Asian Journal of Plant Sciences

ISSN 1682-3974

OPEN ACCESS Asian Journal of Plant Sciences

ISSN 1682-3974
DOI: 10.3923/ajps.2020.54.62

Review Article
Role of Endophytic Microbes Against Plant Pathogens: A Review

Pavithra G., Sumant Bindal, Meenakshi Rana and Seweta Srivastava

School of Agriculture, Lovely Professional University, 144 411 Phagwara , Punjab, India

Abstract
Endophytes are considered as plant mutualists which are living asymptomatically within plant tissues have been found in virtually all plant species. Endophytes receive nutrition and protection from the host plant while the host plant may benefit from enhanced competitive abilities and increased resistance to herbivores, pathogens and various abiotic stresses. This review focuses on the biology of endophytic fungi, their discovery, isolation, identification and diversity and their biological activities in environmental and agricultural sustainability. It also considers and their medicinal applications especially in the production of anticancer, antimicrobial, antioxidant and antiviral compounds. Endophytic fungi are one of the most creative groups of secondary metabolite producers that play important biological roles for human life. They are potential sources of novel natural agents for exploitation in the pharmaceutical industry, agriculture and in environmental applications. So, in this review we summarize their potential role against some important plant pathogens.

Key words: Agriculture, antimicrobial, eco-friendly, endophyte, sustainable, natural agents, active form

Citation: G. Pavithra, Sumant Bindal, Meenakshi Rana and Seweta Srivastava, 2020. Role of endophytic microbes against plant pathogens: A Review. Asian J. Plant Sci., 19: 54-62.

Corresponding Author: Seweta Srivastava, School of Agriculture, Lovely Professional University, 144 411 Phagwara, Punjab, India

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Many plant pathogens invade plants, including fungi, bacteria nematode and viruses, which are the most obvious threats to sustainable food production. It is not economically feasible to routinely use chemicals to eradicate the plant disease. Using these chemicals consistently, it leaves harmful residues and can bring resistance to pathogens[1]. Consequently, knowledge has been developed for safer non-chemical methods to monitor lucrative plant disease, which poses less threat to human health and the environment[2]. Replacing fungicides with bio-control agents is a choice for controlling plant pests, producing food for protection and significantly reducing pollution[3-5]. As an alternative for host-plant resistance and pesticide-based pest and pathogen control, the proper application of naturally occurring microorganisms to suppress pathogen populations and increase the production of significant crops. Endophytic microorganisms, which grow in the intercellular spaces of higher plants, are recognized in terms of diversity and pharmaceutical potential as one of the most chemically promising groups of microorganisms[6].

In particular, plants are infected with different micro-organisms. Endophytic species are those which colonize the internal tissue of the plant and display no external sign of infection or negative effect on the host[7]. Endophytic microorganisms are recognized as one of the most chemically promising diversity and pharmaceutical potential groups of microorganisms growing in the intercellular spaces of higher plants[6]. Beneficial endophytic microorganisms include fungi and bacteria that colonize the internal tissues of plants without causing visible damage to their hosts[8,9]. Although, disease symptoms of host plant can be caused by endophytes under stress conditions[7,10]. Of the nearly 300 000 plant species that exist on the earth, each individual plant is host to one or more endophytes[11]. In addition, endophytic microorganisms are not known to be saprophytes as they are associated with living tissues and may contribute to the plant's well-being in some way. Endophytes occur in a number of tissue types in a wide range of plants, actively colonizing the plant with bacterial colonies and biofilms, latently living in intercellular spaces, in the vascular tissue or in cells[12]. Endophytes are the microorganisms that reside in the tissues of living plants, are relatively unstudied and potential sources of novel natural products for exploitation in agriculture. This comprehensive review is based on critical study of different research works and investigations all around the globe and also depicts endophytic role of various microbes in enhancing crop productivity and maintaining soil health aiming towards sustainability of agriculture in long run.

What is an endophyte?: The word endophytes' derived from Greek word endon and phyton and the meaning of endon-within and phyton means-plant .The term endophytes was first coined by de Bary (1886). Plants are generally associated with diversified microorganisms. Endophytic are those mico organisms which grow in the intercellular spaces of higher plants and are accepted as in terms of diversity and pharmaceutical potential and displaying no external sign of infection or without causing negative effect on their host[6-8]. Based on differences in evolution, taxonomy, plants host and ecological functions, endophytes are divided into 2 main groups clavicipitaceous and non-clavicipitaceous. Clavicipitaceous are able to infect only some species of grasses and non-clavicipitaceous are found in the asymptomatic tissues of other higher plants[13]. Plants comprise huge and diverse niches for endophytic organisms. Of the nearly 300 000 plant species that exist on the earth, each individual plant is host to one or more endophytes[11]. Fungi and bacteria have been studied for biological control they are different from plant pathogenic microorganisms because they, do not cause diseases to plants and are distinct from epiphytic microorganisms which live on the surface of plant organs and tissues[14].

Isolation of endophytic fungi: The most important phase for the isolation of endophytic fungi that are living in plant tissues is surface sterilization and the plant parts under examination should be slice into tiny pieces to assist sterilization and isolation procedures. To accomplish complete surface sterilization, there are numerous techniques to eradicate the majority of the epiphytic fungi from the external tissues and support the growth of the internal mycota, according to the type of tissue as well as its specific location[15].

Identification of endophytes: Endophytic fungi can be readily identified on the basis of morphological methods, using characters of the phenotype of the fungal culture, i.e., colony or hyphae, the characters of the spore, or reproductive structure if these features were discernible[16-18]. The majority of endophytic fungi are supposed to be the ascomycetes and asexual fungi[19]. These isolates cab be stimulated to sporulate on medium contains stripes or extract of host plant[20]. Sterile isolates should be examined on a regular basis for fruiting bodies over a period of 3-4 months and the isolates that failed to sporulate are called to as mycelia sterilia, are divided into different morphotypes according to their culture properties. These groups of fungi are significantly common in endophytes studies[21,22].

Fungi as producers of biologically active metabolites: Fungi have been used as a tool for producing novel metabolites and more than 20,000 bioactive metabolites are of microbial origin[23]. Fungi is a good source of producing biologically active secondary metabolites, which are directly used as drugs or function as lead structures for synthetic modifications[24-30]. A number of antibiotics as shown in Table 1 and many medicinal drugs from microbial origin are recognized such as the antibiotic penicillin from *Penicillium* sp., the immunosuppressant cyclosporine from *Tolypocladium inflatum* and *Cylindrocarpon lucidum*, the antifungal agent griseofulvin from *Penicillium griseofulvum* fungus, the cholesterol biosynthesis inhibitor lovastatin from *Aspergillus terreus* fungus and β-lactam antibiotics from various fungal taxa, has shifted the focus of drug discovery from plants to microorganisms.

Table 1: Antibiotic produced by fungal endophytes

Antibiotics	Occurrence of host	Fungal endophyte	Target pathogens	References
Pyrrocidines A, B	Maize	*Acremonium zeae*	*Aspergillus flavus, Fusarium verticillioides*	Wicklow *et al.*[56]
Massariphenone, ergosterol peroxide	*Rehmannia glutinosa*	*Verticillium* sp.	*Pyricularia oryzae* P-2b	You *et al.*[57]
Cadinane sesquiterpenes	*Cassia spectabilis*	*Phomopis cassiae*	*Cladosporium sphaerospermum, Cladosporium cladosporioides*	Silva *et al.*[58]
Tetrahydrofuran, 2-methyl furan, 2-butanone, aciphyllene	Tropical tree	*Muscodor albus*	*Stachybotrys chartarum*	Atmosukarto *et al.*[59]
Fusicoccane diterpenes	*Taxus cuspidata*	*Periconia* sp.	*Bacillus subtilis, Staphylococcus aureus, Klebsiella pneumoniae, Salmonella typhimurium*	Kim *et al.*[60]
3-O-Methylalaternin, altersolanol A	*Urospermum picroides*	*Ampelomyces* sp.	*Staphylococcus aureus, S. epidermidis, Enterococcus faecalis*	Aly *et al.*[61]
Aliphatic compounds	*Excoecaria agallocha*	*Phomopsis* sp.	*Candida albicans, Fusarium oxysporum*	Huang *et al.*[62]
	Ginkgo biloba	*Chaetomium globosum*	*Mucor miehei*	Qin *et al.*[63]
	Quercus variabilis	*Cladosporium* sp.	*Trichophyton rubrum, Candida albicans, Aspergillus niger, Epidermophyton floccosum, Microsporum canis*	Wang *et al.*[64]
Flavonoids	*Juniperus cedre*	*Nodulisporium* sp.	*Bacillus megaterium, Microbotryum violaceum, Septoria tritici, Chlorella fusca*	Dai *et al.*[65]
Alkaloids	*Garcinia dulcis*	*Phomopsis* sp.	*Mycobacterium tuberculosis*	Rukachaisirikul *et al.*[66]
	Ginkgo biloba	*Chaetomium globosum*	*Mucor miehei*	Qin *et al.*[63]
	Maize	*Acremonium zeae*	*Aspergillus avus, Fusarium verticillioides*	Wicklow *et al.*[56]
Peptides	*Acrostichum aureurm*	*Penicillium* sp.	*Staphylococcus aureus, Candida albicans*	Cui *et al.*[67]
	Pinus sylvestris and *Fagus sylvatica*	*Cryptosporiopsis* sp., *Pezicula* sp.	Yeasts	Noble *et al.*[68]
	Tripterigium wiflordii	*Cryptosporiopsis quercina*	*Candida albicans*	Strobel *et al.*[69]
	Tropical tree and vine species in several of the world's rainforests	*Muscodor albus*	*Candida albicans*	Strobel *et al.*[69]
Phenols	*Cerbera manghas[*	*Penicillium* sp.	*Staphylococcus aureus*	Han *et al.*[70]
	Saurauia scaberrinae	*Phoma species*	*Staphylococcus aureus*	Hoffman *et al.*[71]
	Unidentified	*Pestalotiopsis adusta*	*Fusarium culmorum, Gibberella zeae* and *Verticillium aiboatrum*	Li *et al.*[72]
Quinones	*Callicarpa acuminate*	*Edenia gomezpompae*	*Phythophtora capsici, Phythophtora parasitica, Fusarium oxysporum, Alternaria solani*	Macias-Rubalcava *et al.*[73]
	Unidentified	*Pestalotiopsis adusta*	*Fusarium culmorum, Gibberella zeae, Verticillium aiboatrum*	Li *et al.*[72]
	Urospermum picroides	*Ampelomyces* sp.	*Staphylococcus aureus, Staphylococcus* epidermidis and *Enterococcus faecalis*	Aly *et al.*[61]
Steroids	*Artemisia annua*	*Colletotrichum* sp.	*Phytophthora capisici, Rhizoctonia cerealis, Gaeumannomyces graminis* var. *tritici, Helminthosporium sati6um*	Lu *et al.*[74]
	Juniperus cedre	*Nodulisporium* sp.	*Bacillus megaterium, Microbotryum violaceum, Septoria tritici, Chlorella fusca*	Dai *et al.*[65]
Terpenoids	*Cassia spectabilis*	*Phomopis cassiae*	*Cladosporium sphaerospermum, Cladosporium cladosporioides*	Silva *et al.*[58]
	Daphnopsis americana	Not identified	*Staphylococcus aureus, Enterococcus faecalis*	Brady *et al.*[75]
	Daphnopsis americana	Not mentioned	*Staphylococcus aureus, Enterococcus faecalis*	Brady *et al.*[76]
	Taxus cuspidate	*Periconia* sp.	*Bacillus subtilis, Staphylococcus aureus, Klebsiella pneumoniae, Salmonella typhimurium*	Kim *et al.*[60]

Mechanisms of diseases control displayed by endophytes: Many studies recently found that endophyte fungal have the ability to protect host from diseases and limit the damage caused by pathogen microorganism[31-33]. The common methods of these researches were *in vitro* coculture with pathogens and endophytes or comparison of the survival rate of plant inoculated with fungal endophytes with endophyte-free plant.

Antimicrobials and their activities produced from endophytes

Antifungal activity of endophytes: Endophytic fungi are those that found inside the living plant tissues or organs, without causing them any damaging symptoms[8] and provide the greater host plant resistance to biotic or abiotic stresses. The Phylum mainly Ascomycota, Basidiomycota and Zygomycota include fungal species which have been reported to be endophytic in nature for example several studies displayed that endophytes are an alternative to switch synthetic pesticides, considering the increasing incidence of chemical resistance in fungal pathogens and promising environmental and mammalian toxicities[4,5]. The endophytic fungi seem to produce bioactive compounds, originally isolated from the host plants, as well as bioactive metabolites that are clearly different from other plants and feature that are unique structural characteristics, which may have potential to use in agriculture and medicine[5,34,35]. Several metabolites, such as alkaloids, terpenoids, steroids, isocoumarins and chromones, phenolics and volatiles isolated and characterized from endophytic fungi display antifungal activity against plant pathogenic fungi[4]. The culture filtrates of antagonists/endophytes, which were obtained from 2-3 weeks old cultures, produced antibiotics that strongly suppressed conidial germination of the pathogen. This suggests that the antibiotics possibly played an important role in suppressing conidial germination and infection by the pathogen[36].

Antibacterial activity of endophytes (against phytobacteria): Bacterial endophytes are well-known as one of bioactive compounds providers, such as the secondary metabolite compounds with various biological activities[37]. Endophytes live in the intercellular space[38]. The unique features of bacterial endophytes such as their shorter life cycle than their host plants, which can save production time, using bacterial endophytes. *Pseudomonas aeruginosa* is bacteria that cause urinary tract infections, meningitis, diarrhea, entrokolitis necrosis and pneumonia[39] whereas, *Klebsiella pneumonia* causes pneumonia, urinary tract infections and sepsis in patients with vulnerable immune system[40]. *Bacillus cereus* produces diarrhea-causing enterotoxins. On the other hand, Methicillin-resistant *Staphylococcus aureus* (MRSA) has a mutated gene that is resistant to almost all beta-lactam antibiotics. Meanwhile, *S. aureus* can cause septicaemia, pneumonia, endocarditis, osteomyelitis, gastroenteritis and abscesses[41]. The present study aims to obtain the bacterial endophytes isolates from *S. polycephalum*, where the most potent isolate could be used as antibacterial agent against bacterial pathogens such as *P. aeruginosa*, *K. pneumoniae*, MRSA and *B. cereus*. This study could be as an alternative to over-used of synthetic antibiotics thus it can be medically accountable (Table 1).

Antiviral activity of endophytes: Endophytic and marine fungi growing in unique environments are being constantly explored for their bioactive natural products possessing cytotoxic, anticancer, antibacterial or antifungal potential since past decade[42-44]. Fungi also potentially contain and/or produce several effective molecules that could also be used as antivirals for other hosts[45]. Presently, there is a rather limited understanding of the antiviral mechanisms of fungal products on virus infection. Thus, more detailed knowledge on the actual molecular targets is crucial in order to develop these molecules further to efficiently combat virus infections in the future.

Nematicidal activity of endophytes: Endophytic fungi can protect their host plants by producing natural compounds which are dangerous to nematodes. The first antagonistic activity of endophytic fungi against plant parasitic nematodes was observed in tall fescue (*F. arundinacea*) infected by *Pratylenchus scribneri*. The antagonistic activity of fungal endophyte, *F. oxysporum* was observed; in the roots of tomato plant reduced 60% infection of *Meloidogyne incognita* successfully. The bacterial endophyte *Burkholderia ambifaria*, isolated from corn root, produced some toxic metabolites which inhibited egg hatching and mobility of second-stage juveniles of *M. incognita*[46]. The successful results of nematicidal activity of an arbuscular mycorrhiza, *Glomus coronatum* and an endophytic fungus, *F. oxysporum*, against the *M. incognita* in tomato plant were also shown[47]. Similarly another important parasitic nematode *Radopholus similis* cause on banana and other plants by dual culture techniques the antagonistic effect of endophytic fungi was shown against *R. similis* population[48].

Insecticidal activity of endophytes: Some endophytic fungi can protect their host plants from pathogens and pests[31]. The foliar endophytes are toxic to insects and vertebrates by producing alkaloids[49]. Webber firstly reported the endophytic fungi, Phomopsis oblonga to protect elm trees against the beetle *Arthrocnemum brevilineum*[50]. The insecticidal activity of endophytic fungi (*Acremonium coenophialum*) was showed against aphids (*Rhopalosiphum padi*, *Schizaphis graminum*) and milkweed bug (*Oncopeltus fasciatus*)[51].

There are different genera of entomopathogenic fungus such As acremonium, beauveria, cladosporium, clonostachys and paecilomyces, were isolated from the coffee plants, among them *B. bassiana* and *Clonostachys rosea* were pathogenic to coffee berry borer[52]. Larvicidal and growth inhibitory activities of *B. bassiana* against *Spodoptera litura* was also exhibited by many scientists[53]. The endophytic fungi *Claviceps purpurea* possess a significant insecticidal activity against A. gossypii[54]. The *Cladosporium oxysporum* showed insecticidal activity against *A. fabae*[55].

Advantages of the endophytes in agriculture: There are several advantage of endophytes such as: Endophytes encourage the plants growth, increase plant disease resistance, improve the plants ability to withstand environmental stresses and recycle nutrients[77]. Endophytes are rich source of secondary metabolites with multi-fold importance[15]. Among the other endophytes microorganism, fungal endophytes produce large number of secondary activities[78]. Endophytes have strong fungicidal, bactericidal and cytotoxic metabolites[64].

Endophytes produce some enzymes which are used for various practical application like degradation and bio-transformation of organic compound[79-80]. The derivatives of endophytes are used in biotechnological application[81]. Due to its antimicrobial, anticancer and antiviral activities it has been significance in the field of pharmaceutical science[82].

Plant growth stimulants: Endophytes promote the plant growth through a variety of mechanisms, as endophytic metabolites provide a variety of fitness to host plants enhanced by increasing plant resistance to biotic and abiotic stresses, as well as enhance plant growth. Many endophytes are capable of solubilization of phosphate, enhance uptake of phosphorus (P), nitrogen fixation, production of siderophores and plant hormones such as auxin, abscisins, ethylene, gibberellins and indole acetic acid (IAA), which are important for plant growth regulations[79,83-88]. Gibberellic acid (GA) is a potent phytohormone, that regulates plant growth. Fungal endophyte, *Cladosporium sphaerospermum* from the plant, *Glycine max* (L) Merr. produce GA3, GA4 and GA7. It induced plant growth in rice and soybean[89]. A pestalotin analogue isolated from the *Pestalotiopsis microspora* exhibited significant gibberellin activity against Distylium chinense seeds and increase germination rate (85.56%)[90]. The Fusarium tricinctum and *A. alternata* derivatives of indole acetic acid (IAA) enhanced the plant growth[91].

Crop protection: Endophytic fungi are also capable of inducing resistance to diseases and many mechanisms have been proposed for this resistance. The mechanisms of endophyte induced resistance are related to the nutritional status of the host and to increase the fitness of plants by enhancing their tolerance to abiotic stress[92]. Endophytic fungi *Cryptosporiopsis* cf. *quercina* and *Colletotrichum* sp., are found effective against phytopathogens such as *Rhizoctonia cerealis*, *Phytophthora capsici*, *Pyricularia oryzae* and *Gaeumannomyces graminis*[93]. *Trichoderma* and *Aspergillus* are used to manage many soil-borne plant pathogens[94]. *Trichoderma* has long been considered as one of the most promising endophyte/bio-control agent for several plant pathogens[95,96]. Sixteen fungal endophytic species with 2 strains of *Aspergillus flavus* i.e., brown and green were isolated from physic nut seeds during one year of storage[97].

CONCLUSION

Endophytic fungi have wide application in different fields. It has the potential to produce many bioactive compounds. The secondary metabolites produced by the endophytic fungi have the ability to act as bio-control agent. Endophytic fungi isolated from the medicinal plants would be a promising source for many pharmaceutical ingredients. Plants are the major preliminary source for pharmaceutical drug products. Isolating a compound from the plants and large scale production of a product is expensive and time consuming. But endophytic fungi originated from medicinal plants have the capability to produce valuable compounds and can be easily cultured and large scale production is possible through fermentation process. In future the products from the endophytic fungi will be a cheap source for medical, agriculture and other industries. It is sure that the research on endophytic fungi will lead to isolate more novel compounds.

SIGNIFICANCE STATEMENT

The study on different endophytic fungi and bacteria show brilliant prospect for successive studies for sustainability of soils and agriculture ultimately.

REFERENCES

1. Vinale, F., K. Sivasithamparam, E.L. Ghisalberti, R. Marra, S.L. Woo and M. Lorito, 2008. *Trichoderma*-plant-pathogen interactions. Soil Biol. Biochem., 40: 1-10.
2. Cook, R.J. and R.R. Granados, 1991. Biological Control: Making it Work. In: Agricultural Biotechnology at the Crossroads, MacDonald, M.J.F. (Ed.)., National Agricultural Biotechnology Council, Ithaca, New York, USA., pp: 213-227.
3. Barakat, R.M. and M.I. Al-Masri, 2005. Biological control of gray mold disease (*Botrytis cinerea*) on tomato and bean plants by using local isolates of *Trichoderma harzianum*. Dirasat Agric. Sci., 32: 145-156.
4. Kumar, S. and N. Kaushik, 2012. Metabolites of endophytic fungi as novel source of biofungicide: A review. Phytochem. Rev., 11: 507-522.
5. Wang, X., M.M. Radwan, A.H. Tara´wneh, J. Gao and D.E. Wedge *et al*., 2013. Antifungal activity against plant pathogens of metabolites from the endophytic fungus *Cladosporium cladosporioides*. J. Agric. Food Chem., 61: 4551-4555.
6. Wagenaar, M.M. and J. Clardy, 2001. Dicerandrols, new antibiotic and cytotoxic dimers produced by the fungus *Phomopsis longicolla* isolated from an endangered mint. J. Nat. Prod., 64: 1006-1009.
7. Schulz, B. and C. Boyle, 2005. The endophytic continuum. Mycol. Res., 109: 661-686.
8. Petrini, O., 1991. Fungal Endophytes of Tree Leaves. In: Microbial Ecology of Leaves andrews, J.H. and S.S. Hirano (Eds.). Springer Verlag, New York, USA., pp: 179-197.
9. Saikkonen, K., S.H. Faeth, M. Helander and T.J. Sullivan, 1998. Fungal endophytes: A continuum of interactions with host plants. Ann. Rev. Ecol. System, 29: 319-343.
10. Clay, K. and C. Schardl, 2002. Evolutionary origins and ecological consequences of endophyte symbiosis with grasses. Am. Nat., 160: 99-127.
11. Strobel, G.A., A. Stierle, D. Stierle and W.M Hess, 1993. *Taxomyces andreanae* a proposed new taxon for a bulbilliferous hyphomycete associated with pacific yew. Mycotaxon, 47: 71-78.
12. Ulrich, K., A. Ulrich and D. Ewald, 2008. Diversity of endophytic bacterial communities in poplar grown under field conditions. FEMS Microbiol. Ecol., 63: 169-180.
13. Rodriguez, R.J., J.F. White Jr., A.E. Arnold and R.S. Redman, 2009. Fungal endophytes: Diversity and functional roles. New Phytol., 182: 314-330.
14. Hallmann, J., A. Quadt-Hallmann, W.F. Mahaffee and J.W. Kloepper, 1997. Bacterial endophytes in agricultural crops. Can. J. Microbiol., 43: 895-914.
15. Strobel, G. and B. Daisy, 2003. Bioprospecting for microbial endophytes and their natural products. Microbiol. Mol. Biol. Rev., 67: 491-502.
16. Wei, J.C., 1979. Hand Book of Fungi Identification. Technology Press, Shanghai.
17. Carmichael, J.W., W.B. Kendrick, I.L. Conners and L. Sigler, 1980. Genera of Hyphomycetes. University of Alberta Press, Alberta, ISBN-13: 9780888640635, Pages: 386.
18. Barnett, H.L. and B.B. Hunter, 1998. Illustrated Genera of Imperfect Fungi. 3rd Edn., The Ameriacn Phytopthological Society, St. Paul Minnesota, USA.
19. Huang, Y., J. Wang, G. Li, Z. Zheng and W. Su, 2001. Antitumor and antifungal activities in endophytic fungi isolated from pharmaceutical plants *Taxus mairei*, *Cephalataxus fortunei* and *Torreya grandis*. FEMS Immunol. Med. Microbiol., 31: 163-167.
20. Matsushima, T., 1971. Microfungi of the Solomon Islands and Papua-New Guinea. Matsushima, Kobe, Japan, Pages: 78.
21. Lacap, D.C., K.D. Hyde and E.C.Y. Liew, 2003. An evaluation of the fungal morphotype concept based on ribosomal DNA sequences. Fungal Diversity, 12: 53-66.
22. Guo, L.D, K.D. Hyde and E.C.Y. Liew, 1998. A method to promote sporulation in palm endophytic fungi. Fungal Divers., 1: 109-113.
23. Berdy, J., 2005. Bioactive microbial metabolites: A personal view. J. Antibiot., 58: 1-26.
24. Kock, J.L.F., T. Strauss, C.H. Pohl, D.P. Smith and P.J. Botes *et al*., 2001. Bioprospecting for novel oxylipins in fungi: The presence of 3-hydroxy oxylipins in Pilobolus. Antonie Leeuwenhoek, 80: 93-99.
25. Bode, H.B., B. Bethe, R. Höfs and A. Zeeck, 2002. Big effects from small changes: Possible ways to explore nature's chemical diversity. ChemBioChem, 3: 619-627.
26. Donadio, S., P. Monciardini, R. Alduina, P. Mazza and C. Chiocchini *et al*., 2002. Microbial technologies for the discovery of novel bioactive metabolites. J. Biotechnol., 99: 187-198.
27. Chin, Y.W., M.J. Balunas, H.B. Chai and A.D. Kinghorn, 2006. Drug discovery from natural sources. AAPS J., 8: E239-E253.
28. Gunatilaka, A.A.L., 2006. Natural products from plant-associated microorganisms: Distribution, structural diversity, bioactivity and implications of their occurrence. J. Nat. Prod., 69: 509-526.
29. Mitchell, A.M., G.A. Strobel, W.M. Hess, P.N. Vargas and D. Ezra, 2008. *Muscodor crispans*, a novel endophyte from *Ananas ananassoides* in the Bolivian Amazon. Fungal Divers., 31: 37-43.
30. Stadler, M. and N.P. Keller, 2008. Paradigm shifts in fungal secondary metabolite research. Mycol. Res., 112: 127-130.
31. Arnold, A.E., L.C. Mejia, D. Kyllo, E.I. Rojas, Z. Maynard, N. Robbins and E.A. Herre, 2003. Fungal endophytes limit pathogen damage in a tropical tree. Proc. Natl. Acad. Sci. USA., 100: 15649-15654.
32. Ganley, R.J., R.A. Sniezko and G. Newcombe, 2008. Endophyte-mediated resistance against white pine blister rust in *Pinus monticola*. For. Ecol. Manage., 255: 2751-2760.

33. Mejia, L.C., E.I. Rojas, Z. Maynard, S.V. Bael and A.E. Arnold *et al*., 2008. Endophytic fungi as biocontrol agents of *Theobroma cacao* pathogens. Biol. Control, 46: 4-14.
34. Stierle, A., G. Strobel, D. Stierle, P. Grothaus and G. Bignami, 1995. The search for a taxol-producing microorganism among the endophytic fungi of the pacific yew, *Taxus brevifolia*. J. Nat. Prod., 58: 1315-1324.
35. Puri, S.C., V. Verma, T. Amna, G.N. Qazi and M. Spiteller, 2005. An endophytic fungus from *Nothapodytes foetida* that produces camptothecin. J. Nat. Prod., 68: 1717-1719.
36. Kumar, R., A. Sinha, S. Srivastava and S. Singh, 2014. Evaluation of substrates for mass multiplication of green manure associated fungi for biological control of soil borne phytopathogens. Indian Phytopathol., 67: 396-401.
37. Brooks, G.F., J.S. Butel, S.A. Morse, 2007. Mikrobiologi Kedokteran Jawetz. 23rd Edn., Melnick & Adelberg, Jakarta, Indonesia, (In Indonesian), pp: 251-254.
38. Agustina, S., 2015. Peningkatan resistensi kultur bakteri *Staphylococcus aureus* terhadap amoxicillin menggunakan metode adaptif gradual. J. Farm. Indonesia, Vol. 7. 10.35617/jfi.v7i3.167.
39. Sunarti, S., 2015. Persebaran Syzygium endemik Jawa. Pros. Semin. Nasional Biodivers. Indonesia, 1: 1093-1098.
40. Desriani, D., U.M. Safira, M. Bintang, A. Rivai and P. Lisdiyanti, 2014. Isolasi dan karakterisasi bakteri endofit dari tanaman binahong dan katepeng China. J. Kesehatan Andalas, 3: 89-93.
41. Krishnan, P., R. Bhat, A. Kush and P. Ravikumar, 2012. Isolation and functional characterization of bacterial endophytes from *Carica papaya* fruits. J. Applied Microbiol., 113: 308-317.
42. Mayer, A.M.S., A.D. Rodriguez, O. Taglialatela-Scafati and N. Fusetani, 2013. Marine pharmacology in 2009-2011: Marine compounds with antibacterial, antidiabetic, antifungal, anti-inflammatory, antiprotozoal, antituberculosis and antiviral activities; affecting the immune and nervous systems and other miscellaneous mechanisms of action. Mar. Drugs, 11: 2510-2573.
43. Cheung, R.C.F., J.H. Wong, W.L. Pan, Y.S. Chan and C.M. Yin *et al*., 2014. Antifungal and antiviral products of marine organisms. Applied Microbiol. Biotechnol., 98: 3475-3494.
44. Singh, R.P., P. Kumari and C.R.K. Reddy, 2015. Antimicrobial compounds from seaweeds associated bacteria and fungi. Applied. Microbiol. Biotechnol., 99: 1571-1586.
45. Linnakoski, R., D. Reshamwala, P. Veteli, M. Cortina-Escribano, H. Vanhanen and V. Marjomäki, 2018. Antiviral agents from fungi: Diversity, mechanisms and potential applications. Front. Microbiol., Vol. 9. 10.3389/fmicb.2018.02325.
46. Li, W., D.P. Roberts, P.D. Dery, S.L.F. Meyer, S. Lohrke, R.D. Lumsden and K.P. Hebbar, 2005. Broad spectrum anti-biotic activity and disease suppression by the potential biocontrol agent *Burkholderia ambifaria* BC-F. Crop Prot., 21: 129-135.
47. Diedhiou, P.M., J. Hallmann, E.C. Oerke and H.W. Dehne, 2003. Effects of arbuscular mycorrhizal fungi and a non-pathogenic *Fusarium oxysporum* on *Meloidogyne incognita* infestation of tomato. Mycorrhiza, 13: 199-204.
48. Zum Felde, A., L.E. Pocasangre, C.A. Carnizares Monteros, R.A. Sikora, F.E. Rosales and A.S. Riveros, 2006. Effect of combined inoculations of endophytic fungi on the biocontrol of *Radopholus similis*. InfoMusa, 15: 12-18.
49. Schardl, C. L., 2001. *Epichloë festucae* and related mutualistic symbionts of grasses. Fungal Genet. Biol., 33: 69-82.
50. Webber, J., 1981. A natural biological control of Dutch elm disease. Nature, 292: 449-451.
51. Johnson, M.C., D.L. Dahlman, M.R. Siegel, L.P. Bush, G.C.M. Latch, D.A. Potter and D.R. Varney, 1985. Insect feeding deterrents in endophyte-infected tall fescue. Applied Environ. Microbiol., 49: 568-571.
52. Posada, F. and F.E. Vega, 2006. Inoculation and colonization of coffee seedlings (*Coffea Arabica* L.) with the fungal entomopathogen *Beauveria bassiana* (Ascomycota: Hypocreales). Mycoscience, 47: 284-289.
53. Baskar, K., G.A. Raj, P.M. Mohan, S. Lingathurai, T. Ambrose and C. Muthu, 2012. Larvicidal and growth inhibitory activities of entomopathogenic fungus, *Beauveria bassiana* against Asian Army Worm, *Spodoptera litura* Fab. (Lepidoptera: Noctuidae). J. Entomol., 9: 155-162.
54. Shi, Y.W., X. Zhang and K. Lou, 2013. Isolation, characterization and insecticidal activity of an endophyte of drunken horse grass, *Achnatherum inebrians*. J. Insect Sci., Vol. 13. 10.1673/031.013.15101.
55. Bensaci, O.A., H. Daoud, N. Lombarkia and K. Rouabah, 2015. Formulation of the endophytic fungus *Cladosporium oxysporum* Berk. & MA Curtis, isolated from *Euphorbia bupleuroides* subsp. luteola, as a new biocontrol tool against the black bean aphid (*Aphis fabae* Scop.). J. Plant Prot. Res., 55: 80-87.
56. Wicklow, D.T., S. Roth, S.T. Deyrup and J.B. Gloer, 2005. A protective endophyte of maize: *Acremonium zeae* antibiotics inhibitory to *Aspergillus flavus* and *Fusarium verticillioides*. Mycol. Res., 109: 610-618.
57. You, F., T. Han, J.Z. Wu, B.K. Huang and L.P. Qin, 2009. Antifungal secondary metabolites from endophytic *Verticillium* sp. Biochem. Syst. Ecol., 37: 162-165.
58. Silva, G.H., C.M. de Oliveira, H.L. Teles, P.M. Pauletti and I. Castro-Gamboa *et al*., 2010. Sesquiterpenes from *Xylaria* sp., an endophytic fungus associated with *Piper aduncum* (Piperaceae). Phytochem. Lett., 3: 164-167.
59. Atmosukarto, I., U. Castillo, W.M. Hess, J. Sears and G. Strobel, 2005. Isolation and characterization of *Muscodor albus* I-41.3 s, a volatile antibiotic producing fungus. Plant Sci., 169: 854-861.
60. Kim, S., D.S. Shin, T. Lee and K.B. Oh, 2004. Periconicins, two new fusicoccane diterpenes produced by an endophytic fungus *Periconia* sp. with antibacterial activity. J. Natural Prod., 67: 448-450.

61. Aly, A.H., R. Edrada-Ebel, V. Wray, W.E. Muller and S. Kozytska *et al*., 2008. Bioactive metabolites from the endophytic fungus *Ampelomyces* sp. isolated from the medicinal plant *Urospermum picroides*. Phytochemistry, 69: 1716-1725.
62. Huang, Z., X. Cai, C. Shao, Z. She and X. Xia *et al*., 2008. Chemistry and weak antimicrobial activities of phomopsins produced by mangrove endophytic fungus *Phomopsis* sp. ZSU-H76. Phytochemistry, 69: 1604-1608.
63. Qin, J.C., Y.M. Zhang, J.M. Gao, M.S. Bai, S.X. Yang, H. Laatsch and A.L. Zhang, 2009. Bioactive metabolites produced by *Chaetomium globosum*, an endophytic fungus isolated from *Ginkgo biloba*. Bioorg. Med. Chem. Lett., 19: 1572-1574.
64. Wang, F.W., R.H. Jiao, A.B. Cheng, S.H. Tan and Y.C. Song, 2007. Antimicrobial potentials of endophytic fungi residing in *Quercus variabilis* and brefeldin A obtained from *Cladosporium* sp. World J. Microbiol. Biotechnol., 23: 79-83.
65. Dai, J., K. Krohn, U. Flörke, S. Draeger and B. Schulz *et al*., 2006. Metabolites from the endophytic fungus *Nodulisporium* sp. from *Juniperus cedre*. Eur. J. Org. Chem., 15: 3498-3506.
66. Rukachaisirikul, V., U. Sommart, S. Phongpaichit, J. Sakayaroj and K. Kirtikara, 2008. Metabolites from the endophytic fungus *Phomopsis* sp. PSU-D15. Phytochemistry, 69: 783-787.
67. Cui, H.B., W.L. Mei, C.D. Miao, H.P. Lin, K. Hong and H.F. Dai, 2008. Antibacterial constituents from the endophytic fungus *Penicillium* sp. 0935030 of mangrove plants *Acrostichum aureum*. Chem. J. Chinese Univ., 33: 407-410.
68. Noble, H.M., D. Langley, P.J. Sidebottom, S.J. Lane and P.J. Fisher, 1991. An echinocandin from an endophytic *Cryptosporiopsis* sp. and *Pezicula* sp. in *Pinus sylvestris* and *Fagus sylvatica*. Mycol. Res., 95: 1439-1440.
69. Strobel, G.A., R.V. Miller, C. Martinez-Miller, M.M. Condron, D.B. Teplow and W.M. Hess, 1999. Cryptocandin, a potent antimycotic from the endophytic fungus *Cryptosporiopsis* cf. quercina. Microbiology, Vol. 145. 10.1099/13500872-145-8-1919.
70. Han, Z., W.L. Mei, H.B. Cui, Y.B. Zeng, H.P. Lin and K. Hong, 2008. Antibacterial constituents from the endophytic fungus *Penicillium* sp. of mangrove plant *Cerbera manghas*. Chem. J. Chinese Univ., 29: 749-752.
71. Hoffman, A.M., S.G. Mayer, G.A. Strobel, W.M. Hess and G.W. Sovocool *et al*., 2008. Purification, identification and activity of phomodione, a furandione from an endophytic *Phoma* species. Phytochemistry, 69: 1049-1056.
72. Li, E., L. Jiang, L. Guo, H. Zhang and Y. Che, 2008. Pestalachlorides A-C, antifungal metabolites from the plant endophytic fungus *Pestalotiopsis adusta*. Bioorg. Med. Chem., 16: 7894-7899.
73. Macias-Rubalcava, M.L., B.E. Hernandez-Bautista, M. Jimenez-Estrada, M.C. Gonzalez and A.E. Glenn *et al*., 2008. Naphthoquinone spiroketal with allelochemical activity from the newly discovered endophytic fungus *Edenia gomezpompae*. Phytochemistry, 69: 1185-1196.
74. Lu, H., W.X. Zou, J.C. Meng, J. Hu and R.X. Tan, 2000. New bioactive metabolites produced by *Colletotrichum* sp., an endophytic fungus in *Artemisia annua*. Plant Sci., 151: 67-73.
75. Brady, S.F., S.M. Bondi and J. Clardy, 2001. The guanacastepenes: A highly diverse family of secondary metabolites produced by an endophytic fungus. J. Am. Chem. Soc., 123: 9900-9901.
76. Brady, S.F., M.P. Singh, J.E. Janso and J.J. Clardy, 2000. *Guanacastepene*, a fungal-derived diterpene antibiotic with a new carbon skeleton. J. Am. Chem. Soc., 122: 2116-2117.
77. Sturz, A.V. and J. Nowak, 2000. Endophytic communities of rhizobacteria and the strategies required to create yield enhancing associations with crops. Applied Soil Ecol., 15: 183-190.
78. Zhang, H.W., Y.C. Song and R.X. Tan, 2006. Biology and chemistry of endophytes. Nat. Prod. Rep., 23: 753-771.
79. Firakova, S., M. Sturdikova and M. Muckova, 2007. Bioactive secondary metabolites produced by microorganisms associated with plants. Biologia, 62: 251-257.
80. Pimentel, M.R., G. Molina, A.P. Dionisio, M.R. Marostica Junior and G.M. Pastore, 2011. The use of endophytes to obtain bioactive compounds and their application in biotransformation process. Biotechnol. Res. Int., Vol. 2011. 10.4061/2011/576286.
81. Tomita, F., 2003. Endophytes in Southeast Asia and Japan: their taxonomic diversity and potential applications. Fungal Diversity, 14: 187-204.
82. Selim, K.A., A.A. El-Beih, T. AbdEl-Rahman and A.I. El-Diwany, 2012. Biology of endophytic fungi. Curr. Res. Environ. Applied Mycol., 2: 31-82.
83. Goodman, R.N., Z. Kiraly and K.R. Wood, 1986. The Biochemistry and Physiology of Plant Disease. University of Missouri Press, Columbia, Missouri, ISBN-13: 978-0826203496, Pages: 435.
84. Barraquio, W.L., L. Revilla and J.K. Ladha, 1997. Isolation of endophytic diazotrophic bacteria from Wetland rice. Plant Soil, 194: 15-24.
85. Malinowski, D.P., D.K. Brauer and D.P. Belesky, 1999. The endophyte *Neotyphodium coenophialum* affects root morphology of tall fescue grown under phosphorus deficiency. J. Agron. Crop Sci., 183: 53-60.
86. Malinowski, D.P. and D.P. Belesky, 2000. Adaptation of endophyte-infected cool-season grasses to environmental stresses: Mechanisms of drought and mineral stress tolerance. Crop Sci., 40: 923-940.
87. Loiret, F.G., E. Ortega, D. Kleiner, P. Ortega-Rodes, R. Rodes and Z. Dong, 2004. A putative new endophytic nitrogen-fixing bacterium *Pantoea* sp. from sugarcane. J. Applied Microbiol., 97: 504-511.

88. Sandhiya, G.S., T.C. Sugitha, D. Balachandar and K. Kumar, 2005. Endophytic colonization and in planta nitrogen fixation by a diazotrophic *Serratia* sp. in rice. Indian J. Exp. Biol., 43: 802-807.
89. Hamayun, M., S.A. Khan, N. Ahmad, D.S. Tang and S.M. Kang *et al*., 2009. *Cladosporium sphaerospermum* as a new plant growth-promoting endophyte from the roots of *Glycine max* (L.) Merr. World J. Microbiol. Biotechnol., 25: 627-632.
90. Li, X., Z. Guo, Z. Deng, J. Yang and K. Zou, 2015. A new α-pyrone derivative from endophytic fungus *Pestalotiopsis microspora*. Records Natural Prod., 9: 503-508.
91. Khan, A.R., I. Ullah, M. Waqas, R. Shahzad and S.J. Hong *et al*., 2015. Plant growth-promoting potential of endophytic fungi isolated from *Solanum nigrum* leaves. World J. Microbiol. Biotechnol., 31: 1461-1466.
92. Azcon-Aguilar, C. and J.M. Barea, 1997. Arbuscular mycorrhizas and biological control of soil-borne plant pathogens-an overview of the mechanisms involved. Mycorrhiza, 6: 457-464.
93. Li, J.Y., G.A. Strobel, J.K. Harper, E. Lobkovsky and J. Clardy, 2000. Cryptocin, a potent tetramic acid antimycotic from the endophytic fungus *Cryptosporiopsis* cf. *Quercina*. Org. Lett., 2: 767-770.
94. Srivastava, S., V.P. Singh, R. Kumar, M. Srivastava, A. Sinha and S. Simon, 2011. *In vitro* evaluation of carbendazim 50% WP, antagonists and botanicals against *Fusarium oxysporum* f. sp. *psidii* associated with rhizosphere soil of Guava. Asian J. Plant Pathol., 5: 46-53.
95. Kumar, R., A. Sinha, S. Srivastava and M. Srivastava, 2011. Variation in soil mycobiota associated with decomposition of *Sesbania aculeata* L. Asian J. Plant Pathol., 54: 37-45.
96. Katyayani, K.K.S., S. Bindal, S. Yaddanapudi, V. Kumar, M. Rana and S. Srivastava, 2019. Evaluation of bio-agents, essential oils and chemicals against *Fusarium* wilt of tomato. Int. J. Curr. Micro-Biol. Applied Sci., 8: 1913-1922.
97. Srivastava, S., A. Sinha and C.P. Srivastava, 2011. Screening of seed-borne mycoflora of *Jatropha curcas* L. Res. J. Seed Sci., 4: 94-105.