and Gibberellins	*Cannabis sativa*	Biofertilizer	Not indicated	Lubna et al. [41]
Lasiodiplodia theobromae SNFF	γ-lacton , Auxin (IAA), Auxin (ICA), and Di keto piperazine	*Solanum nigrum*	Hepatoprotective, Anti-inflammatory, and Anticancer	Stems, Leaves, and Fruits	El-Hawary et al. [42]
Colletotrichum gloeosporioides A12	Colletotricones A and B	*Aquilaria sinensis*	Cytotoxic	Not indicated	Liu et al. [43]
Fusarium sp. PN8 and *Aspergillus* sp. PN17	Saponins, Ginsenoside Re, Rd and 20(S)-Rg3	*Panax notoginseng*	Antimicrobial	Roots and Seeds	Jin et al. [44]
Aspergillus clavatonanicus strain MJ31	Polyketide synthase (PKS) and Non-ribosomal peptide synthetase (NRPS)	*Mirabilis jalapa* L	Antimicrobial	Roots	Mishra et al. [45]
Trichoderma sp. 307	Depsidone, Botryorhodine H, together with three known analogues, Botryorhodines C, D and G	*Clerodendruminerme*	Cytotoxic	Stem bark	Zhang et al. [46]

Endophytic Fungal Strains	Metabolites / Compounds	Host Plant	Biocontrol / Activity	Site of Isolation	References
Aspergillus japonicus CAM231	Pyrone derivative, Hydroxy neovasinin, One phenol derivative, Asperolan, together with two known compounds neovasifurarone B and variecolin	*Garcina preussii*	Cytotoxic and Antibacterial	Leaves	Jouda et al. [47]

Table 3. Endophytic actinomycetes strains, their hosts, site of isolation, and biocontrol/activity.

Endophytic Actinomycetes Strain	Metabolites / Compounds	Host Plant	Biocontrol / Activity	Site of Isolation	References
Streptomyces antimycoticus NR_041080	Not indicated	*Mentha longifolia* L	Cytotoxic	Leaves	Salem et al. [49]
Fodinicola acaciae sp. MK323078	Indole-3-acetic acid (IAA)	*Acacia mangium* Willd	Plant growth-promoting	Roots	Phạm et al. [50]
Streptomyces sp. HAAG3-15	Azalomycin B	Cucumber	Antifungal	Roots	Cao et al. [51]
Actinomycete strain GKU 173^T	Phospholipids contained di phosphatidyl glycerol (DPG), Phosphatidyl ethanolamine (PE), and Phosphatidyl inositol (PI)	*Acacia mangium*	Plant growth-promoting	Roots	Phạm et al. [50]
B. japonicum SAY3-7 *B. elkanii* BLY3-8	Not indicated	Not indicated	Biofertilizer	Not indicated	Htwe et al. [52]
Streptomyces sp. KIB-H1289 KM187147.1	Lorneic acid E	*Betula mandshurica Nakai*	Inhibitory effects on Tyrosinase	Bark	Yang et al. [53]
Nocardiopsis sp. GRG1 (KT235640)	Not indicated	Brown Algae	Antibacterial	Leaves	Rajivgandhi et al. [54]

4. ENDOPHYTIC ACTINOMYCETES

Endophytic actinomycetes that colonize plant tissues have attracted a lot of attention because of their potential for stimulating plant growth, as well as contributing to soil and plant survival, by manufacturing certain responsive metabolites. They also counteract pathogenic microbes that live within the same plant species [48]. The metabolites of endophytic actinomycetes reported in previous studies and their beneficial activities are presented below in Table 3.

5. APPLICATIONS OF ENDOPHYTES

Endophytes and their bioactive compounds including polysaccharides, peptides, flavonoids, phenolic acids, and indole derivatives have key importance in pharmaceutical, agricultural, and biotechnological industries due to their numerous types of activities [4] (Figure 2).

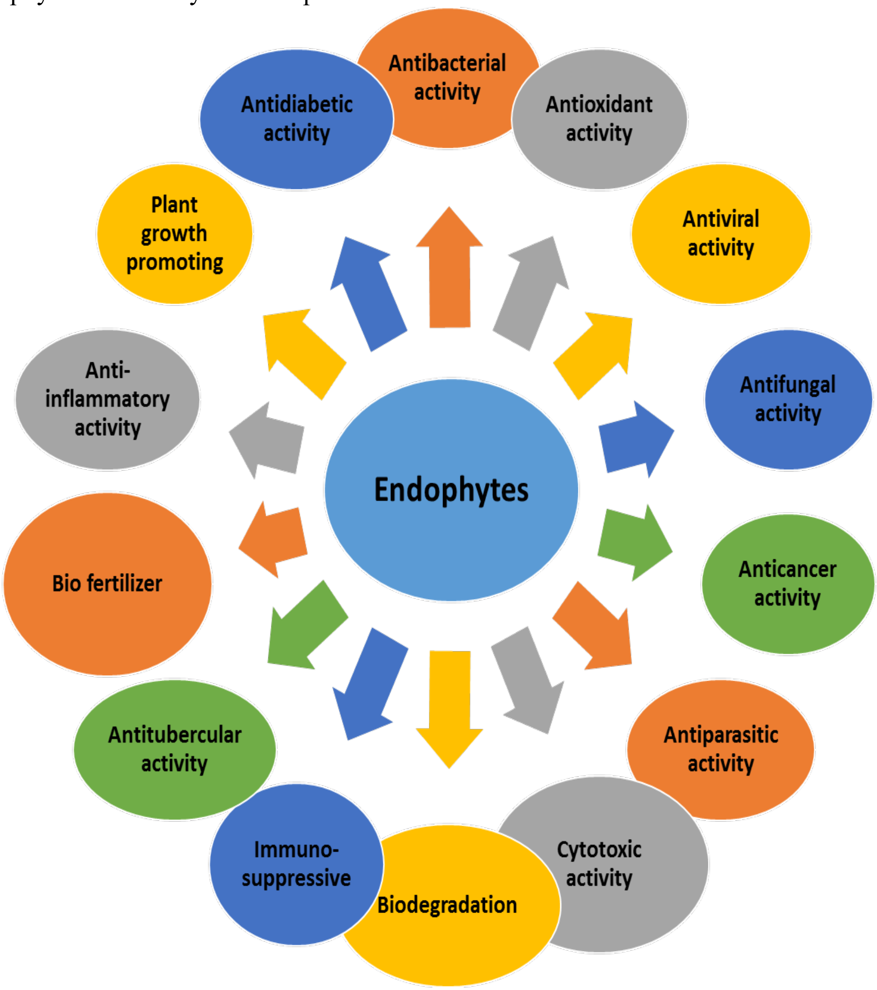

Figure 2. Applications of Endophytes [55–69]

5.1. Antibacterial Activity

Endophytes exhibit a high potential against a vast number of bacterial pathogens. For example, endophytes produce alkaloids which are mostly produced by *Streptococcus* species showing antibacterial activity [10]. The literature reveals that endophytes show antibacterial activities against *Staphylococcus aureus, Escherichia coli*, *Klebsiella pneumonia* [55], *Listeria monocytogenes*, *Pseudomonas aeruginosa* [56], *Salmonella typhi*, *Streptococcus pneumoniae*, *Vibrio cholerae* [57], MRSA [58], vancomycin-resistant *Enterococcus,* and penicillin-resistant *S. pneumoniae* [59].

5.2. Antifungal Activity

The previously reported studies also revealed that endophytes microbiome and its bioactive compounds show antifungal activity against various fungal phytopathogens and human fungal pathogens. They also promote the growth of plants either by increasing the availability of nutrients to the plants or via plant hormone production [3]. According to previous studies, endophytes showed high inhibition against *Candida albicans*, *Aspergillus fumigatus* [60], *Trichophyton rubrum* [61], and *T. mentagrophytes* [45].

5.3. Antiviral Activity

Endophytic microbes also produce various types of antiviral compounds, such as alternariol, alternariol-(9)-methyl ether, 1,1-diphenyl-2-picrylhydrazyl [62], cyclosporine U, cytonic acid A, and B, S39163/F-I, podophyllotoxin, sequoiatones C-F, and CR377 [63]. The antiviral activity of endophytic microbe metabolites have been reported against human immunodeficiency virus (HIV) [64], dengue virus, cytomegalovirus [65], herpes simplex virus, and influenza virus [63].

5.4. Antioxidant Activity

Previously reported studies revealed the antioxidant activity of polysaccharides produced by endophytic microbes [63]. For example, the endophytic fungi *Cephalosporin* spp., *Xylaria* spp., *Chaetomium* spp., and *Pestalotiopsis microspore*, were reported for their antioxidant action [66, 67].

5.5. Anticancer Activity

The endophytic metabolites also exhibit anticancer activities. For example, the taxol isolated from *Taxomyces andreanae* [63], phenylpropanoid's amide isolated from *Penicillium brasilianum* [68], and chartreusin isolated from *Streptomyces* spp. [22] have been reportedly involved in anticancer activities.

5.6. Anti-parasitic Activity

Endophytes and their bioactive metabolites also show a high potential against various parasites. According to a previously reported study, endophytes inhibit the growth of *Plasmodium* spp., *Trypanosoma* spp., and *Leishmania* [69]. Besides these activities, endophytes also have cytotoxic, biodegradation, antidiabetic, immunosuppressive, antitubercular, biofertilizer, and anti-inflammatory properties, and they also promote the growth of plants.

6. CONCLUSION

This study concludes that endophytes are present in all the plant species discussed in this study. They benefit their hosts by creating a variety of metabolites that offer protection and survival value. Literature shows that endophytes represent a fresh and promising source of innovative natural compounds for use in modern medicine, agriculture, and industry. Furthermore, endophytes are a dependable and promising source of innovative and effective bioactive chemicals used for the therapeutic treatment of human illnesses. In this study, endophytes were empirically proved *in vitro* to have at least one of the following activities namely anticancer, antibacterial, antifungal, antitumor, or antioxidant.

6.1. Future Research Directions

Future research on beneficial endophytic strains should focus more on field trials and practical applications to generate high quality endophytes. Furthermore, little is known about the processes behind endophytes and medicinal plant interactions. Several topics for future research are recommended, including the introduction of advanced strategies for the isolation and production of endophytes to create a functional library of endophytes, investigating the effects of uncultivable endophytes, and strategies for establishing the association of symbiotic endophytes with host plants.

The types of the endophytic microbiome have been described in this review, as well as their beneficial effects. This knowledge may be used to extract improved bioactive compounds from endophytes and can serve as a foundation for future research.

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