The Fungal Endobiome of Medicinal Plants: A Prospective Source of Bioactive Metabolites

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Sanjana Kaul, Suruchi Gupta, Supriya Sharma, and Manoj K. Dhar

Abstract

Fungal endobiome has over the period of time evolved from being defined just as the microbes living within plants indicating not only their location but also the type of association that they have with the host. They are the organisms that live asymptomatically within the internal tissues of the plant and exhibit a variety of relationships with their host ranging from symbiotic to pathogenic. They have a very intimate and also a co-evolutionary relationship with their host and therefore have the potential to influence the physiology of the plant. Endophytes from medicinal plants especially represent an important and potential source of bioactive compounds. Endophytic fungi under the influence of multiplexed interactions within its niche, viz., host plant, produce a plethora of secondary metabolites which belong to diverse chemical groups including terpenoids, alkaloids, phenylpropanoids, polyketides, peptides, flavonoids, steroids, lignans, etc. Terpenoids and polyketides are most commonly purified from endophytes, whereas flavonoids and lignans are rare. Due to chemical diversity of their secondary metabolites, endophytic fungi have been explored for medicinal, agricultural, and industrial uses. These are proven useful for novel drug discovery and can be used as potential sources of pharmaceutical leads. These metabolites are known to possess a wide variety of biological activities like antimicrobial, antioxidant, immunomodulatory, anticancerous, antidiabetic, acetylcholinesterase, etc. Endophytes are viewed as an outstanding source for bioprospecting new drugs, and their importance lies in the fact that they represent an ecological group which is less explored and develop in special and sequestered environments. Their diversity and specialized habituation make them an exciting field to search for novel bioactive compounds.

S. Kaul (✉) • S. Gupta • S. Sharma • M.K. Dhar
School of Biotechnology, University of Jammu, Jammu 180006, Jammu & Kashmir, India
e-mail: sanrozie@rediffmail.com

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Keywords
Fungal endophytes • Endobiome • Bioactive compounds • Medicinal plants • Bioactivity

Contents

Abbreviations

AgNPs	Silver nanoparticles
DPPH	1, 1-Diphenyl-2-picrylhydrazyl base pairs
IC_{50}	Half maximal inhibitory concentration
MDR	Multidrug resistance
ml	Milliliter
MLR	Mixed lymphocyte reaction assay
sp.	Species
WHO	World Health Organization
α	Alpha
μg	Microgram

7.1 Introduction

7.1.1 Endobiome

The plant endobiome consists of various microorganisms residing inside the endosphere, i.e., internal compartments of the plant. Various studies have significantly advanced the understanding of the composition and structure of plant microbiomes which indicate that abiotic factors, as well as plant–microbe, microbe–microbe, and plant–plant interactions, contribute to plant endobiome composition and structure. The community structure of the endobiome depends on the combination of ability to colonize and the allocation of plant resources. The drivers for which include soil, host plant, and microbes. Factors such as latitude, elevation, temperature, and precipitation can also interact and influence the endobiome composition. The interactions between the endobiome and plant are highly complex and dynamic and can be beneficial (mutualistic), neutral (commensalism), or detrimental (parasitic). Consequently, the plant endobiome dramatically affects plant health and productivity (Turner et al. 2013; Berg et al. 2014; Schlaeppi and Bulgarelli 2015). The plant microbiome is known to induce or prime plant defenses against a broad range of pathogens and insect herbivores. Studies on the plant–microbe interaction involved in endosphere provide an alternative for the manipulations of different biosynthetic pathways responsible for the production of various bioactive and novel molecules of commercial importance. Additionally, the plant endobiome is a crucial player in global biogeochemical cycles, participating significantly in the biochemical cycling of the products of photosynthesis. Therefore, manipulation of plant endobiome is believed to have the potential to interfere with plant disease development, promote plant secondary metabolite production, and ease chemical inputs, leading to more sustainable agricultural practices and enhanced productivity.

Fungal endobiome can precisely be called as the endophytes and is defined functionally by their occurrence within tissues of plants without causing any immediate overt effects (Bacon and White 2000; Hyde and Soytong 2008). Endophytes are ubiquitous and have been found in all the species of plants studied to date. Host–endophyte interactions fall within a continuum ranging from mutualism to commensalism and ultimately pathogenicity. Mutualistic relationship provides benefit to both the partners. Endophytes get nutrition and shelter from the host, while endophyte contributes to the well-being of the host by providing adequate nutrient supply, improved growth, and resistance from herbivores, pathogens, drought, salinity, etc. Colonization of host plants by endophytic fungi can have a profound effect on the plant ecology, fitness, and plant community health (Gopalakrishnan et al. 2015). Enormous biological diversity coupled with their capability to biosynthesize secondary metabolites has provided the impetus for a number of investigations on endophytes. They are particularly interesting due to their easy biological utilization on the large commercial scale and have proven to be a promising source of novel and biologically active natural products, extracellular enzymes, and plant growth-promoting agents of biotechnological interest.

7.1.2 Fungal Endophytes

Over the period of time, the research on endophytes has taken a long leap, but the basic definition given by various researchers remains more or less the same, i.e., "Microbes that exist within the living tissues of plants intercellularly or intracellularly, at least for a part of their life cycle without causing any harm to their host are known as endophytes" (Nisa et al. 2015). Endophytes in Greek means "within plant" (endo = within, phytes = plants). The term endophyte was first coined by De Bary in 1866 (Jain and Pundir 2015). The endophytic microorganisms which constitute the plant endobiome include bacteria, fungi, and actinomycetes which form a range of relationships with their host plant including symbiotic, mutualistic, commensalism, parasitic, etc. (Stepniewska and Kuzniar 2013; Swarnalatha et al. 2015). The infection caused by endophytes within the invading tissues of the host plant is inconspicuous and symptomless unless endophytes become pathogenic under stressful conditions. Some endophytes assume a quiescent state either for the whole lifetime or for an extended period of time. A harmonious symbiotic association generally exists between plant and endophyte in which both of them are benefitted. Most of the mycologists use the term "endophyte" strictly for those fungi that never cause any visible disease symptoms at any specific moment. Endophytes get nutrition and shelter inside the host and in return provide resistance to the concerned host against biotic and abiotic stresses. They can have a profound effect on the plant ecology, fitness, and plant community health. They reside entirely within host tissues and emerge during host senescence unlike mycorrhizal fungi that colonizes plant roots and grow into the rhizosphere.

The importance of endophytes lies in the fact that they represent the ecological group with less explored fungal species. Each plant, in turn, is host to one or more endophytes. As documented by Hawksworth (2001), only 1 lakh fungal species is presently known out of estimated 1.5 million fungal species. The remaining undiscovered fungi may be in the form of hidden endophytes. Endophytes develop in special and sequestered environments and represent a huge diversity of microbial adaptations. Their diversity and specialized habituation make them an exciting field of study in the search for new medicines or novel drugs. Endophytic fungal diversity is supposed to be high in tropics as compared to temperate regions. It is assumed that fungi within tropical tree leaves may be hyperdiverse. Their diversity even varies from one location to another.

Another interesting point in studying endophytes is because of the hope it brings, by synthesizing diverse and novel secondary metabolites. The new and bioactive compounds can provide assistance and relief in all aspects of human conditions like drug resistance, treatment of new emerging diseases, and safe bioactive compounds (Kaul et al. 2012). A list of all approved agents has been prepared from 1981 to 2006 in which microbes/endophytes were found to be the main source of a significant number of natural products (Pimentel et al. 2011). Synthesis of new active secondary metabolites by the endophytes may be induced by metabolic interaction between the host plant and endophytes.

The discovery of paclitaxel-producing endophytic fungus *Taxomyces andreanae* from *Taxus brevifolia* (yew trees) increased the importance of endophytes and created an impetus among the researchers for a more comprehensive and elaborative examination in this area (Selim et al. 2012). The presence of a microbial source of the drug could eliminate the need to harvest and extract the slow growing and relatively rare yew trees, and the price for the drug would also be reduced. The drug would be available to cancer patients, since paclitaxel (taxol) could be produced via fermentation in the same way that penicillin is fermented (Strobel 2003). Fermentation of endophytic fungus producing bioactive compounds has several advantages like reproducible and dependable productivity. It can be grown in fermenters to provide an inexhaustible supply of bioactive compound and thus can be exploited commercially. Direct changes in the culture conditions can be explored as a method of optimizing various biosynthetic pathways that lead to the production of derivatives and analogs of novel compounds (Strobel et al. 2004). Later in the years to follow, taxol has been detected in numerous other endophytic fungi, isolated from diverse host plants. In addition to taxol, other medicinally important plant compounds have also been produced by endophytic fungi (Kaul et al. 2012).

There are many assumptions that endophytes uptake plant DNA into their own genome during their long co-evolution with host plants. This adaptation and genetic variation could have led to endophytes with the ability to synthesize phytochemicals originally associated with the host plant. Horizontal gene transfer makes the endophyte capable of producing associated plant compounds. For example, an endophyte *Fusarium solani* could produce precursors of camptothecin. However, in order to synthesize camptothecin, endophyte uses host's strictosidine synthase, an enzyme involved in the synthesis of camptothecin (Kusari et al. 2012). Initially, it was thought and hypothesized that the endophytic fungi do not synthesize paclitaxel independently but derived it from the host and later accumulates it in their cell walls (Heinig et al. 2013). On the contrary, in a recent study, a large set of potential genes involved in paclitaxel synthesis have been reported in *Penicillium aurantiogriseum* NRRL 62421, an endophyte of *Corylus avellana*. This study has however ruled out the possibility of horizontal gene transfer between endophytic fungus and host plant (Yang et al. 2014a).

Host–endophyte association is very important and influences the synthetic ability of endophytes. Under stressful conditions, endophytes affect the host plant in producing defense chemicals against invading pathogens. During this hostile environment, the ability to synthesize diverse and novel bioactive compounds by endophytes also increases. Thus, environment affects host plant which in turn affects endophyte to change its metabolite profile, increasing synthetic ability and overall biological activity of its secondary metabolites (Selim et al. 2012).

7.2 Fungal Endophytes from Medicinal Plants

Since time immemorial, medicinal plants have been used as a source of medicine. They produce unique and divergent secondary metabolites and harbor a distinctive microbiome (Qi et al. 2012). The endophytes that live inside the plant have distinct but similar metabolic pathway for the production of secondary metabolites. Inducing factors from both plants and endophytes affect the accumulation of secondary metabolites. Researchers around the globe have been prompted to explore the medicinal plants for isolation of endophytes. This is because of the importance of secondary metabolites from medicinal plants in pharmaceuticals and their influence on the synthetic ability of endophytes. Endophytes are also known to mimic the bioactive compounds as produced by the plant itself. Therefore, it is significant to bioprospect endophytes from medicinal plants which have been used for centuries as a source of important bioactive compounds. Endophytes isolated from medicinal plants may result in the inexhaustible and cost-effective production of desired compounds and therefore help to conserve the biodiversity. Endophytes from medicinal plants are believed to be the source of unique and novel compounds associated with diverse biological activities (Jain and Pundir 2015). Their capability to biosynthesize bioactive secondary metabolites has provided the impetus on bioprospection of endophytes.

Different workers have investigated and documented the isolation of endophytic fungi and their metabolites from Indian medicinal plants. Eight medicinal plants of Western Ghats of India were sampled for endophyte isolation. Fifteen species were recovered, out of which *Alternaria* sp., *Nigrospora oryzae*, and *Papulospora* sp. showed antimicrobial activity (Raviraja et al. 2006). Similarly, medicinal plants of Jammu and Kashmir, namely, *Digitalis lanata*, *Digitalis purpurea*, *Plantago ovata*, *Dioscorea bulbifera*, and *Crocus sativus*, have been sampled for the isolation of endophytes (Ahmed et al. 2012; Sharma et al. 2015). Furthermore, 30 species of endophytic *Pestalotiopsis* sp. have been isolated from four medicinal plants *Terminalia arjuna*, *T. chebula*, *Azadirachta indica*, and *Holarrhena antidysenterica* (Tejesvi et al. 2007). Likewise, endophytic fungi from *Garcinia atroviridis*, *G. dulcis*, *G.mangostana*, *G. nigrolineata*, and *G. scortechinii* have been documented as the potential source of antimicrobial agents (Phongpaichit et al. 2006). Fungal endophytes isolated from indigenous medicinal plants belonging to North Maharashtra region of India have been investigated for antimicrobial activity. The isolates from roots of *Aloe vera* possess strong antibacterial activity (Jalgaonwala et al. 2010).

Chinese traditional medicinal plants have also been immensely explored for isolation of endophytes. Li et al. (2005) have studied 12 Chinese medicinal plants for fungal endophyte isolation. One hundred thirty endophytic fungi were reported, out of which 9.2% of the isolates exhibited antitumor activity and 30% exhibited antifungal activity. Similarly, Huang et al. (2007) have reported 292 morphologically distinct endophytic fungi from 29 Chinese medicinal plants. The endophytes recovered from *Ginkgo biloba* have shown different bioactivities like antimicrobial, antioxidant, cytotoxic, etc. (Li et al. 2014c; Ye et al. 2013; Yuan et al. 2013). Bioprospecting of fungal endophytes from different medicinal plants for the period 2010–2016 has been tabulated (Table 7.1).

Table 7.1 Fungal endophytes from medicinal plants showing different bioactivities (Period: 2012–2016)

S. no.	Medicinal plants	Fungal endophytes	Bioactivity	References
1.	*Hugonia mystax*	*Aspergillus* sp.	Antimicrobial	Abirami and Boominathan (2016)
2.	*Corchorus olitorius*	*Aspergillus terreus*	Extracellular enzymes	Ahmed et al. (2016a)
3.	Marine habitat	*Aspergillus* sp.	L-asparaginase	Ahmed et al. (2016b)
4.	*Sapium ellipticum*	*Chaetomium* sp.	Antimicrobial	Akone et al. (2016)
5.	*Cymbopogon caesius*	*Curvularia lunata*	Antimicrobial	Avinash et al. (2016)
6.	*Glycyrrhiza glabra*	*Phoma* sp.	Antimicrobial	Arora et al. (2016)
7.	*Catharanthus roseus*	*Alternaria alternata*	Acetylcholinesterase inhibitory	Bhagat et al. (2016)
8.	*Cupressus torulosa*	*Penicillium oxalicum*	Antidiabetic and antimicrobial	Bisht et al. (2016)
9.	*Acanthospermum australe*	*Aspergillus calidoustus*	Antimicrobial	Carvahlo et al. (2016)
10.	*Sonneratia ovata*	*Nectria* sp.	Antidiabetic	Cui et al. (2016)
11.	*Nymphaea nouchali*	*Chaetomium globosum*	Antimicrobial	Dissanayake et al. (2016)
12.	*Eichhornia crassipes*	*Aspergillus austroafricanus*	Antimicrobial	Ebrahim et al. (2016)
13.	*Hydrastis canadensis*	*Alternaria* sp., *Colletotrichum fioriniae*, *Diaporthe eres*, *Diaporthe* sp., *Phoma* sp., and *Pyrenochaeta cava*	Antimicrobial	Egan et al. (2016)
14.	*Tamarix nilotica*	*Aspergillus sydowii, Penicillium chrysogenum,* and *Eupenicillium crustaceum*	Not reported	Gashgari et al. (2016)
15.	*Juniperus procera*	*Aspergillus fumigatus*	Antimicrobial	Gherbawy and Elhariry (2016)
		Hypocrea lutea		
		Penicillium oxalicum and *Preussia* sp.		
16.	*Pteris pellucida*	*Emericella quadrilineata*	Antimicrobial	Goutam et al. (2016)
17.	*Silybum marianum*	*Talaromyces minioluteus*	Antimicrobial	Kaur et al. (2016)

(continued)

Table 7.1 (continued)

S. no.	Medicinal plants	Fungal endophytes	Bioactivity	References
18.	*Calotropis procera, Catharanthus roseus, Euphorbia prostrata, Trigonella foenum-graecum,* and *Vernonia amygdalina*	*Alternaria* sp.	Antimicrobial	Khiralla et al. (2016)
19.	*Mentha viridis*	*Fusarium oxysporum*	Antimicrobial	Kumar et al. (2016)
20.	*Nicotiana tabacum*	*Rhizopycnis vagum*	Antimicrobial	Lai et al. (2016)
21.	*Panax notoginseng*	*Chaetomium globosum*	Acetylcholinesterase inhibitory	Lia et al. (2016)
22.	*Mahonia fortunei*	*Fusarium decemcellulare*	Antimicrobial	Li et al. (2016a, b)
23.	*Cephalotaxus hainanensis*	*Diaporthe* sp., *Phomopsis* sp., *Colletotrichum* sp., *Colletotrichum* sp., *Corynespora* sp.	Antimicrobial	Liu et al. (2016)
		Penicillium sp. and *Nemania* sp.		
24.	*Salvia miltiorrhiza*	*Alternaria* sp.	Antimicrobial	Lou et al. (2016)
25.	*Schima wallichii*	*Penicillium simplicissimum and Talaromyces verruculosus*	Antimicrobial	Mishra et al. (2016b)
26.	*Rhizophora annamalayana*	*Trichoderma* sp.	Antimicrobial	Narendran and Kathiresan (2016)
27.	*Pisonia grandis*	*Aspergillus niger, Aspergillus fumigates,* and *Aspergillus japonicus*	Antimicrobial	Nishanthi et al. (2016)
28.	*Garcinia preussii*	*Penicillium* sp.	Antimicrobial	Jouda et al. (2016a)
29.	*Ficus carica*	*Aspergillus tamarii*	Antimicrobial	Ma et al. (2016)
30.	*Cinnamomum iners, Shorea siamensis, Fernandoa adenophylla, Quercus semiserrata*	*Xylaria* sp.	Antimicrobial	Orachaipunlap et al. (2016)
31.	*Cinnamomum malabatrum*	*Colletotrichum gloeosporioides*	Antimicrobial	Packiaraj et al. (2016)

32.	*Houttuynia cordata*	*Chaetomium globosum*	Antimicrobial	Pan et al. (2016)
33.	*Moringa oleifera*	*Aspergillus flavus*	Antimicrobial	Rajeshwari et al. (2016)
34.	*Cupressus torulosa*	*Alternaria alternata*	Extracellular enzyme	Rajput et al. (2016)
35.	*Hypocrea virens*	*Premna serratifolia*	Antimicrobial	Ratnaweera et al. (2016)
36.	*Rauvolfia serpentina*	*Colletotrichum* sp.	Antimicrobial	Singh et al. (2016)
		Fusarium sp.		
		Cladosporium sp.		
37.	*Datura innoxia* and *Hyoscyamus muticus*	*Aspergillus fumigatus, Aspergillus niger, Aspergillus terreus var. africanus,*	Antimicrobial	El-Said et al. (2016)
		Cladosporium cucumerinum, Cladosporium oxysporum, Penicillium aurantiogriseum, and *Penicillium chrysogenum*		
38.	*Acalypha indica*	*Phoma* sp.	Antimicrobial	Sowparthani (2016)
39.	*Santalum album*	*Fusarium oxysporum, Fusarium solani, Histoplasma* sp.,	Antimicrobial	Tapwal et al. (2016)
		Periconia sp. and *Pestalotiopsis* sp.		
40.	*Picea mariana* and *Picea rubens*	*Diaporthe maritime*	Antimicrobial	Tanney et al. (2016)
41.	*Narcissus tazetta*	*Fusarium solani*	Antimicrobial	Wang et al. (2015)
42.	*Huperzia serrata*	*Colletotrichum* sp., *Ascomycota* sp.	Acetylcholinesterase inhibitory	Wang et al. (2016b)
43.	*Eugenia jambolana*	*Aspergillus niger* and *Aspergillus terreus*	Antimicrobial	Yadav et al. (2016)
44.	*Lonicera japonica*	*Fusarium* sp.	Antimicrobial	Zhang et al. (2016b)
45.	*Edgeworthia chrysantha*	*Fusarium oxysporum*	Antimicrobial	Zhang et al. (2016a)
46.	*Sapium ellipticum*	*Penicillium tropicum*	Antimicrobial	Zeng et al. (2016)

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Table 7.1 (continued)

S. no.	Medicinal plants	Fungal endophytes	Bioactivity	References
47.	*Panax notoginseng*	*Acremonium* sp.	Antimicrobial	Zheng et al. (2016)
		Alternaria sp.		
		Arthrinium sp.		
		Aspergillus sp.		
		Botryotinia sp.		
		Chaetomium sp.		
		Cladosporium sp.		
		Colletotrichum sp.		
		Dictyosporium sp.		
		Fusarium sp.		
		Humicola sp.		
		Ilyonectria sp.		
		Mucor sp.		
		Myrothecium sp.		
		Penicillium sp.		
		Periconia sp.		
		Pestalotiopsis sp.		
		Phialophora sp.		
		Phoma sp.		
		Phomopsis sp.		
		Plectosphaerella sp.		
		Thielavia sp. and *Trichoderma* sp.		
48.	*Centaurea stoebe*	*Trichoderma* sp.	Antifungal,	Abdou and Abdelhady (2015)
			Cytotoxic	

49.	*Rhododendron anthopogon*	*Stemphylium* sp.	Antimicrobial	Baral et al. (2015)
		Alternaria sp.		
		Penicillium sp.		
		Aspergillus sp.		
		Trichoderma sp.		
		Papulaspora sp.		
		Hansfordia sp.		
		Wardomyces sp. and *Geaotrichum* sp.		
50.	*Bauhinia forficata*	*Acremonium curvulum*	Antibacterial,	Bezerra et al. (2015)
		Aspergillus ochraceus	Enzymatic	
		Gibberella fujikuroi		
		Myrothecium verrucaria and *Trichoderma piluliferum*		
51.	*Curcuma longa*	44 endophytic fungal isolates	Antioxidant	Bustanussalam et al. (2015)
52.	*Annona crassiflora*	*Rhizoctonia* sp.	Antibacterial	De Mendonca et al. (2015)
53.	*Carapa guianensis*	35 distinct fungal taxa	Antibacterial	Ferreira et al. (2015)
54.	*Mallotus philippensis*	*Alternaria* sp.,	Antimicrobial	Gangwar et al. (2015)
		Pestalotiopsis sp. and *Phomopsis* sp.		
55.	*Curcuma xanthorrhiza*	*Xylaria* sp.	Cytotoxic	Hammerschmidt et al. (2015)
56.	*Kadsura angustifolia*	42 fungal taxa	Extracellular enzymatic	Huang et al. (2015)
57.	*Azadirachta indica*	*Chaetomium* sp.	Antioxidant	Kumaresan et al. (2015)
		Colletotrichum sp.		
		Curvularia sp. and *Trichoderma* sp.		
58.	*Rauwolfia serpentina*	*Aspergillus awamori*	Antibacterial	Nath et al. (2015)
		Penicillium sp. and *Colletotrichum gloeosporioides*		

(continued)

Table 7.1 (continued)

S. no.	Medicinal plants	Fungal endophytes	Bioactivity	References
59.	*Brucea javanica*	*Trichoderma* sp.	Not reported	Nur and Muh Danial (2015)
		Fusarium sp.		
		Aspergillus sp. and *Penicillium* sp.		
60.	*Solanum xanthocarpum*	*Phomopsis vexans*	Lowering blood cholesterol (lovastatin)	Parthasarathya and Sathiyabama (2015)
61.	*Aegle marmelos*	*Aspergillus flavus*	Antioxidant	Patil et al. (2015b)
			Antimicrobial	
62.	*Silybum marianum*	25 fungal taxa	Cytotoxic	Raja et al. (2015)
63.	*Cyperus rotundus*	*Rhizoctonia solani*	Antibacterial	Ratnaweera et al. (2015a)
64.	*Indigofera suffruticosa*	*Nigrospora sphaerica* and *Pestalotiopsis maculans*	Antibacterial	Santos et al. (2015)
65.	*Withania somnifera*	*Fusarium* sp.	Antibacterial	Singh et al. (2015a)
66.	*Limonia acidissima*	*Aspergillus* sp.	Cytotoxic	Siriwardane et al. (2015)
67.	*Huperzia serrata*	*Paecilomyces tenuis*	Anti-Alzheimer's	Su and Yang (2015)
68.	*Bacopa monnieri*	*Aspergillus fumigatus*	Antioxidant and antitubercular	Thakur et al. (2015)
69.	*Alstonia boonei-Ahun, Enantia chlorantha-Awopa,* and *Kigelia africana-Pandoro*	*Aspergillus niger*	Antibacterial	Tolulope et al. (2015)
		Macrophomina sp.		
		Trichoderma sp. and four different *Penicillium* sp.		
70.	*Dracaena draco*	*Botryodiplodia theobromae*	Antibacterial	Zaher et al. (2015a, b)
71.	*Calotropis procera*	*Aspergillus niger*	Antibacterial	Aharwal et al. (2014)
		Cladosporium herbarum, Aspergillus tamari, Drechslera nodulosa, Fusarium solani		
		Aspergillus japonicas, Alternaria alternata, Alternaria tenuissima, Curvularia pallescens, and *Curvularia lunata*		
72.	*Tabebuia argentea*	*Aspergillus niger*	Anticancer	Channabasava and Govindappa (2014)

73.	*Lantana camara*	Three endophytic strains	Enzymatic, phytochemical screening	Desire et al. (2014)
74.	*Capsicum annuum*	*Alternaria alternata*	Cytotoxic	Devari et al. (2014)
75.	*Gloriosa superba*	*Alternaria solani* and *Penicillium funiculosum*	Antimicrobial	Devi et al. (2014)
76.	*Tabebuia argentea*	*Alternaria alternate*	Cytotoxic	Govindappa et al. (2014)
77.	*Garcinia nobilis*	*Penicillium* sp.	Antibacterial	Jouda et al. (2014)
78.	*Bacopa monnieri*	26 endophytes	Antimicrobial cytotoxic	Katoch et al. (2014a, b)
79.	*Xanthium sibiricum*	*Eupenicillium* sp.	Antibacterial	Li et al. (2014a)
80.	*Ginkgo biloba*	*Chaetomium globosum*	Cytotoxic	Li et al. (2014c)
81.	*Datura stramonium*	*Aspergillus* sp.	Antimicrobial	Mahdi et al. (2014)
		Curvularia sp.	Antioxidant	
	Moringa oleifera and *Prosopis chilensis*	*Emericella* sp. and *Chaetomium* sp.		
82.	*Terminalia arjuna*	*Aspergillus flavus,*	Antimicrobial	Patil et al. (2014)
		Diaporthe arengae	Antioxidant	
		Alternaria sp. and *Lasiodiploidia theobromae*		
83.	*Polygala elongata*	*Colletotrichum* sp.	Antioxidant	Pawle and Singh (2014)
84.	*Nothapodytes foetida* and *Hypericum mysorense*	*Bionectria ochroleuca* and *Chaetomium globosum*	Antibacterial	Samaga and Rai (2014)
			Antioxidant	
85.	*Camellia sinensis*	*Colletotrichum* sp. and *Gloeosporioides* sp.	Antifungal	Rabha et al. (2014)
86.	*Cynodon dactylon* and *Dactyloctenium aegyptium*	26 fungal endophytes 30 fungal endophytes	Antimicrobial	Rekha and Shivanna (2014)
			Antioxidant	
87.	*Saraca indica*	*Phomopsis* sp.	Antibacterial	Sandhu et al. (2014)
		Aspergillus terreus		
		Phialophora sp.		
		Alternaria alternata and *Phyllosticta* sp.		

(continued)

Table 7.1 (continued)

S. no.	Medicinal plants	Fungal endophytes	Bioactivity	References
88.	*Cinnamomum mollissimum*	*Phoma* sp.	Antibacterial,	Santiago et al. (2014)
			Antifungal,	
			Cytotoxic	
89.	*Adiantum capillus-veneris*	*Chaetomium globosum*	Cytotoxic	Selim et al. 2014
			Antioxidant	
			Butyrylcholinesterase inhibitory	
90.	*Allium sativum*	*Trichoderma brevicompactum*	Antifungal	Shentu et al. (2014)
91.	*Curcuma longa*	*Penicillium* sp.	Antibacterial	Singh et al. (2014)
92.	*Phyllanthus amarus*	30 endophytic fungi	Antifungal,	Taware et al. (2014)
			Anticancer,	
			Anti-metastatic	
93.	*Crotalaria pallida*	*Alternaria* sp.	Antioxidant	Umashankar et al. (2014)
		Penicillium sp. and *Aspergillus flavus*	Antimicrobial	
94.	*Madhuca indica*	40 taxa	Antibacterial	Verma et al. (2014)
		Dominant: *Phomopsis* sp.		
		Colletotrichum sp. and *Gloeosporioides* sp.		
95.	*Baccharis trimera*	*Diaporthe phaseolorum*	Antimicrobial	Vieira et al. (2014)
		Pestalotiopsis sp. and *Preussia pseudominima*		
96.	*Boswellia ovalifoliolata*	14 fungal species	Not reported	Anitha et al. (2013)
		Dominant:		
	Pterocarpus Santalinus	*Colletotrichum falcatum*		
	Shorea thumbuggaia and *Syzygium alternifolium*			
97.	*Bauhinia guianensis*	*Aspergillus* sp.	Antimicrobial	Pinheiro et al. (2013)
98.	*Pandanus amaryllifolius*	*Colletotrichum* sp.	Antibacterial	Bungihan et al. (2013)
99.	*Camptotheca acuminate*	*Botryosphaeria* sp. and *Fusarium* sp.	Antimicrobial	Ding et al. (2013)

100.	*Moringa oleifera*	*Alternaria* sp.	Not reported	Dhanalakshmi et al. (2013)
		Aspergillus sp.		
		Bipolaris sp.		
		Exophiala sp.		
		Nigrospora sp. and *Penicillium* sp.		
101.	*Ceratonia siliqua*	*Penicillium citrinum*	Cytotoxic	El-Neketi et al. (2013)
102.	*Tabebuia argentea*	*Aspergillus niger*	Antioxidant	Govindappa et al. (2013)
		Aspergillus flavus		
		Penicillium sp.		
		Rhizopus sp. and *Fusarium* sp.		
103.	*Kigelia africana*	*Cladosporium* sp.	Antibacterial	Idris et al. (2013)
		Aspergillus flavus		
		Aspergillus sp. and *Curvularia lunata*		
104.	*Antidesma madagascariense*	*Aspergillus* sp. *Guignardia* sp.	Not reported	Jeewon et al. (2013)
		Fusarium sp.		
		Penicillium sp.		
		Pestalotiopsis sp. and *Trichoderma* sp.		
105.	*Withania somnifera*	*Chaetomium globosum*	Antifungal	Kumar et al. (2013)
106.	*Jatropha curcas*	*Colletotrichum truncatum*	Antifungal	Kumar and Kaushik (2013)
		Nigrospora oryzae		
		Fusarium proliferatum		
		Guignardia cammillae		
		Alternaria destruens and *Chaetomium* sp.		
107.	*Cannabis sativa*	30 fungal species	Antifungal	Kusari et al. (2013)
		Dominant:		
		Penicillium copticola		
108.	*Ocimum tenuiflorum*	*Penicillium citrinum*	Antibacterial	Lai et al. (2013)

(continued)

Table 7.1 (continued)

S. no.	Medicinal plants	Fungal endophytes	Bioactivity	References
109.	*Zingiber zerumbet*	*Fusarium oxysporum*	Antioxidant	Nongalleima et al. (2013)
110.	*Erythrina variegata*	*Alternaria* sp.	Antiangiogenic	Pompeng et al. (2013)
111.	*Garcinia* sp.	*Aspergillus fumigates* and *Fusarium* sp.	Antimicrobial	Ruma et al. (2013)
			Antioxidant,	
			Anti-inflammatory	
112.	*Viscum album*	*Aspergillus flavus*	Antioxidant	Sadananda et al. (2013)
		Fusarium oxysporum		
		Fusarium moniliforme and *Trichothecium* sp.		
113.	*Ocimum sanctum*	147 fungal endophytes	Antioxidant	Sharma and Kumar (2013)
114.	*Elaeis guineensis*	*Trichoderma* sp.	Antifungal	Sundram (2013)
115.	*Rhododendron tomentosum*	*Fusarium tricinctum*	Antibacterial	Tejesvi et al. (2013)
116.	*Glycine max*	*Alternaria alternata*	Not reported	Tenguria and Firodiya (2013)
		Phoma sp.		
		Penicillium sp. and *Fusarium* sp.		
117.	*Sauracia scaberrinae*	*Phoma* sp.	Antibacterial	Wijeratne et al. (2013)
118.	*Panax ginseng*	*Nectria* sp.	Antibacterial	Wu et al. (2013b)
		Aspergillus sp.		
		Fusarium sp.		
		Verticillium sp.		
		Engyodontium sp.		
		Plectosphaerella sp.		
		Penicillium sp. and *Cladosporium* sp.		
119.	*Ginkgo biloba*	*Chaetomium globosum*	Antioxidant	Ye et al. (2013)
120.	*Huperzia serrata*	*Ceriporia lacerate*	Cytotoxic (ceriponols A– K)	Ying et al. (2013)
121.	*Ginkgo biloba*	*Penicillium* sp.	Antioxidant	Yuan et al. (2013)
122.	*Taraxacum mongolicum*	*Phoma* sp.	Antibacterial	Zhang et al. (2013a)

123.	*Annona muricata*	*Periconia* sp.	Cytotoxic (periconiasins A–C)	Zhang et al. (2013b)
124.	*Terminalia brownii*	*Rhizophus oryzae*	Antimicrobial	Basha et al. (2012)
		Aspergillus niger and *Aspergillus flavus*		
125.	*Ocimum sanctum* and *Sapindus detergens*	63 endophytic fungal	Antibacterial	Bhagat et al. (2012)
		Isolates	Anticancer	
126.	*Nyctanthes arbor-tristis*	19 endophytic fungi	Antimicrobial	Gond et al. (2012)
		Dominant:		
		Alternaria alternata and *Cladosporium cladosporioides*		
127.	*Sapindus saponaria*	*Cochliobolus intermedius* and *Phomopsis* sp.	Antimicrobial	Garcia et al. (2012)
128.	*Cinnamomum camphora*	20 fungal species	Antimicrobial	Kharwar et al. (2012)
129.	*Dysoxylum binectariferum*	*Fusarium proliferatum*	Anticancer (rohitukine)	Kumara et al. (2012)
130.	*Ophiopogon japonicus*	30 fungal strains	Antimicrobial	Liang et al. (2012)
131.	*Emblica officinalis*	*Phomopsis* sp.	Antioxidant	Nath et al. (2012)
			Antimicrobial	
132.	*Piper hispidum*	21 isolates belonging to 11 genera	Not reported	Orlandelli and Pamphile (2012)
133.	*Trichilia elegans*	*Cordyceps memorabilis*	Antimicrobial	Rhoden et al. (2012)
		Phomopsis longicolla and *Dothideomycetes* sp.		
134.	*Arisaema erubescens*	*Phoma* sp.	Antimicrobial	Wang et al. (2012a)
			Antitumor	
135.	*Curcuma wenyujin*	*Chaetomium globosum*	Antifungal	Wang et al. (2012b)
			Cytotoxic	
136.	*Moringa oleifera*	*Nigrospora* sp.	Antifungal	Zhao et al. (2012a, b)

7.3 Fungal Endobiome as a Source of Bioactive Metabolites

Endophytic fungi exist within a niche where it communicates with diverse communities of microorganisms. Variegated cross talks take place among endophytic fungi, endophytes and host, endophytic fungi and endophytic bacteria, etc. Under the influence of such multiplexed interactions and environmental conditions, a plethora of secondary metabolites is synthesized by the fungal endophytes (Kusari et al. 2014). Secondary metabolites are defined as small molecules that are not necessary for normal growth or development. Although it is not possible to reproduce such an array of diverse metabolites by endophytes under in vitro conditions, however, it is interesting that using controlled fermentation condition, by altering the accessible culture and process parameters (media composition, aeration, pH, incubation period, shaking conditions, inoculum size, etc.), the endophyte can be optimized for the production of surplus biologically active secondary metabolites (Kusari et al. 2012).

Secondary metabolites from endophytes have a tremendous impact on the society and proven useful for novel drug discovery and can be used as a potential source of pharmaceutical leads. These belong to diverse chemical groups including terpenoids, alkaloids, phenylpropanoids, aliphatic, polyketides, peptides, flavonoids, steroids, lignans, etc. Terpenoids and polyketides are most commonly purified from endophytes, whereas flavonoids and lignans are rare (Mousa and Raizada 2013). Due to chemical diversity of their secondary metabolites, endophytic fungi have been explored for medicinal, agricultural, and industrial uses. These metabolites are known for a wide variety of biological activities like antimicrobial, antioxidant, immunomodulatory, anticancerous, antidiabetic, antiviral, etc.

Some of the important categories of bioactive secondary metabolites produced by fungal endophytes of medicinal plants are as follows.

7.3.1 Anticancer Compounds

Cancer is a killer disease affecting more than six million people every year. It is characterized by unregulated cell proliferation. Due to uncontrollable growth of cells, an abnormal mass of tissue is formed which is generally called as a tumor. Antitumor agents are the compounds that are capable of counteracting the formation of malignant. Plant-based compounds have played an important role in the development of several clinically useful anticancer drugs like taxol, vinblastine, vincristine, topotecan, and etoposide (Nirmala et al. 2011). Despite this, there is a need to explore alternative source with more diversity and novelty. Endophytes with their unique secondary metabolites provide tremendous diversity. Active metabolites isolated from endophytes provide anticancer action with minimum side effects. These compounds could be an alternative approach for discovery of novel anticancer drugs (Kharwar et al. 2011; Kaul et al. 2012; Chen et al. 2014). Various anticancer compounds have been reported from fungal endophytes. For the sake of convenience, some of the anticancer compounds from fungal endophytes have been tabulated (Table 7.2).

Table 7.2 Anticancer compounds from endophytic fungi of medicinal plants (2012–2016)

S. no.	Medicinal plants	Fungal endophytes	Anticancer compound	Reference
1.	*Piper hispidum*	*Diaporthe* sp.	(1 → 3,1 → 6)-D-glucans	Orlandelli et al. (2017)
2.	Medicinal plant	*Bipolaris setariae*	Ophiobolin A	Bhatia et al. (2016)
3.	*Acanthospermum australe*	*Aspergillus calidoustus*	Ophiobolin K and 6-epiophiobolin K	Carvalho et al. (2016)
4.	*Uncaria rhynchophylla*	*Colletotrichum gloeosporioides*	Colletotrilactam A–D	Wei et al. (2016)
5.	*Acanthus ilicifolius*	*Aspergillus flavipes*	Meroterpenoids (guignardones)	Bai et al. (2015)
6.	*Hevea brasiliensis*	*Eutypella scoparia*	Cytochalasins	Kongprapan et al. (2015)
7.	*Diphylleia sinensis*	*Aspergillus fumigates*	Fumitremorgin and fumitremorgin D	Liang et al. (2015b)
8.	*Sinopodophyllum emodi*	*Alternaria tenuissima*	Podophyllotoxin	Liang et al. (2015a)
9.	Mangrove plant	*Lasiodiplodia* sp.	Lasiodiplodins	Li et al. (2015b)
10.	*Paris polyphylla var. yunnanensis*	*Aspergillus versicolor*	Versicolols A and B	Zhou et al. 2015
11.	*Tabebuia argentea*	*Aspergillus niger*	Lapachol	Channabasava and Govindappa (2014)
12.	*Tripterygium wilfordii*	*Penicillium* sp.	Penifupyrone	Chen et al. 2014
13.	*Ginkgo biloba*	*Chaetomium globosum*	Chaetoglobosins A, G, V, Vb, and C	Li et al. (2014c)
14.	*Ludwigia prostrata*	*Colletotrichum* sp.	Pyrenocines N–O	Yang et al. (2014b)
15.	*Ceratonia siliqua*	*Penicillium citrinum*	Tanzawaic acids G–H, 6-methylcurvulinic acid, 8-methoxy-3, 5-dimethylisoquinolin-6-ol, and 1,2,3,11b-tetrahydroquinolactacide	El-Neketi et al. (2013)
16.	*Ocimum tenuiflorum*	*Penicillium citrinum*	Two new alkaloids	Lai et al. (2013)
17.	*Miquelia dentata*	*Fomitopsis* sp.	Camptothecin	Shweta et al. (2013)
18.	*Tamarix chinensis*	*Penicillium* sp.	Arisugacins I and J	Sun et al. (2013)
19.	*Mentha pulegium*	*Stemphylium globuliferum*	Altersolanol A	Teiten et al. (2013)

(continued)

Table 7.2 (continued)

S. no.	Medicinal plants	Fungal endophytes	Anticancer compound	Reference
20.	*Taxus chinensis*	*Perenniporia tephropora*	Perenniporin A	Wu et al. (2013a)
21.	*Astragalus lentiginosus*	*Emericella* sp.	Secoemestrin D	Xu et al. (2013)
22.	*Avicennia* sp.	*Penicillium* sp.	4-(methoxymethyl)-7-methoxy-6-methyl-1(3H)-isobenzofuranone	Yang et al. (2013)
23.	*Bruguiera sexangula*	*Pestalotiopsis foedan*	(−)-(4S, 8S)-foedanolide and (+)-(4R, 8R)-foedanolide	Yang and Li (2013)
24.	*Huperzia serrata*	*Ceriporia lacerate*	Ceriponols A–K,	Ying et al. (2013)
25.	*Annona muricata*	*Periconia* sp.	Periconiasins A–C	Zhang et al. (2013)
26.	*Cajanus cajan*	*Hypocrea lixii*	Cajanol	Zhao et al. (2013)

7.3.2 Antioxidant Compounds

Oxidation is an essential process that utilizes oxygen and metabolizes macromolecules for energy production. Paradoxically, this vital mechanism may also lead to cell and tissue damage through production of free radicals and reactive oxygen species. These radicals get stabilized by reacting with cellular components including lipids, proteins, and DNA leading to impairment in their normal structure and function. This ultimately leads to the development of pathologies such as diabetes and cardiovascular and neurodegenerative diseases. An antioxidant is a molecule that slows down the oxidative damage caused by the free radicals and inhibits the deleterious effect caused by oxidation chain reaction. Antioxidant compounds can be obtained from plants, fruits, and vegetables. Since few antioxidants are approved for clinical application due to health safety issues, exploration of novel compounds from endophytes can be considered as an alternative source. Investigation of antioxidant compounds from endophytes gained importance after the discovery of pestacin and isopestacin as antioxidant compounds from endophyte *Pestalotiopsis microspore* residing in *Terminalia morobensis* (Harper et al. 2003). Since then, different studies on isolation of diverse antioxidant compounds have been reported from endophytes.

It is presumed that phenolic and flavonoid compounds are known to possess good antioxidant capacity. Huang et al. (2007) showed a positive correlation between the antioxidant capacity of *Chaetomium* sp., an endophyte of *Nerium oleander*, to phenolic and flavonoid compounds which were the major antioxidant constituents isolated from fungal extract (Huang et al. 2007). Similarly, *Xylaria* sp. isolated from *Ginkgo biloba* has been reported to show antioxidant activity. The activity was due to the presence of phenolic and flavonoid compounds present in the methanolic extract of the fungus (Liu et al. 2007). Similarly, *Chaetomium globosum* (CDW7), an endophyte of *Ginkgo biloba*, has been reported to synthesize antioxidant compound flavipin. The compound has been reported to be used in the therapy for free radical-associated diseases (Ye et al. 2013). Yuan et al. (2013) also isolated *Penicillium* sp. from roots of *Ginkgo biloba*. Six known metabolites have been obtained from this endophyte out of which three compounds, viz., adenosine, adenine, and 2-deoxyadenosine, exhibited potential DPPH scavenging activity.

Some new metabolites possessing antioxidant activity have also been reported from endophytes. In a recent study, phomopsidone A, a novel pentacyclic depsidone, has been reported from mangrove endophytic fungus *Phomopsis*. The compound exhibited antioxidant activity in addition to antifungal and cytotoxic activities (Zhang et al. 2014). Huang et al. (2012) also reported a new isobenzofuranone derivative 4, 6-dihydroxy-5-methoxy-7-methylphthalide from *Cephalosporium* sp. AL031 endophytic in *Sinarundinaria nitida*.

An exopolysaccharide, rhamnogalactan was obtained from endophyte *Fusarium solani* SD5 isolated from *Alstonia scholaris*. The compound showed the significant free radical scavenging effect on DPPH radicals with an IC_{50} value of 578.5 μg/ml (Mahapatra and Banerjee 2014). In another study endophytes for antioxidant compounds glutaminase enzyme possessing free radical scavenging activity were isolated from the endophytic fungus *Penicillium citrinum*. The IC_{50} value of enzyme for DPPH, reducing power, nitric oxide, and hydroxyl radical scavenging activity were found to be 94.65, 117.73, 87.26, and 105.62, respectively (Sajitha et al. 2014). Antioxidant compounds palmarumycins C2 and C3 from endophyte *Berkleasmium* sp. Dzf12 and terrain from *Aspergillus terreus* have been reported in different studies (Mou et al. 2012; Al-Trabolsy et al. 2014). An antioxidant compound graphislactone A was obtained from endophyte *Cephalosporium* sp. IFB-E00, a resident of *Trachelospermum jasminoides*. The compound was confirmed to have stronger antioxidant activity in vitro as compared to butylated hydroxytoluene and ascorbic acid which were used as positive control (Song et al. 2005). Cajaninstilbene acid, a natural antioxidant, has been reported from *Fusarium*, an endophyte of pigeon pea *Cajanus cajan* (Zhao et al. 2012).

7.3.3 Antimicrobial Compounds

Secondary metabolites produced by fungal endophytes having antimicrobial activity are a promising way to overcome the increasing threat of drug-resistant microbes. These can also be used as food preservatives in the control of food spoilage and food-borne diseases (Liu et al. 2007). Antimicrobial metabolites (antibiotics) are low-molecular-weight organic compounds produced by microorganisms that are active at low concentrations against other microorganisms not required for its growth. They are produced as an adaptation for a specific function in nature and are the most frequent bioactive natural products isolated from endophytes.

Penicillium sp. has always been the important source of antimicrobial compounds. The literature reviewed revealed several examples where antimicrobial compounds have been reported from diverse species of *Penicillium*. Five new picolinic acid derivatives penicolinates A–E have been isolated from an endophytic fungus *Penicillium* sp. BCC16054. Penicolinates B and C have displayed activity against *Bacillus cereus* and *Candida albicans* (Intaraudom et al. 2013). Chemical investigation of *Penicillium citrinum*, a fungal endophyte of *Ocimum tenuifolium*, has led to the isolation of two new alkaloids along with 14 known polyketides and 4 known alkaloids. Perinadine A, alternariol, and citrinin were found to be moderately active against *Staphylococcus aureus* (Lai et al. 2013). Another *Penicillium* sp. isolated as endophyte of *Curcuma longa* has been reported to exhibit antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli* (Singh et al. 2014). *Staphylococcus aureus* was also susceptible to antimicrobial compounds isolated from *Penicillium* sp., an endophyte of *Acrostichum aureum.* The compounds have been identified as cyclo(pro-Thr), cyclo(pro-Tyr), and liquiritigenin (Cui et al. 2008).

Various species of *Aspergillus* isolated as endophytes from different medicinal plants have been described as the promising source of antimicrobial compounds. *Aspergillus* sp. from *Bauhinia guianensis* yielded alkaloidal antimicrobial compounds pseurotin and fumigaclavine C. The latter was found to be active against *Bacillus subtilis* (Pinheiro et al. 2013). Nigerasterols A–B and malformins A–C have been isolated from culture extract of *Aspergillus niger*, an endophyte of mangrove plant *Avicennia marina*. Malformins A–C displayed weak activity against *S. aureus* (Liu et al. 2013). Another mangrove endophyte *Aspergillus* sp. yielded antimicrobial compound asperterpenoid A. It exhibited strong inhibitory activity against *Mycobacterium tuberculosis* (Huang et al. 2013). *Aspergillus* sp. isolated from *Melia azedarach* afforded seven metabolites. All the isolated compounds have been evaluated against several phytopathogenic fungi and pathogenic bacteria. Compounds asperpyrone A, asperazine, and rubrofusarin B were found to inhibit fungal pathogen *Aspergillus solani*. Asperpyrone A also exhibited antibacterial activity against *Staphylococcus aureus* and *Bacillus subtilis* with MICs of 25 mm (Xiao et al. 2014b).

A large number of diverse antimicrobial compounds have been reported from *Xylaria* residing in different host plants as endophytes. 7-Amino-4-methylcoumarin was obtained from *Xylaria* sp. YX-28, an endophyte of *Ginkgo biloba*, displayed antibacterial and antifungal activity against many pathogenic organisms (Liu et al. 2007). Three compounds chaetomugilin D, chaetomugilin A, and chaetoglobosin C were isolated from *Chaetomium globosum* endophytic in *Ginkgo biloba*. All of them exhibited significant activity against *Artemia salina* and *Mucor miehei* (Qin et al. 2009). Compounds 2-hexyl-3-methyl butanodioic acid and cytochalasin D possessing antifungal activity were recovered from endophytic *Xylaria* sp. The endophyte was isolated from *Palicourea marcgravii* (Cafeu et al. 2005). Likewise, *Xylaria* F0010, an endophyte of *Abies holophylla*, was found to be a potential producer of antifungal antibiotic agent griseofulvin. The compound has been used for the treatment of human and veterinary mycotic diseases (Park et al. 2005).

Endophytic *Phoma* sp. isolated from different medicinal plants has been reported to be a promising source of antimicrobial compounds. Santiago et al. (2012) have reported a polyketide compound 5-hydroxyramulosin from *Phoma* sp., an endophyte of *Cinnamomum mollissimum*. The isolated compound exhibited antifungal activity against *Aspergillus niger*. In another study mycelial extract of *Phoma* sp. NRRL 46751, inhabiting *Sauracia scaberrinae*, afforded three new alkaloids: phomapyrrolidones A–C out of which phomapyrrolidones B and C exhibited weak activity against *Mycobacterium tuberculosis* (Wijeratne et al. 2013). Similarly, a compound phomodione, an usnic acid derivative, was reported to be produced by *Phoma* sp. isolated from *Saurauia scaberrinae*. The compound displayed antibacterial activity against *Staphylococcus aureus* (Hoffman et al. 2008). Bioassay-guided fractionation of culture filtrate of fungal endophyte *Phoma*, isolated from *Taraxacum mongolicum*, led to the isolation of 2-hydroxy-6-methyl benzoic acid. The compound showed antibacterial activity against five bacterial test pathogens: *Escherichia coli*, *Staphylococcus aureus*, *Aeromonas hydrophila*, *Edwardsiella tarda*, and *Pasteurella multocida* (Zhang et al. 2013a). Four compounds, phomafuranol, phomalacton, (3R)-5-hydroxymellein, and emodin, were isolated from ethyl acetate extract of *Phoma* sp., a marine endophyte isolated from plant *Fucus serratus* (Hussain et al. 2014).

A broad diversity of endophytic fungi exists in the rhizome of *Paris polyphylla var. yunnanensis*, a medicinal plant used in traditional Chinese medicine. *Fusarium* sp. Ppf4 from this plant yielded two sterols and one fatty acid by bioassay-guided fractionation. The compounds were elucidated as 5alpha, 8alpha-epidioxyergosta-6, 22-dien-3beta-ol and ergosta-8(9), 22-dien-3beta, 5alpha, 6beta, 7alpha-tetraol and displayed antimicrobial activity (Huang et al. 2009). *Fusarium redolens* DzF2 was isolated from Chinese medicinal plant *Dioscorea zingiberensis*. Beauvericin was obtained using bioautographic antibacterial assay. The compound displayed activity against six test bacteria: *Bacillus subtilis*, *Staphylococcus haemolyticus*, *Pseudomonas lachrymans*, *Agrobacterium tumefaciens*, *Escherichia coli*, and *Xanthomonas vesicatoria* (Xu et al. 2010). Taynung et al. (2011) have reported four compounds, 1-tetradecene, 8-octadecanone, 8-pentadecanone, and octylcyclohexane and 10-nonadecanone, from *Fusarium solani* isolated from *Taxus baccata*. All the compounds showed antibacterial as well as antifungal activity. *Fusarium tricinctum* was isolated from *Rhododendron tomentosum*. Transcriptome of this endophyte was sequenced; 12,006 contigs were assembled. On analyzing transcriptomic library, it yielded a peptide resin. The compound was found to be active against *Staphylococcus carnosus*, *Candida albicans*, and *Candida utilis* (Tejesvi et al. 2013).

Colletotrichum is one of the important genus frequently isolated as an endophyte from different hosts. The endophyte has been investigated during different studies for the isolation of antimicrobial compounds. Colletotriolide a new macrolide was obtained from *Colletotrichum* sp. residing in *Pandanus amaryllifolius*. The compound showed low activity against *E. coli* (Bungihan et al. 2013). Similarly, Chithra et al. (2014) have reported the ability of *Colletotrichum gloeosporioides* to produce piperine, a compound originally synthesized by the host plant *Piper nigrum*. The compound has antimicrobial activity. One new compound 2-phenylethyl 1H–indol-3-yl-acetate was obtained from endophyte *Colletotrichum gloeosporioides* isolated from *Michelia champaca.* The compound possessed antifungal activity against *Cladosporium cladosporioides* and *C. sphaerospermum* (Chapla et al. 2014). Some of the antimicrobial compounds isolated from fungal endobiome have been discussed, and the rest of the data has been tabulated (Table 7.3).

7.3.4 Immunomodulatory Compounds

Immunomodulatory compounds are those compounds that help in modulating the immune system either by stimulating it or suppressing it. Immunosuppressive compounds are required to deal with autoimmune disorders and allograft rejection in transplant patients. Immunomodulatory drugs play a key role in the treatment of cancer. Due to the emergence of new autoimmune disorders and their role in the treatment of cancer, an intensive search is going on for more effective agents that provide aid in this regard. Since fungal endophytes have the capacity to produce novel compounds, these could prove a useful source for potentially active immunomodulatory compounds (Kaul et al. 2012). Several immunomodulatory compounds have been reported from fungal endophytes in the recent past.

Table 7.3 Antimicrobial compounds from fungal endophytes comprising the endobiome of some medicinal plants

S. no.	Medicinal plants	Fungal endophytes	Extract/compound isolated	Reference
1.	*Hugonia mystax*	*Aspergillus* sp.	Ethanol	Abirami and Boominath (2016)
2.	*Sapium ellipticum*	*Chaetomium* sp.	Polyketides	Akone et al. (2016)
3.	*Cymbopogon caesius*	*Curvularia lunata*	Ethyl acetate	Avinash et al. (2016)
4.	*Glycyrrhiza glabra*	*Phoma* sp.	Thiodiketopiperazine derivatives	Arora et al. (2016)
5.	*Cupressus torulosa*	*Penicillium oxalicum*	Methanol and chloroform	Bisht et al. (2016)
6.	*Acanthospermum australe*	*Aspergillus calidoustus*	Ophiobolin K and 6-epiophiobolin K	Carvahlo et al. (2016)
7.	Mangrove plants	*Talaromyces amestolkiae*	Isocoumarins and benzofurans	Chen et al. (2016)
8.	*Nymphaea nouchali*	*Chaetomium globosum*	Chaetoglobosin A and C	Dissanayake et al. (2016)
9.	*Hydrastis canadensis*	*Alternaria* sp., *Colletotrichum fioriniae,* *Diaporthe eres, Diaporthe* sp., *Sordariomycetes* sp., *Magnaporthales* sp., *Phoma* sp., and *Pyrenochaeta cava*	Alternariol, alternariol monomethyl ether, 50 epi-equisetin, equisetin, 10–11 dehydrocurvularin, macrosphelide A, cordipyridone A verticillin A, aurofusarin	Egan et al. (2016)
10.	*Eichhornia crassipes*	*Aspergillus austroafricanus*	Diphenyl ether	Ebrahim et al. (2016)
11.	*Datura innoxia* and *Hyoscyamus muticus*	*Aspergillus fumigatus, A. niger, A. terreus var. africanus, Cladosporium cucumerinum, C. oxysporum, Penicillium aurantiogriseum,* and *P. chrysogenum*	Chloroform	El-Said et al. (2016)
12.	*Juniperus procera*	*Aspergillus fumigatus*, *Hypocrea lutea*, *Penicillium oxalicum*, and *Preussia* sp.	Methanol	Gherbawy and Elhariry (2016)
13.	*Pteris pellucida*	*Emericella quadrilineata*	Benzyl benzoate	Goutam et al. (2016)
14.	*Glycosmis mauritiana*	*Penicillium* sp.	AgNP	Govindappa et al. (2016a)

(continued)

Table 7.3 (continued)

S. no.	Medicinal plants	Fungal endophytes	Extract/compound isolated	Reference
15.	*Curcuma longa*	*Phoma herbarum*	Gentisyl alcohol	Gupta et al. (2016)
16.	*Garcinia preussii*	*Aspergillus japonicus*	Variecolin and neovasifuranone B	Jouda et al. (2016b)
17.	*Silybum marianum*	*Talaromyces minioluteus*	Talarolutins A–D: Meroterpenoids	Kaur et al. (2016)
18.	*Calotropis procera, Catharanthus roseus, Euphorbia prostrata, Trigonella foenum-graecum,* and *Vernonia amygdalina*	*Byssochlamys spectabilis* and *Alternaria* sp.	Ethyl acetate	Khiralla et al. (2016)
19.	*Menthe viridis*	*Fusarium oxysporum*	Broth	Kumar et al. (2016)
20.	*Nicotiana tabacum*	*Rhizopycnis vagum*	Dibenzo-α-pyrone derivatives	Lai et al. (2016)
21.	*Mahonia fortune*	*Fusarium decemcellulare*	Pentapeptides and lipopeptide	Li et al. (2016b)
22.	*Cephalotaxus hainanensis*	*Diaporthe* sp., *Phomopsis* sp., *Colletotrichum* sp., *Corynespora* sp., *Penicillium* sp., and *Nemania* sp.	Ethyl acetate	Liu et al. (2016)
23.	*Salvia miltiorrhiza*	*Alternaria* sp.	Alternariol 9-methyl ether	Lou et al. (2016)
24.	*Ficus carica*	*Aspergillus tamarii*	Cyclic pentapeptide: malformin E	Ma et al. (2016)
25.	*Melastoma malabathricum*	*Diaporthe phaseolorum*	Ethyl acetate	Mishra et al. (2016a)
26.	*Schima wallichii*	*Penicillium simplicissimum* and *Talaromyces verruculosus*	Ethyl acetate	Mishra et al. (2016b)
27.	*Rhizophora annamalayana*	*Trichoderma* sp.	Ethyl acetate	Narendran and Kathiresan (2016)
28.	*Cinnamomum iners, Shorea siamensis, Fernandoa adenophylla,* and *Quercus semiserrata*	*Xylaria* sp.	Ethyl acetate	Orachaipunlap et al. (2016)

29.	*Cinnamomum malabatrum*	*Colletotrichum gloeosporioides*	Phenol 3, 5- dimethoxy acetate, 4′-isopropylidene-bis-(2-cyclohexyl) phenol, N-didehydrohexacarboxyl-2, 4, 5-trimethylpiperazine and 1, 2, 4-triazolium ylide	Packiaraj et al. (2016)
30.	*Houttuynia cordata*	*Chaetomium globosum*	Ethyl acetate	Pan et al. (2016)
31.	*Moringa oleifera*	*Aspergillus flavus*	Fenaclone	Rajeshwari et al. (2016)
32.	*Hypocrea virens*	*Premna serratifolia*	Epidithiodioxopiperazine, gliotoxin, bisdethiobis(methylthio)gliotoxin	Ratnaweera et al. (2016)
33.	*Rauvolfia serpentina*	*Colletotrichum* sp., *Fusarium* sp., and *Cladosporium* sp.	Methanol	Singh et al. (2016)
34.	*Acalypha indica*	*Phoma* sp.	Terpenoids	Sowparthani (2016)
35.	*Santalum album*	*Fusarium oxysporum, Fusarium solani, Histoplasma* sp., *Periconia* sp., and *Pestalotiopsis* sp.	Distilled water, ethanol	Tapwal et al. (2016)
36.	*Picea mariana* and *Picea rubens*	*Diaporthe maritima*	Dihydropyrones, phomopsolides, alpha-pyrone	Tanney et al. (2016)
37.	*Schinus terebinthifolius*	*Alternaria* sp.	E-2-hexyl-cinnamaldehyde and two compounds of the pyrrolopyrazine alkaloids	Tonial et al. (2016)
38.	*Buxus sinica*	*Colletotrichum* sp.	Colletotrichone A	Wang et al. (2016a, b)
39.	*Eugenia jambolana*	*Aspergillus niger* and *A. terreus*	Ethyl acetate	Yadav et al. (2016)
40.	*Lonicera japonica*	*Fusarium* sp.	Methanol	Zhang et al. (2016b)
41.	*Sapium ellipticum*	*Penicillium tropicum*	Cyclohexapeptide, penitropeptide, and a new polyketide, penitropone	Zeng et al. (2016)

(continued)

Table 7.3 (continued)

S. no.	Medicinal plants	Fungal endophytes	Extract/compound isolated	Reference
42.	*Panax notoginseng*	*Acremonium* sp.	Ethyl acetate	Zheng et al. (2016)
		Alternaria sp.		
		Arthrinium sp.		
		Aspergillus sp.		
		Botryotinia sp.		
		Chaetomium sp.		
		Cladosporium sp.		
		Colletotrichum sp.		
		Dictyosporium sp.		
		Fusarium sp.		
		Humicola sp.		
		Ilyonectria sp.		
		Mucor sp.		
		Myrothecium sp.		
		Penicillium sp.		
		Periconia sp.		
		Pestalotiopsis sp.		
		Phialophora sp.		
		Phoma sp.		
		Phomopsis sp.		
		Plectosphaerella sp.		
		Thielavia sp. and *Trichoderma* sp.		
43.	*Edgeworthia chrysantha*	*Fusarium oxysporum*	Beauvericin	Zhang et al. (2016a)
44.	*Mallotus philippensis*	*Alternaria* sp., *Pestalotiopsis* sp., and *Phomopsis* sp.	Ethyl acetate	Gangwar et al. (2015)

45.	*Bauhinia forficata*	*Aspergillus ochraceus,*	Ethyl acetate	Bezerra et al. (2015)
		Gibberella baccata, Penicillium commune, and *P. glabrum*		
46.	*Caesalpinia echinata*	*Xylaria* sp.	Ethyl acetate	Campos et al. (2015)
		Nectria sp.		
		Fusarium sp., *Epicoccum* sp.		
		Talaromyces sp. and *Aspergillus* sp.		
47.	*Carapa guianensis*	*Diaporthe mayteni, Endomelanconiopsis, Colletotrichum* sp., *Guignardia mangiferae, Pestalotiopsis* sp., and *Diaporthe melonis*	Ethanol	Ferreira et al. (2015)
48.	*Asclepias sinaica*	*Penicillium chrysogenum* and *Alternaria alternate*	Ethyl acetate	Fouda et al. (2015)
49.	*Dioscorea composita*	*Fusarium* sp. and *Alternaria* sp.	Steroidal saponins	Gupta et al. (2015)
50.	*Opuntia humifusa*	*Biscogniauxia mediterranea*	5-Methylmellein	Silva-Hughes et al. (2015)
51.	*Senecio kleinia*	*Phoma* sp.	Sclerodione, atrovenetinone	Hussain et al. (2015)
52.	*Avicennia officinalis*	*Acremonium* sp., *Cladosporium* sp., *Curvularia* sp., and *Saccharomyces* sp.	Ethyl acetate	Job et al. (2015)
53.	*Tridax procumbens*	*Alternaria* sp.	Methanol, chloroform, ethyl acetate, and petroleum ether	Kumar et al. (2015)
54.	*Tectona grandis*	*Diaporthe phaseolorum*	Ethyl acetate	Kumala et al. (2015)
55.	*Mahonia fortune*	*Diaporthe* sp.	Tetracyclic Triterpenoid	Li et al. (2015a)
56.	*Taxus chinensis*	*Pestalotiopsis microspora*	α-Pyrone derivative	Li et al. (2015c)
57.	*Tephrosia purpurea*	*Penicillium griseofulvum* and *Aspergillus oryzae*	Broth	Luo et al. (2015)

(continued)

Table 7.3 (continued)

S. no.	Medicinal plants	Fungal endophytes	Extract/compound isolated	Reference
58.	*Avicennia marina*	*Penicillium brocae*	Sulfide diketopiperazines	Meng et al. (2015)
59.	*Rauwolfia serpentina*	*Colletotrichum gloeosporioides, Penicillium* sp., and *Aspergillus awamori*	Ethanol	Nath et al. (2015)
60.	*Panax ginseng*	*Phoma terrestris*	N-amino-3-hydroxy-6-meth oxyphthalimide and 5H–dibenz [B, F] azepine	Park et al. (2015)
61.	*Mikania glomerata*	*Diaporthe citri*	Ethyl acetate	Polonio et al. (2015)
62.	*Crescentia cujete*	*Nigrospora sphaerica, Fusarium oxysporum, Gibberella moniliformis,* and *Beauveria bassiana*	Aspirin and diethyl phthalate	Prabukumar et al. (2015)
63.	*Artemisia annua*	*Cladosporium* sp.	*Ethyl acetate*	Purwantini et al. (2015)
64.	*Aegle marmelos, Coccinia indica, Moringa oleifera*	*Cladosporium oxysporum*	Taxol	Raj et al. (2015)
65.	*Combretum latifolium*	*Gliomastix polychroma*	Ethyl acetate	Rao et al. (2015b)
66.	*Cryptolepis buchanani*	*Phomopsis liquidambaris*	Ethyl acetate	Rao et al. (2015a)
67.	*Opuntia dillenii*	*Fusarium* sp.	Equisetin	Ratnaweera et al. (2015b)
68.	*Cyperus rotundus*	*Rhizoctonia solani*	Solanioic acid	Ratnaweera et al. (2015a)
69.	*Abies* sp.	*Lophodermium pinastri, L. seditiosum,* and *Phoma herbarum*	Methanol, ethyl acetate, and dichloromethane	Ravnikar et al. (2015)
	Cedrus sp., *Juniperus* sp., *Larix* sp., *Metasequoia* sp., *Picea* sp.,			
	Pinus sp.			
	Taxus sp., *Sambucus* sp., *Calluna* sp., and *Centaurea* sp.			
70.	*Calophyllum apetalum*	*Myrothecium* sp.	Methanol	Ruma et al. (2015)
	Garcinia morella			

71.	*Rhizophora mucronata, Excoecaria agallocha*	*Fusarium proliferatum*	Ethyl acetate	Salini et al. (2015)
72.	*Indigofera suffruticosa*	*Nigrospora sphaerica* and *Pestalotiopsis maculans*	Methanol, ethyl acetate	Santos et al. (2015)
73.	*Cinnamomum camphora*	*Muscodor tigerii*	4-Octadecylmorpholine, 1-tetradecanamine, N,N-dimethyl ,and 1,2- benzenedicarboxylic acid, mono(2-ethylhexyl) ester.	Saxena et al. (2015)
74.	*Tsuga heterophylla*	*Gloeosporium* sp.	6-Pentyl-2H-pyran-2-one	Schaible et al. (2015)
75.	*Caesalpinia sappan, Alternanthera sessilis*	*Trichoderma* sp., *Aspergillus* sp., *Fusarium* sp., and *Trichoderma* sp.	Ethyl acetate	Srinivas et al. (2015)
	Sapindus laurifolius			
	Basella alba and *Acalypha indica*			
76.	*Prosopis juliflora*	*Colletotrichum gloeosporioides* and *Paecilomyces lilacinus*	Ethyl acetate	Srivastava and Anandrao (2015)
77.	*Phragmites communis*	*Phoma* sp.	Barceloneic acid C	Xia et al. (2015)
78.	*Cephalotaxus hainanensis*	*Neonectria macroconidia, Xylaria* sp., and *Verticillium bulbillosum*	Ethyl acetate	Yang et al. (2015)
79.	*Swietenia macrophylla*	*Aspergillus terreus*	Di-n-octyl phthalate	Yin et al. (2015)
80.	*Dracaena draco*	*Botryodiplodia theobromae*	Dipeptides (maculosin and L,L-cyclo(leucylprolyl)), alkaloid (norharman), coumarin and isocoumarins (bergapten, meranzin, and monocerin), sesquiterpene (dihydrocumambrin A), aldehyde (formyl indanone), fatty alcohol (halaminol A), and fatty acid amide (palmitoleamide, palmitamide, capsi-amide and oleamide)	Zaher et al. (2015a)
81.	*Ginkgo biloba*	*Aspergillus* sp.	Xanthoascin	Zhang et al. (2015a)
82.	*Acanthus ilicifolius*	*Aspergillus flavipes*	Phenyl derivatives: aromatic butyrolactones, flavipesins A and B	Bai et al. (2014)

(continued)

Table 7.3 (continued)

S. no.	Medicinal plants	Fungal endophytes	Extract/compound isolated	Reference
83.	*Xanthium sibiricum*	*Eupenicillium* sp.	Eupenicinicols A and B, butylitaconic acid, and (2S)-hexylitaconic acid	Li et al. (2014a)
84.	Australian dry rainforests	*Preussia* sp.	Ethyl acetate	Mapperson et al. (2014)
85.	*Hyptis dilatata*	*Pestalotiopsis mangiferae*	Polyhydroxylated macrolide: mangiferaelactone	Ortega et al. (2014)
86.	*Tribulus terrestris*	*Aspergillus fumigatiaffinis*	Neosartorin	Ola et al. (2014)
87.	*Vitex negundo*	*Pestalotiopsis* sp., *Fusarium* sp., *Fusarium* sp., and *Alternaria* sp.	Ethyl acetate	Palanichamy et al. (2014)
	Justicia gendarussa, Ocimum basalicum			
	Costus spicatus and *Glycosmis pentaphylla*			
88.	*Aloe vera*	*Talaromyces wortmannii*	Methanol	Pretsch et al. (2014)
89.	*Anoectochilus setaceus*	*Xylaria* sp.	Helvolic acid	Ratnaweera et al. (2014)
90.	*Plumeria acuminate* and *Plumeria obtusifolia*	*Colletotrichum gloeosporioides* and *Fusarium oxysporum*	Ethyl acetate	Ramesha and Srinivas (2014)
91.	*Nothapodytes foetida*	*Bionectria ochroleuca*	Ethyl acetate	Samaga et al. (2014)
92.	*Cupressus arizonica, C. sempervirens var. cereiformis,* and *Thuja orientalis*	*Alternaria alternata, A. pellucid,* and *A. tangelonis*	Methanol	Soltani and Moghaddam (2014)
93.	*Allium sativum*	*Trichoderma brevicompactum*	Extract	Shentu et al. (2014)
94.	*Madhuca indica*	*Aschersonia* sp.	Ethyl acetate	Verma et al. (2014)
95.	*Pinus wallichiana*	*Tritirachium oryzae, Truncatella spadicea,* and *Fusarium larvarum*	Methanol	Qadri et al. (2014)
96.	*Melia azedarach*	*Botryosphaeria dothidea*	Pycnophorin, stemphyperylenol	Xiao et al. (2014a)
97.	*Brguiera sexangula var. rhynchopetala*	*Stemphylium* sp.	Pyrone derivatives, infectopyrones A and B	Zhou et al. (2014b)
98.	*Bruguiera gymnorrhiza*	*Penicillium* sp.	Penibruguieramine A:Pyrrolizidine alkaloid	Zhou et al. (2014a)
99.	*Rhizophora stylosa*	*Aspergillus nidulans*	Aniquinazolines A–D	An et al. (2013)

100.	Amazon rainforest biome	*Chaetomium globosum*,	Pyrrocidine C	Casella et al. (2013)
		Xylaria cubensis and *Lewia infectoria*		
101.	Amazon forests	*Xylaria feejeensis*	Xyolide	Baraban et al. (2013)
102.	*Camptotheca acuminata*	*Botryosphaeria dothidea*	9-Methoxycamptothecin	Ding et al. (2013)
103.	*Vitex negundo*	*Phomopsis* sp.	Ethyl acetate, methanol, hexane	Desale and Bodhankar (2013)
104.	*Ceratonia siliqua*	*Penicillium citrinum*	Alkaloids and polyketides	El-Neketi et al. (2013)
105.	*Trichilia elegans*	*Phomopsis longicolla*	3-Nitropropionic acid	Flores et al. (2013)
106.	*Artabotrys odoratissimus*, *Cassia auriculata*, *Guazuma ulmifolia*, and *Terminalia catappa*	*Phomopsis* sp.	Ethyl acetate	Gopinath et al. (2013)
107.	*Cannabis sativa*	*Aspergillus niger*, *A. flavus*, *A. nidulans*, *Penicillium chrysogenum*, *P. citrinum*, *Phoma* sp.	Ethanol	Gautam et al. (2013)
		Rhizopus sp., *Colletotrichum* sp., *Cladosporium* sp., and *Curvularia* sp.		
108.	*Rhizophora stylosa*	*Alternaria tenuissima*	Tricycloalternarene 3, djalonensone	Hong et al. (2013)
109.	*Ocimum tenuiflorum*	*Penicillium citrinum*	Polyketides and alkaloids	Lai et al. (2013)
110.	*Ulmus macrocarpa*	*Microsphaeropsis arundinis*	Arundinols A–C and Arundinones A and B	Luo et al. (2013)
111.	*Bauhinia guianensis*	*Aspergillus* sp.	Alkaloids: fumigaclavine C and pseurotin A	Pinheiro et al. (2013)
112.	Forests of Western Ghats	*Xylaria* sp.	Ethyl acetate	Rajulu et al. (2013)
113.	*Cymodocea serrulata*, *Halophila ovalis*, and *Thalassia hemprichii*	*Hypocreales* sp., *Trichoderma* sp., and *Penicillium* sp., *Fusarium* sp. and *Stephanonectria* sp.	Ethyl acetate	Supaphon et al. (2013)

(continued)

Table 7.3 (continued)

S. no.	Medicinal plants	Fungal endophytes	Extract/compound isolated	Reference
114.	*Triticum durum*	*Aspergillus* sp., *Alternaria* sp., *Penicillium* sp., *Cladosporium* sp., *Chaetomium* sp., and *Phoma* sp.	Ethyl acetate	Sadrati et al. (2013)
115.	*Dioscorea zingiberensis*	*Berkleasmium* sp.	Palmarumycins C3 and C4	Mou et al. (2013)
116.	*Cedrus deodara, Pinus roxburghii,* and *Abies pindrow*	*Trichophaea abundans, Diaporthe phaseolorum* and *Fusarium redolens*	Methanol	Qadri et al. (2013)
117.	*Ficus pumila*	*Phomopsis* sp.	Ethyl acetate	Rakshith et al. (2013)
118.	*Theobroma cacao*	*Epicoccum* sp.	Polyketides: Epicoccolides	Talontsi et al. (2013)
119.	*Rhododendron tomentosum*	*Fusarium tricinctum*	Polypeptides	Tejesvi et al. (2013)
120.	*Panax ginseng*	*Fusarium* sp.	Triterpenoid saponin	Wu et al. (2013b)
121.	*Rheum palmatum*	*Fusarium solani*	Rhein	You et al. (2013)
122.	*Taraxacum mongolicum*	*Phoma* sp.	2-Hydroxy-6-methylbenzoic acid	Zhang et al. (2013a)
123.	*Clidemia hirta*	*Cryptosporiopsis* sp.	1-(2,6-Dihydroxyphenyl)pentan-1-one (2) and (Z)-1-(2-(2- butyryl-3-hydroxyphenoxy)-6-hydroxyphenyl)-3-hydroxybut-2-en-1-one	Zilla et al. (2013)

Pestalotiopsis sp. isolated from *Taxus brevifolia* (Yew tree) has been reported for immunosuppressive pestalotiopsins A and B (Pulici et al. 1996). Another immunosuppressive compound cytochalasin U has been produced by *Pestalotia* sp. isolated from *Cassia fistula* (Burres et al. 1992).

Subglutinols A and B, two immunosuppressive compounds, have been obtained from *Fusarium subglutinans*, inhabiting *Tripterygium wilfordii*. Both the compounds were nontoxic and very potent in the thymocyte proliferation (TP) assays and mixed lymphocyte reaction (MLR) (Lee et al. 1995). Cyclosporine-A, an immunosuppressive drug isolated from endophyte, was found to be 104 times more potent in the TP assay and roughly as potent in the MLR assay (Bentley et al. 2000). Similarly, *Pestalotiopsis leucothoe* from *Tripterygium wilfordii* has been documented to produce three compounds designated as BS, GS, and YS. All the compounds showed variable effects on T and B cells and monocytes. Hence, these represent a new source of immunomodulatory compounds for the treatment of human immune-mediated diseases. However, the structure of the compounds has not been elucidated yet (Kumar et al. 2005). Another potent immunosuppressive fungal metabolite used for the treatment of autoimmune diseases and organ transplantations has been documented to be produced by fungal endophytes *Penicillium*, *Aspergillus*, *Byssochlamys*, and *Septoria* species. The compound was identified as mycophenolic acid (Larsen et al. 2005).

Ren et al. (2008) have recorded collutelin-A and cyclosporine-A from *Colletotrichum dematium* inhabiting *Pteromischum* sp. growing in the tropical forests of Costa Rica. The compound displayed strong immunosuppressive activity by inhibiting CD4 T-cell activation of interleukin-2 production, whereas cyclosporine-A showed moderate activity in the same experiment.

Recently, an endophyte *Phomopsis longicolla* yielded four tetrahydroxanthone dimers, of which phomoxanthone A showed immunostimulation and pro-apoptotic activity. The compound exhibited immunostimulation by activating T lymphocytes, NK cells, and macrophages (Ronsberg et al. 2013). Similarly, *Botryosphaeria dothidea* isolated from *Kigelia africana* has been evaluated for its immunomodulatory potential. It was found to suppress T-cell proliferation by 50% and also inhibited TNF-α production (Katoch et al. 2014). These examples depict the potentiality of endophytes for exploring rare and uncommon immunomodulatory compounds.

7.3.5 Antidiabetic Compounds

Diabetes mellitus is the highest cause of death among other chronic diseases. It cannot be cured but controlled. In 2015, about 415 million people had diabetes worldwide, with type II diabetes accounting for about 90% of the cases (Cui et al. 2016). It can cause complications such as cardiovascular disorders, kidney failure, impotency, blindness, and gangrene. One of the strategies used to cure this is by inhibiting digestion of complex carbohydrates in the small intestine into glucose, resulting in the reduction of intake of glucose into the blood. Alpha-glucosidase and alpha-amylase inhibitors are known to possess such activity. Medicinal plants for diabetes are a potential source of microbes producing alpha-glucosidase inhibitors.

α-Glucosidase is an important enzyme for breaking down complex carbohydrates for absorption; α-glucosidase inhibitors such as acarbose, miglitol, and voglibose, all originating from natural products, are widely used to treat type II diabetes, indicating that natural products are an important source of antidiabetic drugs.

Syncephalastrum sp. isolated from *Adhatoda beddomei* exhibits antidiabetic activity by inhibiting α-amylase (Prabavathy and Valli 2013). The alpha-glucosidase inhibitory activity of endophytic fungi isolated from *Cassia siamea* has also been reported (Munim et al. 2013). α-Amylase inhibitor from endophytic fungi of antidiabetic medicinal plants of the Western Ghats retards the liberation of glucose from dietary complex carbohydrates and delays the absorption of glucose. Antidiabetic activity of ethanolic and acetone extracts of endophytic fungi *Syncephalastrum racemosum* isolated from the seaweed *Gracilaria corticata* by alpha-amylase inhibition has been reported (Ushasri and Anusha 2015). Similarly, endophytic *Alternaria* sp. isolated from *Viscum album* exhibited strong antidiabetic activity on alloxan-induced diabetic rats (Govindappa et al. 2015). The additional examples of antidiabetic activity of fungal endophytes have been tabulated (Table 7.4).

7.3.6 Acetylcholinesterase Inhibitory Activity of Fungal Endophytes

Alzheimer's disease is a neurodegenerative disease of the central nervous system. The first clinical manifestation is recent memory dysfunction, which is followed by persistent intellectual impairment, loss of judgment and reasoning abilities, aphasia, and movement dysfunction. A study found that of the 10–15% of elderly people with different degrees of dementia, approximately 60–70% of the cases are due to Alzheimer's disease. However, the pathogenesis of senile dementia is not clear. Cholinergic nerve injury is the most accepted hypothesis of Alzheimer's disease pathogenesis, and if this is true, acetylcholinesterase inhibitors could be developed to effectively improve Alzheimer's disease treatment.

The use of acetylcholinesterase inhibitors is the most effective approach to treating the cognitive symptoms of Alzheimer's disease (Zhang et al. 2011) and has other possible therapeutic applications in the treatment of Parkinson's disease, senile dementia, and ataxia (Zhang et al. 2011; Singh et al. 2012). Acetylcholinesterase inhibitors such as eserine, tacrine, donepezil, rivastigmine, and galantamine are the drugs currently approved for the treatment of Alzheimer's disease (Anand and Singh 2013). The additional examples of acetylcholinesterase inhibitory activities of endophytic fungal isolates have been tabulated (Table 7.5).

Table 7.4 Antidiabetic activity of endophytic fungi isolated from medicinal plants

S. no.	Medicinal plants	Fungal endophytes	Bioactivity	Extract/compounds isolated	References
1.	*Cupressus torulosa*	*Penicillium oxalicum*	Alpha-amylase inhibitory activity	Chloroform and methanol	Bisht et al. (2016)
2.	*Mangrove plants*	*Talaromyces amestolkiae*	α-Glucosidase inhibitory and antibacterial	Isocoumarins and benzofurans	Chen et al. (2016)
3.	*Sonneratia ovate*	*Nectria* sp.	α-Glucosidase inhibitory activity	Polyketides: Nectriacid B, nectriacid C	Cui et al. (2016)
4.	*Hintonia latiflora*	*Xylaria feejeensis*	α-Glucosidase inhibitors	Pestalotin 4′-O-methyl-β-mannopyranoside and 3S,4R-(+)-4-hydroxymellein	Chavez et al. (2015)
5.	*Viscum album*	*Alternaria* sp.	Antidiabetic	Lectin(N-acetylga lactosamine)	Govindappa et al. (2015)
6.	*Sonneratia apetala*	*Aspergillus* sp.	Antidiabetic	Methanol	Liu et al. (2015b)
				Isocoumarin derivatives	
				Aspergifuranone	
7.	*Cerbera manghas*	*Penicillium* sp.	α-Glucosidase inhibitory	(±)-penifupyrone and phenolic compounds	Liu et al. (2015a)
8.	*Acacia nilotica*	*Aspergillus awamori*	Antidiabetic	Peptide	Singh and Kaur 2016)
9.	*Tinospora. cordifolia*	*Cladosporium* sp.	α-Glucosidase inhibitors	Phenolic compound	Singh et al. (2015b)
10.	*Gracilaria corticata*	*Syncephalastrum racemosum*	Antidiabetic	Ethanol, acetone	Ushasri and Anusha (2015)
11.	*Momordica charantia* and *Trigonella foenumgraceum*	*Trichoderma atroviride* and *Stemphylium globuliferum*	Antidiabetic	Ethyl acetate	Pavithra et al. (2014)
12.	*Morus alba*	*Alternaria* sp.	Antidiabetic	Ethyl acetate	Zheng et al. (2014)
13.	*Salvadora oleoides*	*Aspergillus* sp.	Antidiabetic	2, 6-Di-tert-butyl-p-cresol and phenol, 2, 6-bis (1, 1-dimethylethyl)-4-methyl	Dhankar et al. (2013)
14.	*Ficus religiosa*	*Dendrophion nanum*	Antidiabetic	Herbarin (naphthoquinones)	Mishra et al. (2013)
15.	*Catharanthus roseus*	Fungal endophytes	Antidiabetic	Ethyl acetate	Rosaline and Agastian (2013)
16.	*Coscinium fenestratum*	*Fusarium solani*	Antidiabetic	Berberine	Vinodhini and Agastian (2013)

Table 7.5 Acetylcholinesterase inhibitory activity of endophytic fungi isolated from medicinal plants

S. no.	Medicinal plants	Fungal endophytes	Activity	Extract/compounds isolated	References
1.	*Catharanthus roseus*	*Alternaria alternata*	Acetylcholinesterase inhibitory	Altenune	Bhagat et al. (2016)
2.	*Panax notoginseng*	*Chaetomium globosum*	Acetylcholinesterase inhibitory	3-Methoxy epicoccone, epicoccolides B	Li et al. (2016a)
3.	*Huperzia serrata*	*Colletotrichum* sp.,	Acetylcholinesterase inhibitory	Ethanol	Wang et al. (2016b)
4.	*Phlegmariurus phlegmaria*	*Ceriporia lacerate*	Acetylcholinesterase inhibitory	Chloroform	Zhang et al. (2015b)
5.	*Huperzia serrata*	*Paecilomyces tenuis YS-13*	Acetylcholinesterase inhibitory	Huperzine A	Su and Yang (2015)

7.3.7 Endophytes as a Source of Silver Nanoparticles

Nanotechnology is the ability to work at atomic, molecular, and supramolecular levels. It involves production, manipulation, and use of material ranging from less than a micron. Nanoparticles have a wide range of applications in diverse fields like catalysis, sensors, medicine, etc., and these depend on the physical and optical properties of the particles. As the field of nanotechnology is progressing, the knowledge of physical and chemical characteristics of nanoparticles has greatly increased. The most well-known nanoparticles are made from silver metal. Silver is used in medical fields as a topical bactericide. Silver nanoparticles possess broad-spectrum multifunctional activities and have the promising therapeutic potential to be used for the treatment of burns and variety of infections. The emphasis is being given to their use in prophylaxis and treatment of different types of cancers and microbial infections. The silver nanoparticles can change the 3D structure of proteins by interfering with S–S bond and block the functional operations of microorganisms (Sunkar and Nachiyar 2013). In the recent years apart from silver, gold nanoparticles have also been the focus of interest because of their emerging applications in the areas such as bioimaging and biosensors (Alappat et al. 2012).

Silver nanoparticles can be synthesized using chemical approaches, but it leads to the presence of traces of toxic chemicals absorbed on the surface which is undesirable in the medical applications (Bharathidasan and Panneerselvam 2012). Moreover, a lot of hazardous by-products are generated using this approach. Considering these facts, an alternative approach for nanomaterial synthesis has to be thought of. An important aspect in the field of nanotechnology is to develop a reliable and eco-friendly process for the synthesis of nanoscale materials.

Green technology is emerging nowadays and involves the use of microorganisms in the synthesis of nanoparticles (Razavi et al. 2015). The synthesis of nanoparticles using biological systems provides new routes to develop nanoparticles with desired

Table 7.6 Nanoparticle producing endophytic fungi isolated from medicinal plants

S. no.	Endophyte	Plant	Nanoparticle	Activity	References
1.	*Penicillium* sp.	*Calophyllum apetalum*	Ag-Nps	Not reported	Chandrappa et al. (2016)
2.	*Aspergillus versicolor*	*Centella asiatica*	Ag-Nps	Antimicrobial Antioxidant	Netala et al. (2016)
3.	*Fusarium solani*	*Withania somnifera*	Ag-Nps	Antibacterial Cytotoxic	Vijayan et al. (2016)
4.	*Colletotrichum* sp.	*Andrographis paniculata*	Ag-Nps	Antibacterial	Azmath et al. (2016)
5.	*Fusarium* sp.	*Withania somnifera*	Ag-Nps	Antibacterial	Singh et al. (2015a)
6.	*Penicillium* sp. and *Alternaria* sp.	*Gloriosa superba*	Ag-Nps	Antibacterial	Devi et al. (2014)
7.	*Cryptosporiopsis ericae*	*Potentilla fulgens*	Ag-Nps	Antimicrobial	Devi and Joshi (2014)
8.	*Penicillium* sp.	*Curcuma longa*	Ag-Nps	Antimicrobial	Singh et al. (2014)
9.	*Epicoccum nigrum*	*Phellodendron amurense*	Ag-Nps	Antifungal	Qian et al. (2013)
10.	*Penicillium* sp.	*Centella asiatica*	Ag-Nps	Antimicrobial	Devi et al. (2012)

properties for making their exploitation possible in diverse fields (Pugazhenthiran et al. 2009). The nonpathogenic and eco-friendly behavior of endophytes makes them as good candidates for the synthesis of nanoparticles (Kaul et al. 2014). Fungal endophytes can be exploited for large-scale extracellular synthesis of nanoparticles which makes the downstream processing easier (Verma et al. 2011). Various studies on fungal endobiome described their ability to synthesize nanoparticles particularly silver nanoparticles (Ag-Nps) (Table 7.6).

7.3.8 Antitubercular Compounds

Tuberculosis is currently a major public health problem due to the advent of multidrug-resistant (MDR) forms of bacilli as well as human immunodeficiency virus epidemics. The World Health Organization (WHO) estimated that currently 50 million people are infected and 1,500 people die each hour from tuberculosis worldwide. After emergence and spread of *Mycobacterium tuberculosis*-resistant strains to multiple drugs, the search for new antimycobacterial agents is timely. The globe recognized medicinal plants as a repository for fungal endophytes with metabolites containing the novel molecular structure and biologically active compounds against various human pathogenic diseases for potential use in modern medicine. Endophytic fungi are a good source for exploring the possibility of new antimycobacterial drugs. Recently, polyketide such as penialidin C has been isolated from endophytic

Penicillium sp. of *Garcinia nobilis* that exhibits significant activity against *Mycobacterium tuberculosis* (Jouda et al. 2016a).

A new isofuranonaphthalenone isolated from endophytic fungus *Nodulisporium* sp. of *Antidesma ghaesembilla* displayed antimycobacterial activity with IC_{50} values of 3.125 μg/mL (Prabpai et al. 2015). Asperlones A and B, dinaphthalenone derivatives, asperterpenoid A, and alterporriol-type dimmers from mangrove endophytic fungus *Aspergillus* sp. and *Alternaria* sp., respectively, exhibited potent inhibitory effects against *Mycobacterium tuberculosis* protein tyrosine phosphatase B (MptpB) with IC_{50} values of 4.24 ± 0.41, 8.70, and 2.2 μM, respectively (Xia et al. 2014, 2015; Huang et al. 2013). Peniphenones A−D from endophytic *Penicillium dipodomyicola* of *Acanthus ilicifolius* exhibited strong inhibitory activity against *Mycobacterium tuberculosis* protein tyrosine phosphatase B (MptpB) (Li et al. 2014b).

Numerous secondary metabolites are known from endophytic strains of *Phoma* sp. Phomapyrrolidones A−C, alkaloids from the endophytic fungus *Phoma* sp. of *Saurauia scaberrinae*, possess significant antitubercular activity (Wijeratne et al. 2013). Penicolinates A–E from endophytic *Penicillium* sp. of grasses belonging to Poaceae family were found to possess antitubercular activity (Intaraudom et al. 2013). Colletotriolide, a macrolide isolated from *Colletotrichum* sp. endophytic to *Pandanus amaryllifolius*, exhibited an inhibition of greater than 90% at 128 μg/mL for *M. tuberculosis* (Bungihan et al. 2013).

7.3.9 Antihelminthic, Antiplasmodial, and Antileishmanial Compounds

Parasitic diseases such as malaria and leishmaniasis affect millions of people worldwide and pose a major health problem in developing countries. Malaria and leishmaniasis have affected major population with increasing number of new cases each year. Leishmaniasis is caused by protozoan parasites that belong to the genus *Leishmania* and is transmitted by the bite of certain species of sand fly (subfamily *Phlebotominae)*. Most of the current drugs used to treat parasitic diseases are decades old and have many limitations, including the emergence of drug resistance. For leishmaniasis, either the first-line pentavalent antimonials or second-line drugs such as amphotericin B are available, which are costly and have serious side effects and are getting resistant to pathogens after treatment for several weeks, and hence there is a need for new antileishmanial agents with improved efficacy and fewer side effects for both visceral and cutaneous leishmaniasis.

Malaria remains the world's most devastating human parasitic infection, afflicting more than 500 million people and causing about 2.5 million deaths each year. It is an infectious disease caused by the main four protozoan species of the genus *Plasmodium* (*Plasmodium falciparum*, *P. malariae*, *P. ovale*, and *P. vivax*) (Mendis et al. 2009). The increasing resistance to existing antimalarial drugs demands the exploration of novel drugs and treatment efforts to eliminate this deadly disease. Natural products contain a great variety of chemical structures and have been screened for antiplasmodial activity as potential sources of new antimalarial drugs (De Silva et al. 2013).

The development of anthelmintic resistance in helminths reported in a number of countries gives a clear indication that control programs based exclusively on their use are not sustainable. The development of integrated programs to control helminths is vital, but such control programs require viable alternatives to the use of anthelmintics. The history of herbal medicine is almost as old as human civilization. Medicinal plants have served through ages, as a constant source of medicaments for the exposure of a variety of diseases. The endophytic fungi act as an alternative to provide a rich source of anthelmintics, antibacterials, and insecticides.

Screening of mangrove endophytic fungi for antimalarial natural products displays the most favorable bioactivity profile (Calcul et al. 2013). Two unusual dibenzofurans, preussiafurans A–B, isolated from the fungus *Preussia* sp. occurring in *Enantia chlorantha* possessed antiplasmodial activity against erythrocytic stages of chloroquine-resistant *Plasmodium falciparum* (Talontsi et al. 2014). Reduced perylenequinone derivatives from an endophytic *Alternaria* sp. isolated from *Pinus ponderosa* were found to have antileishmanial and antimalarial activities (Idris et al. 2015). Meroterpenoid, isocoumarin, and phenol derivatives isolated from seagrass endophytic fungi *Pestalotiopsis* sp. exhibited antimalarial activity (Arunpanichlert et al. 2015).

Chemical and biological investigation for the endophytic fungus *Nigrospora sphaerica* led to the isolation of nigrosphaerin A, a new isochromene derivative with moderate antileishmanial activity having IC50 values of 30.2, 26.4, and 36.4 μg/ml, respectively (Metwaly et al. 2013). Enniatins (ENs), a group of antibiotics commonly produced by various strains of *Fusarium*, are six-membered cyclic depsipeptides formed by the union of three molecules of D-α-hydroxyisovaleric acid and three N-methyl-L-amino acids. The endophyte *Fusarium tricinctum* isolated from the fruits of *Hordeum sativum* showed antileishmanial activities (Zaher et al. 2015b).

The genus *Aspergillus* represents a diverse group of fungi, which are among the most abundant fungi in the world. Biologically active metabolites from endophytic fungus *A. terreus* isolated from the roots of *Carthamus lanatus* were found to have antileishmanial activity. Terrenolide S, a new butenolide derivative, together with (22E,24R)-stigmasta-5,7,22-trien-3-β-ol and stigmast-4- ene-3-one exhibited antileishmanial activity toward *Leishmania donovani* with IC50 values of 27.27, 15.32, and 27.27 μM, respectively, and IC90 values of 167.03, 40.56, and 14.68 μM, respectively (Elkhayat et al. 2016).

7.3.10 Extracellular Enzymes

Among a large number of microorganisms capable of producing useful enzymes, filamentous fungi are of particular interest due to their easy cultivation and high production of extracellular enzymes. Fungal enzymes are gaining importance in agriculture, industry, and human health as they are often more stable (at high temperature and extreme pH) than the enzymes derived from plants and animals (Maria et al. 2005). Fungal endophytes known to be the treasure of new compounds represent an interesting alternative to be explored for enzyme production with different potentialities (Bhagobaty and Joshi 2012). Diverse array of extracellular enzymes produced by endophytes include cellulases, chitinases, amylases, lipases and proteases, pectinases, laccase, etc., having wide application in various industrial processes such as baking, brewing, textile, confectionaries, paper, pulp and leather, manufacturing corn syrup, hydrolyzing milk proteins, removing stains, separating racemic mixtures of amino acids, bioremediation, and biosensing (Kaul et al. 2014). The extracellular enzyme production varies among the fungal isolates. By optimizing the conditions, these isolates can prove to be a novel source of industrially relevant enzymes.

Different studies have been carried out on the screening of endophytes for enzyme production. For example, 50 fungal strains isolated from medicinal plants (*Alpinia calcarata, Bixa orellana*, *Calophyllum inophyllum*, and *Catharanthus roseus*) were screened for their ability to produce extracellular enzymes such as amylase, cellulase, laccase, lipase, pectinase, and protease on solid media. Variation in the enzyme production was recorded among the isolates. The array of enzymes produced by different fungal isolates often depends on the host and their ecological factors (Sunitha et al. 2013).

Endophytic fungi isolated from *Opuntia ficus-indica* were analyzed for preliminary screening for enzyme production. Among the 24 isolates which were studied, *Aspergillus japonicus* presented pectinolytic activity, and cellulase activity was exhibited by *Xylaria* (Bezerra et al. 2012).

Similarly, 30 fungal endophytes isolated from indigenous monocotyledonous and dicotyledonous plants have been evaluated for amylase, cellulase, protease, lipase, and laccase activity, and most of them showed positive results (Patel et al. 2013). Endophytes from *Lantana camara* have been screened for amylase, lipase, and laccase production, and three isolates were shown to produce three enzymes (Desire et al. 2014). Fungal endophytes isolated from *Butea monosperma*, a tropical medicinal plant, and *Bacopa monnieri* were found to be potential producers of industrial enzymes such as amylase, cellulase, pectinase, protease, and lipase (Tuppad and Shishupala 2014; Katoch et al. 2014a, b). The extracellular enzymatic activity of endophytic fungi *Cladosporium* sp., *Rhizoctonia* sp., *Aspergillus* sp., *Chaetomium* sp., *Biosporous* sp., *Fuzarium* sp., *Curvularia* sp., *Cladosporium* sp., and *Colletotrichum* sp. isolated from medicinal plants *Azadirachta indica*, *Citrus limon*, *Gossypium hirsutum*, *Magnolia champaca*, *Datura stramonium*, *Piper betle*, and *Phyllanthus emblica* has been reported (Patil et al. 2015a). Endophytic fungi from leaves of *Calophyllum inophyllum* produce extracellular enzymes such as amylase, protease, lipase, and cellulase (Patil et al. 2015a). Endophytic microbial resources producing extracellular enzymes can establish a unique niche for ecological adaptation during symbiosis with the host frankincense tree *Boswellia sacra* (Khan et al. 2016). A few more examples of common enzymes isolated from fungal endobiome of medicinal plants are enlisted below (Table 7.7).

Table 7.7 Extracellular enzymes produced by fungal endophytes of medicinal plants

S. no.	Fungal endophytes	Medicinal plants	Enzyme	References
1.	*Corchorus olitorius*	*Aspergillus terreus*	Xylanase	Ahmed et al. (2016a)
2.	Marine habitat	*Aspergillus* sp.	L-asparaginase	Ahmed et al. (2016b)
3.	*Cupressus torulosa*	*Alternaria alternate*	Protease	Rajput et al. (2016)
4.	*Artemisia annua*	*Aspergillus* sp.	Amylolytic	Ogbonna et al. (2015)
5.	*Eurotium* sp.	*Curcuma longa*	Asparaginase	Jalgaonwala and Mahajan (2014)
6.	*Preussia minima*	*Eremophila longifolia*	Amylase	Zaferanloo et al. (2014a)
7.	*Alternaria alternate* and *Phoma herbarum*	*Eremophila longifolia*	Protease	Zaferanloo et al. (2014b)
8.	*Sordaria humana*	*Cedrus deodara* and *Pinus roxburghii*	Cellulase	Syed et al. (2013)

7.4 Conclusions

Fungal endobiome of medicinal plants is considered as an important and viable component of microbial biodiversity that offers a plethora of advantages to its host plant by producing bioactive secondary metabolites. In the continuous search for novel drug sources, endophytic fungi have proven to be a promising, largely untapped reservoir of natural products. A perusal of the literature indicates many ethnomedicinal plant species known to harbor potential endophytes that produce bioactive metabolites. Therefore, it is significant to bioprospect endophytes from medicinal plants for bioactive secondary metabolites. Bioactive metabolites from fungal endobiome could be a resolute solution to the present-day problems like the emergence of new diseases and resistance to existing drugs. The ability of endophytes to produce bioactive metabolites is influenced by its interaction with the host plant and its cross talk with other microbiota associated with the host. So it is very much significant to understand the mechanisms underlying the plant–microbe interaction. Improvization of isolation and purification methods needs to be done for commercial production of bioactive metabolites. Many novel and valuable compounds with antioxidant, anticancer, antimicrobial, immunomodulatory, and antidiabetic activities have been reported from fungal endophytes. This proves that fungal endobiome of medicinal plants certainly holds in them great potential to improve future in medicinal cure along with various industrial applications.

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References

Abdou R, Abdelhady MI (2015) Anticancer endophytic metabolites of the medicinal plant *Centaurea stoebe*. World J Pharm Pharm Sci 4:220–230

Abirami G, Boominathan M (2016) Antimicrobial activity of endophytic fungi isolated from medicinal plant *Hugonia mystax L.* J Acad Ind Res 4(12):257–262

Aharwal RP, Kumar S, Sandhu SS (2014) Isolation and antibacterial property of endophytic fungi isolated from Indian medicinal plant *Calotropis procera* (Linn.) R. Br. World J Pharm Pharm Sci 3(5):678–691

Ahmed M, Hussain M, Dhar MK, Kaul S (2012) Isolation of microbial endophytes from some ethnomedicinal plants of Jammu and Kashmir. J Natl Prod Plant Resour 2:215–220

Ahmed SA, Saleh SAA, Mostafa FA, Aty AAA, Ammar HAM (2016a) Characterization and valuable applications of xylanase from endophytic fungus *Aspergillus terreus* KP900973 isolated from *Corchorus olitorius*. Biocat Agri Biotechnol 7:134–144

Ahmed MMA, Dahab NA, Taha T, Hassan SMJ (2016b) Production, purification and characterization of L-Asparaginase from marine endophytic *Aspergillus* sp. ALAA-2000 under submerged and solid state fermentation. Microb Biochem Technol 7(3):165–172

Akone SH, Mandi A, Kurtan T, Hartmann R, Lin W, Daletos G, Proksch P (2016) Inducing secondary metabolite production by the endophytic fungus *Chaetomium* sp. through fungal-bacterial co-culture and epigenetic modification. Tetrahedron. doi:10.1016/j.tet.2016.08.022

Alappat CF, Kannan KP, Vasanthi NS (2012) Biosynthesis of Au nanoparticles using the endophytic fungi isolated from *Bauhinia variegata* L. Eng Sci Tech Int J 2:377–380

Al-Trabolsy ZBKA, Anouar EH, Zakaria NSS, Zulkeflee M, Hasan MH, Zin MM, Ahmad R, Sultan S, Weber JFF (2014) Antioxidant activity, NMR, X-ray, ECD and UV/vis spectra of (+)-terrein: experimental and theoretical approaches. J Mol Struct 1060:102–110

An CY, Li XM, Luo H, Li CS, Wang MH, Xu GM, Wang BG (2013) 4-Phenyl-3,4-dihydroquinolone derivatives from *Aspergillus nidulans* MA-143, an endophytic fungus isolated from the mangrove plant *Rhizophora stylosa*. J Nat Prod 76:1896–1901

Anand P, Singh B (2013) A review on cholinesterase inhibitors for Alzheimer's disease. Arch Pharm Res 36(4):375–399

Anitha D, Vijaya T, Pragathi D, Reddy NV, Mouli KC, Venkateswarulu N, Bhargav DS (2013) Isolation and characterization of endophytic fungi from endemic medicinal plants of Tirumala hills. Int J Life Sc Bt Pharm Res 2:367–373

Arora P, Wani ZA, Nalli Y, Ali A, Riyaz-UlHassan R (2016) Antimicrobial potential of thiodiketopiperazine derivatives produced by *Phoma* sp., an endophyte of *Glycyrrhiza glabra Linn*. Microb Ecol. doi:10.1007/s00248-016-0805

Arunpanichlert J, Rukachaisirikul V, Phongpaichit S, Supaphon O, Sakayaroj J (2015) Meroterpenoid, isocoumarin, and phenol derivatives from the seagrass-derived fungus *Pestalotiopsis* sp. PSU-ES194. Tetrahedron 71:882–888

Avinash KS, Ashwini HS, Babu HNR, Krishnamurthy YL (2016) Antimicrobial potential of crude extract of *Curvularia lunata*, an endophytic fungi isolated from *Cymbopogon caesius*. J Mycol doi.org/10.1155/2015/185821

Azmath P, Baker S, Rakshith D, Satish S (2016) Mycosynthesis of silver nanoparticles bearing antibacterial activity. Saudi Pharm J. doi:10.1016/j.jsps.2015.01.008

Bacon CW, White J (eds) (2000) Microbial endophytes. CRC Press, Boca Raton

Bai ZQ, Lin X, Wang Y, Wang Y, Zhou X, Yang B, Liu J, Yang X, Wang Y, Liu Y (2014) New phenyl derivatives from endophytic fungus *Aspergillus flavipes* AIL8 derived of mangrove plant *Acanthus ilicifolius*. Fitoterapia 95:194–202

Bai ZQ, Lin X, Wang J, Zhou X, Liu J, Yang B, Yang X, Liao S, Wang L, Liu Y (2015) New meroterpenoids from the endophytic fungus *Aspergillus flavipes* AIL8 derived from the mangrove plant *Acanthus ilicifolius*. Mar Drugs 13(1):237–248

Baraban EG, Morin JB, Phillips GM, Phillips AJ, Strobel SA, Handelsman J (2013) Xyolide, a bioactive nonenolide from an Amazonian endophytic fungus, *Xylaria feejeensis*. Tetrahedron Lett 54:4058–4060

Baral B, Shrestha VG, Laxmi Maharjan B, Teixeira Da Silva JA (2015) Phytochemical and antimicrobial characterization of *Rhododendron anthopogon* from high Nepalese Himalaya. Bot Lith 20(2):142–152

Basha N, Ogbaghebriel A, Yemane K, Zenebe M (2012) Isolation and screening of endophytic fungi from Eritrean traditional medicinal plant *Terminalia brownii* leaves for antimicrobial activity. Int J Green Pharm 6(1):40

Bentley R (2000) Mycophenolic acid: a one hundred year odyssey from antibiotic to immunosuppressant. Chem Rev 100(10):3801–3826

Berg G, Grube M, Schloter M, Smalla K (2014) Unraveling the plant microbiome: looking back and future perspectives. Front Microbiol 5:148. doi:10.3389/fmicb.2014.00148

Bezerra DP, Santos MGS, Svedese VM, Lima DMM, Fernandes MJS, Paiva LM, Souza-Motta CM (2012) Richness of endophytic fungi isolated from *Opuntia ficus*-indica Mill. (Cactaceae) and preliminary screening for enzyme production. World J Microbiol Biotechnol 28(5):1989–1995

Bezerra JDP, Nascimento CCF, Barbosa RDN, da Silva DCV, Svedese VM, Silva-Nogueira EB, Gomes BS, Paiva LM, Souza-Motta CM (2015) Endophytic fungi from medicinal plant *Bauhinia forficata*: diversity and biotechnological potential. Braz J Microbiol 46(1):49–57

Bhagat J, Kaur A, Sharma M, Saxena AK, Chadha BS (2012) Molecular and functional characterization of endophytic fungi from traditional medicinal plants. World J Microbiol Biotechnol 28(3):963–971

Bhagat J, Kaur A, Kaur R, Yadav A.K, Sharma V, Chadha BS (2016) Cholinesterase inhibitor (Altenuene) from an endophytic fungus *Alternaria alternata*: optimization, purification and characterization. J App Microbiol 121(4): 1015–1025

Bhagobaty RK, Joshi SR (2012) Enzymatic activity of fungi endophytic on five medicinal plant species of the pristine sacred forests of Meghalaya. India Biotechnol Bioprocess Engg 17(1):33–40

Bharathidasan R, Panneerselvam A (2012) Biosynthesis and characterization of silver nanoparticles using endophytic fungi *Aspergillus concius*, *Penicillium janthinellum* and *Phomosis* sp. Int J Pharma Sci Res 3:3163–3169

Bhatia DR, Dhara P, Mutalik V, Deshmukh SK, Verekar SA, Desaic DC, Kshirsagar R, Thiagarajand P, Agarwala V (2016) Anticancer activity of Ophiobolin a, isolated from the endophytic fungus *Bipolaris setariae*. Nat Prod Res 30(12):1455–1458

Bisht R, Sharma D, Agarwal PK (2016) Antimicrobial and antidiabetic activity of an *Penicillium oxalicum* isolated from *Cupressus torulosa*. Int J Biotechnol Biomed Sci 2(2):119–122

Bungihan ME, Tan MA, Takayama H, Cruz TED, NoNatlo MG (2013) A new macrolide isolated from the endophytic fungus *Colletotrichum* sp. Phil Sci Lett 6(1):57–73

Burres NS, Premachandran U, Humphrey PE, Jackson M, Chen RH (1992) A new immunosuppressive cytochalasin isolated from a *Pestalotia* sp. J Antibiot 45(8):1367–1369

Bustanussalam Rachman F, Septiana E, Lekatompessy SJR, Sukiman HI, Simanjuntak P (2015) Screening for endophytic fungi from turmeric plant (*Curcuma longa* L.) of Sukabumi and Cibinong with potency as antioxidant compounds producer. Pak J Biol Sci. doi:10.3923/pjbs.2015

Cafeu MC, Silva GH, Teles HL, Bolzani VDS, Araujo AR (2005) Antifungal compounds of *Xylaria sp*. an endophytic fungus isolated from *Palicourea marcgravii* (Rubiaceae). Quim Nova 28(6):991–995

Calcul L, Waterman C, Ma WS, Lebar MD, Harter C, Mutka T, Morton L, Maignan P, Olphen AV, Kyle DE, Vrijmoed L, Pang KL, Pearce C, Baker BJ (2013) Screening mangrove endophytic fungi for antimalarial natural products. Mar Drugs 11(12):5036–5050

Campos FF, Junior PAS, Romanha AJR, Araujo MSS, Siqueira EPP, Resende JM, Alves TMA, Martins-Filho OA, dos Santos VL, Rosa CA, Zani CLZ, Cruz BB, de Janeiro R (2015) Bioactive endophytic fungi isolated from *Caesalpinia echinata* lam. (Brazilwood) and identification of beauvericin as a trypanocidal metabolite from *Fusarium* sp. Mem Inst Oswaldo Cruz, Rio de Janeiro 110(1):65–74

Carvalho CR, Vieira MLA, Cantrell CL, Wedge DE, Alves TMA, Zanic CL, Pimentad RS, Juniore PAS, Murtae SMF, Romanhae AJ, Rosaa CA, Rosaa LH (2016) Biological activities of ophiobolin K and 6-epi-ophiobolin K produced by the endophytic fungus *Aspergillus calidoustus*. Nat Prod Res 30(4):478–481

Casella TM, Eparvier V, Mandavid H, Bendelac A, Odonne G, Dayan L, Duplais C, Espindola LS, Stien D (2013) Antimicrobial and cytotoxic secondary metabolites from tropical leaf endophytes: isolation of antibacterial agent pyrrocidine C from *Lewia infectoria* SNB-GTC2402. Phytochemistry 96:370–377

Chandrappa CP, Govindappa M, Chandrasekar N, Sarkar S, Ooha S, Channabasava R (2016) Endophytic synthesis of silver chloride nanoparticles from *Penicillium* sp. of *Calophyllum apetalum*. Adv Nat Sci Nanosci Nanotechnol 7:025016

Channabasava, Govindappa M (2014) First report of anticancer agent, lapachol producing endophyte, *Aspergillus niger* of *Tabebuia argentea* and its in vitro cytotoxicity assays. Bangladesh J Pharmacol 9(1):129–139

Chapla VM, Zeraik ML, Leptokarydis IH, Silva GH, Bolzani VS, Young MC, Pfenning LH, Araujo AR (2014) Antifungal compounds produced by *Colletotrichum gloeosporioides*, an endophytic fungus from *Michelia champaca*. Molecules 19:19243–19252

Chavez JR, Figueroa M, Gonzalez MC, Glenn AE, Mata R (2015) α-Glucosidase inhibitors from a *Xylaria feejeensis* associated with *Hintonia latiflora*. J Nat Prod 78:730–735. doi:10.1021/np500897y

Chen MJ, Fu YW, Zhou QY (2014) Penifupyrone, a new cytotoxic funicone derivative from the endophytic fungus *Penicillium* sp. HSZ-43. Nat Prod Res 28(19):1544–1548

Chen S, Liu Y, Liu Z, Cai R, Lu Y, Huang X, She Z (2016) Isocoumarins and benzofurans from the mangrove endophytic fungus *Talaromyces amestolkiae* possess α-glucosidase inhibitory and antibacterial activities. RSC Adv 6(31):26412–26420

Chithra S, Jasim B, Sachidanandan P, Jyothis M, Radhakrishnan EK (2014) Piperine production by endophytic fungus *Colletotrichum gloeosporioides* isolated from *Piper nigrum*. Phytomedicine 21:534–540

Cui HB, Mei WL, Miao CD, Lin HP, Kui H, Dai HF (2008) Antibacterial constituents from the endophytic fungus *Penicillium* sp. 0935030 of a mangrove plant *Acrostichum aureurm*. Chin J Antibiot 33:407–410

Cui H, Liu Y, Nie Y, Liu Z, Chen S, Zhang Z, Lu Y, He L, Huang X, She Z (2016) Polyketides from the mangrove-derived endophytic fungus *Nectria* sp. hn001 and their α-glucosidase inhibitory activity. Mar Drugs 14(5):86. doi:10.3390/md14050086

De Mendonca AN, Feliphe BHMP, Lemes RML, Ruiz ALTG, de Carvalho JE, Ikegaki M (2015) Potential antimicrobial and antiproliferative activity of the crude extract of the endophytic fungus *Rhizoctonia* sp. from *Annona crassiflora*. Afr J Pharm Pharmacol 9(10):327–332

De Silva DD, Rapior S, Sudarman E, Stadler M, Xu J, Alias SA, Hyde KD (2013) Bioactive metabolites from macrofungi: ethnopharmacology, biological activities and chemistry. Fungal Divers 62:1–40

Desale MG, Bodhankar MG (2013) Antimicrobial activity of endophytic fungi isolated from *Vitex negundo* Linn. Int J Curr Microbiol App Sci 2(12):389–395

Desire MH, Bernard F, Forsah MR, Assang CT, Denis ON (2014) Enzymes and qualitative phytochemical screening of endophytic fungi isolated from *Lantana camara* Linn. leaves. J Appl Biol Biotechnol 2(06):001–006

Devari S, Jaglan S, Kumar M, Deshidi R, Guru S, Bhushan S, Taneja SC (2014) Capsaicin production by *Alternaria alternata*, an endophytic fungus from *Capsicum annum*; LC–ESI–MS/MS analysis. Phytochemistry 98:183–189

Devi LS, Joshi SR (2014) Evaluation of the antimicrobial potency of silver nanoparticles biosynthesized by using an endophytic fungus, *Cryptosporiopsis ericae* PS4. J Microbiol 52(8):667–674

Devi NN, Shankar D, Sutha S (2012) Biomimetic synthesis of silver nanoparticles from an endophytic fungus and their antimicrobial efficacy. Int J Biomed Adv Res 3(5):409–415

Devi LS, Bareh DA, Joshi SR (2014) Studies on biosynthesis of antimicrobial silver nanoparticles using endophytic fungi isolated from the ethno-medicinal plant *Gloriosa superba* L. Proc Natl Acad Sci India Section B: Biol Sci 84(4):1091–1099

Dhanalakshmi R, Umamaheswari S, Sugandhi P, Prasanth DA (2013) Biodiversity of the endophytic fungi isolated from *Moringa oleifera* of Yercaud hills. Int J Pharm Sci Res 4(3):1064–1068

Dhankhar S, Dhankhar S, Yadav JP (2013) Investigations towards new antidiabetic drugs from fungal endophytes associated with *Salvadora oleoides* Decne. Med Chem 9(4):624–632

Ding X, Liu K, Deng B, Chen W, Li W, Liu F (2013) Isolation and characterization of endophytic fungi from *Camptotheca acuminate*. World J Microbiol Biotechnol 29:1831–1838

Dissanayake RK, Ratnaweera PB, Williams DE, Wijayarathne CD, Wijesundera RLC, Andersen RJ, de Silva ED (2016) Antimicrobial activities of endophytic fungi of the Sri Lankan aquatic plant *Nymphaea nouchali* and chaetoglobosin A and C, produced by the endophytic fungus *Chaetomium globosum*. Mycology 7(1):1–8. doi.org/10.1080/21501203.2015.1136708

Ebrahim W, El-Neketi M, Lewald LI, Orfali RS, Lin W, Rehberg N, Kalscheuer R, Daletos G, Proksch P (2016) Metabolites from the fungal endophyte *Aspergillus austroafricanus* in axenic culture and in fungal–bacterial mixed cultures. J Nat Prod 79(4):914–922. doi:10.1021/acs.jnatprod.5b00975

Egan JM, Kaur A, Raja HA, Kellogg JJ, Oberlies NS, Dompeipen EJ, Simanjuntak P (2016) Antimicrobial fungal endophytes from the botanical medicine golden seal (*Hydrastis canadensis*). Uni Phytochem Lett 17:219–225

Elkhayata ES, Ibrahim SRM, Mohamed GA, Rosse SA (2016) Terrenolide S, a new antileishmanial butenolide from the endophytic fungus *Aspergillus terreus*. Nat Prod Res 30(7):814–820

El-Neketi M, Ebrahim W, Lin W, Gedara S, Badria F, Saad HEA, Lai D, Proksch P (2013) Alkaloids and Polyketides from *Penicillium citrinum*, an endophyte isolated from the Moroccan plant *Ceratonia silique*. J Natl Prod 76(6):1099–1104

El-Said AHM, Shebany YM, Hussein MA, El-Dawy EGA (2016) Antimicrobial and L-asparaginase activities of endophytic fungi isolated from *Datura innoxia* and *Hyoscyamus muticus* medicinal plants. Europ J Biol Res 6(3):135–144

Ferreira MC, Vieira MDLA, Zani CL, de Almeida Alves TM, Junior PAS, Murta SM, Romanha AJ, Carvalho AGDO, Zilli JE, Vital MJS, Rosa CA, Rosa LH (2015) Molecular phylogeny, diversity, symbiosis and discovery of bioactive compounds of endophytic fungi associated with the medicinal Amazonian plant *Carapa guianensis* Aublet (Meliaceae). Biochem Syst Ecol 59:36–44

Flores AC, Pamphile JA, Sarragiotto MH, Clemente E (2013) Production of 3-nitropropionic acid by endophytic fungus *Phomopsis longicolla* isolated from *Trichilia elegans* and evaluation of biological activity. World J Microbiol Biotechnol 29:923–932

Fouda AH, Hassan SD, Eid AM, Ewais EE (2015) Biotechnological applications of fungal endophytes associated with medicinal plant *Asclepias sinaica* (Bioss.) Annals Agri Sci 60(1):95–104

Gangwar V, Verma C, Gautam MK, Nath G (2015) Isolation and evaluation of antimicrobial activities of endophytic fungal extract from *Mallotus philippinensis* Muell. Appl Microbiol 1(1):1000103

Garcia A, Rhoden SA, Bernardi-Wenzel J, Orlandelli RC, Azevedo JL, Pamphile JA (2012) Antimicrobial activity of crude extracts of endophytic fungi isolated from medicinal plant *Sapindus saponaria* L. J Appl Pharm Sci 2(10):35–40

Gashgari R, Gherbawy Y, Ameen F, Alsharari S (2016) Molecular characterization and analysis of antimicrobial activity of endophytic fungi from medicinal plants in Saudi Arabia. Jundishapur J Microbiol 9(1):e26157. doi:10.5812/jjm.26157

Gautama AK, Kant M, Thakur Y (2013) Isolation of endophytic fungi from *Cannabis sativa* and study their antifungal potential. Arch Phytopath Plant Prot 46(6):627–635

Gherbawy YA, Elhariry HM (2016) Endophytic fungi associated with high-altitude *Juniperus* trees and their antimicrobial activities. Plant Biosystems 150(1):131–140

Gond SK, Mishra A, Sharma VK, Verma SK, Kumar J, Kharwar RN, Kumar A (2012) Diversity and antimicrobial activity of endophytic fungi isolated from *Nyctanthes arbor-tristis*, a well –known medicinal plant of India. Mycoscience 53:113–121

Gopalakrishnan S, Sathya A, Vijayabharathi R, Varshney RK, Gowda CL, Krishnamurthy L (2015) Plant growth promoting rhizobia: challenges and opportunities. 3. Biotech 5(4):355–377

Gopinath K, Senthilkumar V, Arumugam A, Kumaresan S (2013) Antimicrobial activity of extracellular metabolite of endophytic fungi *Phomopsis* spp. isolated from four different medicinal plants of India. Int J App Biol Pharm Tech 4(2):40–46

Goutam J, Kharwar RN, Tiwari VK, Mishra A, Singh S (2016) Isolation and identification of antibacterial compounds isolated from endophytic fungus *Emericella qaudrilineata* (RS-5). Nat Prod Chem Res 4:2. doi.org/10.4172/2329-6836.1000205

Govindappa M, Channabasava R, Kumar KS, Pushpalatha KC (2013) Antioxidant activity and phytochemical screening of crude endophytes extracts of *Tabebuia argentea* Bur. & K. Sch. Am J Plant Sci 4:1641–1652

Govindappa M, Prathap S, Vinay V, Channabasava R (2014) Chemical composition of methanol extract of endophytic fungi, *Alternaria sp.* of Tebebuia argentea and their antimicrobial and antioxidant activity. Int J Biol Pharm Res 5(11):861–869

Govindappa M, Sadananda TS, Channabasava RYL, Chandrappa CP, Padmalatha RS, Prasad SK (2015) In vitro and in vivo antidiabetic activity of lectin (N-acetylgalactosamine, 64 kDa) isolated from endophytic fungi, *Alternaria* species from *Viscum album* on alloxan induced diabetic rats. Integr Obes Diabetes 1(1):11–19

Govindappa M, Farheen H, Chandrappa CP, Rai RV, Raghavendra VB (2016a) Mycosynthesis of silver nanoparticles using extract of endophytic fungi, *Penicillium* species of *Glycosmis mauritiana*, and its antioxidant, antimicrobial, anti-inflammatory and tyrokinase inhibitory activity. Adv Nat Sci Nanosci Nanotechnol 7(3):035014

Govindappa M, Channabasava R, Chandrappa CP, Sadananda TS (2016b) In vitro antidiabetic activity of three fractions of methanol extracts of *Loranthus micranthus*, identification of phytoconstituents by GC-MS and possible mechanism identified by GEMDOCK method. Asian J Biomed Pharm Res 4:34–41

Gupta S, Kaul S, Dhar MK (2015) Exploring the antimicrobial potential of fungal endophytes of *Dioscorea composita*: a north-west Himalayan medicinal plant. ENVIS Bull Himal Ecol 23:113–118

Gupta S, Kaul S, Singh B, Vishwakarma RA, Dhar MK (2016) Production of gentisyl alcohol from *Phoma herbarum* endophytic in *Curcuma longa* L. and its antagonistic activity towards leaf spot pathogen *Colletotrichum gloeosporioides*. Appl Biochem Biotechnol 10.1007/s12010-016-2154-0

Hammerschmidt L, Ola A, Muller WE, Lin W, Mandi A, Kurtan T, Proksch P, Aly AH (2015) Two new metabolites from the endophytic fungus *Xylaria sp.* isolated from the medicinal plant *Curcuma xanthorrhiza*. Tetrahedron Lett 56(10):1193–1197

Harper JK, Arif AM, Ford EJ, Strobel GA, Porco JA, Tomer DP, Oneill KL, Heider EM, Grant DM (2003) Pestacin: a 1, 3-dihydro isobenzofuran from *Pestalotiopsis microspora* possessing antioxidant and antimycotic activities. Tetrahedron 59:2471–2476

Hawksworth DL (2001) The magnitude of fungal diversity: the 1.5 million species estimate revisted. Mycol Res 105:1422–1432

Heinig U, Scholz S, Jennewein S (2013) Getting to the bottom of taxol biosynthesis by fungi. Fungal Divers 60:161–170

Hoffman AM, Mayer SG, Strobel GA, Hess WM, Sovocool GW, Grange AH, Harper JK, Arif AM, Grant DM, Kelley EG (2008) Purification, identification and activity of Phomodione, a furandione from an endophytic *Phoma* species. Phytochemistry 69(4):1049–1056

Hong S, Shushan G, Xiaoming L, Chunshun L, Bingui W (2013) Chemical constituents of marine mangrove-derived endophytic fungus *Alternaria tenuissima* EN-192. Chin J Oceanol Limnol 31(2):464–470

Huang WY, Cai YZ, Xing J, Corke H, Sun M (2007) A potential antioxidant resource: endophytic fungi from medicinal plants. Eco Bot 61(1):14–30

Huang Y, Zhao J, Zhou L, Wang M, Wang J, Li X, Chen Q (2009) Antimicrobial compounds from the endophytic fungus *Fusarium* sp. Ppf4 isolated from the medicinal plant *Paris polyphylla* var. yunnanensis. Natl Prod Commun 4(11):1455–1458

Huang XZ, Zhu Y, Guan XL, Tian K, Guo JM, Wang HB, Fu GM (2012) A novel antioxidant isobenzofuranone derivative from fungus *Cephalosporium* sp. AL031. Molecules 17(4):4219–4224

Huang X, Huang H, Li H, Sun X, Huang H, Lu Y, Lin Y, Long Y, She Z (2013) Asperterpenoid A, a new sesterterpenoid as an inhibitor of *Mycobacterium tuberculosis* protein tyrosine phosphatase B from the culture of *Aspergillus* sp. 16-5c. Org Lett 15(4):721–723

Huang Q, An H, Song H, Mao H, Shen W, Dong J (2015) Diversity and biotransformative potential of endophytic fungi associated with the medicinal plant *Kadsura angustifolia*. Res Microbiol 166(1):45–55

Hussain H, Kock I, Al-Harrasi A, Al-Rawahi A, Abbas G, Green IR, Badshah SA, Saleem A, Draeger MS, Schulz B, Krohn K (2014) Antimicrobial chemical constituents from endophytic fungus *Phoma* sp. Asian Pac J Trop Med 7:699–702

Hussain H, John M, Al-Harrasi A, Shah A, Hassan Z, Abbas G, Rana UA, Green IR, Schulz B, Krohn K (2015) Phytochemical investigation and antimicrobial activity of an endophytic fungus *Phoma sp*. J King Saud Univ – Sci 27:92–95

Hyde KD, Soytong K (2008) The fungal endophyte dilemma. Fungal Divers 33:163–173

Idris AM, Al-tahir I, Idris E (2013) Antibacterial activity of endophytic fungi extracts from the medicinal plant *Kigelia africana*. Egypt Acad J Biolog Sci 5(1):1–9

Idris A, Tantry MA, Ganai BA, Kamili AN, Williamson JS (2015) Reduced perylenequinone derivatives from an endophytic *Alternaria* sp. isolated from *Pinus ponderosa*. Phytochem Lett 11:264–269

Intaraudom C, Boonyuen N, Suvannakad R, Rachtawee P, Pittayakhajonwut P (2013) PenicoliNatles A–E from endophytic *Penicillium sp.* BCC16054. Tetrahedron Lett 54:744–748

Jain P, Pundir RK (2015) Diverse endophytic microflora of medicinal plants. Plant-Growth-Promoting Rhizobacteria (PGPR) and Medicinal Plants, Soil Biology 42, doi: 10.1007/978–3–319-13401-7-17. Springer International Publishing Switzerland D. Egamberdieva et al. (eds.)

Jalgaonwala RE, Mahajan RT (2014) Production of anticancer enzyme asparaginase from endophytic *Eurotium sp.* isolated from rhizomes of *Curcuma longa*. Eur J Exp Biol 4(3):36–43

Jalgaonwala RE, Mohite BV, Mahajan RT (2010) Evaluation of endophytes for their antimicrobial activity from indigenous medicinal plants belonging to North Maharashtra region India. Int J Biol Pharm Res 1:136–141

Jeewon R, Ittoo J, Mahadeb D, Jaufeerally-Fakim Y, Wang HK, Liu AR (2013) DNA based identification and phylogenetic characterisation of endophytic and saprobic fungi from *Antidesma madagascariense*, a medicinal plant in Mauritius. J Mycol doi.org/10.1155/2013/781914

Job N, Manomi S, Philip R (2015) Isolation and characterisation of endophytic fungi from *Avicennia officinalis*. Int J Res Biomed Biotechnol 5(1):4–8

Jouda JB, Kusari S, Lamshoft M, Talontsi FM, Meli CD, Wandji J, Spiteller M (2014) Penialidins A–C with strong antibacterial activities from *Penicillium sp.*, an endophytic fungus harboring leaves of *Garcinia nobilis*. Fitoterapia 98:209–214

Jouda JB, Mawabo IK, Notedji A, Mbazoa CD, Nkenfou J, Wandji J, Nkenfou CN (2016a) Anti-mycobacterial activity of polyketides from *Penicillium* sp. endophyte isolated from *Garcinia nobilis* against *Mycobacterium smegmatis*. Int J Mycobact 5:192–196

Jouda JB, Fopossib JLD, Mbazoaa CDM, Wandji J (2016b) Antibacterial activity of the major compound of an endophytic fungus isolated from *Garcinia preussii*. J App Pharm Sci 6(06):026–029. doi:10.7324/JAPS.2016.60605

Katoch M, Singh G, Sharma S, Gupta N, Sangwan PL, Saxena AK (2014a) Cytotoxic and antimicrobial activities of endophytic fungi isolated from *Bacopa monnieri* (L.) Pennell (Scrophulariaceae). BMC Complement Altern Med 11:14–52

Katoch M, Khajuria A, Sharma PR, Saxena AK (2014b) Immunosuppressive potential of *Botryosphaeria dothidea*, an endophyte isolated from *Kigelia africana*. Pharm Biol 53(1):85–91

Kaul S, Gupta S, Ahmed M, Dhar MK (2012) Endophytic fungi from medicinal plants: a treasure hunt for bioactive metabolites. Phytochem Rev 11:487–505

Kaul S, Ahmed M, Sharma T, Dhar MK (2014) Unlocking the myriad benefits of endophytes: an overview. In: Kharwar RN et al (eds) Microbial diversity and biotechnology in food security. Springer, India. doi:10.1007/978-81-322-1801-2_4

Kaur A, Raja HA, Swenson DC, Agarwal R, Deep G, Falkinham J, Oberlies NH (2016) Talarolutins A–D: Meroterpenoids from an endophytic fungal isolate of *Talaromyces minioluteus*. Phytochemistry 126:4–10

Khan AL, Al-Harrasi A, Al-Rawahi A, Al-Farsi Z, Al-Mamari A, Waqas M, Asaf S, Elyassi A, Mabood F, Shin JH, Lee IJ (2016) Endophytic fungi from Frankincense tree improves host growth and produces extracellular enzymes and indole acetic acid. PLoS One 11(6):e0158207

Kharwar RN, Mishra A, Gond SK, Stierle A, Stierle D (2011) Anticancer compounds derived from fungal endophytes: their importance and future challenges. Natl Prod Rep 28(7):1208–1228

Kharwar RN, Maurya AL, Verma VC, Kumar A, Gond SK, Mishra A (2012) Diversity and antimicrobial activity of endophytic fungal community isolated from medicinal plant *Cinnamomum camphora*. Proc Natl Acad Sci. India Sect B: Biol Sci 82(4):557–565

Khiralla A, Mohamed IE, Tzanova T, Schohn H, Slezack-Deschaumes SS, Hehn A, Andre A, Carre G, Spina R, Lobstein A, Yagi S, Laurain-Mattar D (2016) Endophytic fungi associated with Sudanese medicinal plants show cytotoxic and antibiotic potential. FEMS Microbiol Lett 363. doi: 10.1093/femsle/fnw089

Kongprapan T, Rukachaisirikul V, Saithong S, Phongpaichit S, Poonsuwan W, Sakayaroj J (2015) Cytotoxic cytochalasins from the endophytic fungus *Eutypella scoparia* PSU-H267. Phytochem Lett 13:171–176

Kumala S, DwiYuliani K, Simanjuntak P (2015) Antimicrobial activity of secondary metabolites produced by endophytic fungi isolated from stems of jati tree (tectonagrandis l.f). Int J Pharm Sci Res 6(6):2349–2353

Kumar S, Kaushik N (2013) Endophytic fungi isolated from oil-seed crop *Jatropha curcas* produces oil and exhibit antifungal activity. PLoS One 8(2):e56202. doi:10.1371/journal.pone.0056202

Kumar DSS, Lau CS, Wan JM, Yang D, Hyde KD (2005) Immunomodulatory compounds from *Pestalotiopsis leucothes*, an endophytic fungus from *Tripterygium wilfordii*. Life Sci 78(2):147–156

Kumar S, Kaushik N, Proksch P (2013) Identification of antifungal principle in the solvent extract of an endophytic fungus *Chaetomium globosum* from *Withania somnifera*. SpringerPlus 2(1):37

Kumar A, Jha KP, Kumar R, Kumar K, Sedolkar V (2015) Antibacterial activity, phytochemical and enzyme analysis of crude extract of endophytic fungus, *Alternaria sp.* isolated from an ethnobotanical medicinal plant *Tridax procumbens*. Int J Pharma Phytochem Res 7(6):1111–1115

Kumar S, Upadhyay R, Aharwal RP, Sandhu SS (2016) Antibacterial activity of some isolated endophytic fungi from *Menthe viridis*. Int J App Biol Pharm Tech 7(1)

Kumara PM, Zuehlke S, Priti V, Ramesha BT, Shweta S, Ravikanth G, Vasudeva R, Santhoshkumar TR, Spiteller M, Shaanker RU (2012) *Fusarium proliferatum*, an endophytic fungus from *Dysoxylum binectariferum* Hook. f, produces rohitukine, a chromane alkaloid possessing anti-cancer activity. Anton Leeuw 101(2):323–329

Kumaresan S, Karthi V, Senthilkumar V, Balakumar BS, Stephen A (2015) Biochemical constituents and antioxidant potential of endophytic fungi isolated from the leaves of *Azadirachta indica* A. Juss (Neem) from Chennai. Indian J Acad Ind Res 3(8):355–361

Kusari S, Hertweck C, Spiteller M (2012) Chemical ecology of endophytic fungi: origins of secondary metabolites. Chem Biol 19:792–798

Kusari P, Kusari S, Spiteller M, Kayser O (2013) Endophytic fungi harbored in *Cannabis sativa* L.: diversity and potential as biocontrol agents against host plant-specific phytopathogens. Fungal Divers 60(1):137–151

Kusari S, Singh S, Jayabaskaran C (2014) Biotechnological potential of plant-associated endophytic fungi: hope versus hype. Trends Biotechnol 32(6):297–303

Lai D, Brotz-Oesterhelt H, Müller WEG, Wray V, Proksch P (2013) Bioactive polyketides and alkaloids from *Penicillium citrinum*, a fungal endophyte isolated from *Ocimum tenuiflorum*. Fitoterapia 91:100–106

Lai ND, Wang A, Cao Y, Zhou K, Mao Z, Dong X, Tian J, Xu D, Dai J, Peng Y, Zhou L, Liu Y (2016) Bioactive dibenzo-α-pyrone derivatives from the endophytic fungus *Rhizopycnis vagum*. J Nat Prod. doi:10.1021/acs.jnatprod.6b0032

Larsen TO, Smedsgaard J, Nielsen KF, Hansen ME, Frisvad JC (2005) Phenotypic taxonomy and metabolite profiling in microbial drug discovery. Natl Prod Rep 22(6):672–695

Lee JC, Lobkovsky E, Pliam NB, Strobel G, Clardy J (1995) Subglutinols A and B: immunosuppressive compounds from the endophytic fungus *Fusarium subglutinans*. J Org Chem 60(22):7076–7077

Li H, Qing C, Zhang Y, Zhao Z (2005) Screening for endophytic fungi with antitumour and antifungal activities from Chinese medicinal plants. World J Microbiol Biotechnol 21:1515–1519

Li G, Kusari S, Lamshoft M, Schuffler A, Laatsch H, Spiteller M (2014a) Antibacterial secondary metabolites from an endophytic fungus, *Eupenicillium sp.* LG41. J Natl Prod 77(11):2335–2341

Li H, Jiang J, Liu Z, Lin S, Xia G, Xia X, Ding B, He L, Lu Y, She Z (2014b) Peniphenones A−D from the mangrove fungus *Penicillium dipodomyicola* HN4-3A as inhibitors of *Mycobacterium tuberculosis* phosphatase MptpB. Nat Prod 77:800–806

Li H, Xiao J, Gao YQ, Tang JJ, Zhang AL, Gao JM (2014c) Chaetoglobosins from *Chaetomium globosum*, an endophytic fungus in *Ginkgo biloba*, and their phytotoxic and cytotoxic activities. J Agric Food Chem 62(17):3734–3741

Li G, Kusari S, Kusari P, Kayser O, Spiteller M (2015a) Endophytic *Diaporthe sp.* LG23 produces a potent antibacterial tetracyclic triterpenoid. J Nat Prod 78:2128–2132. doi:10.1021/acs.jnatprod.5b00170

Li J, Xue Y, Yuan J, Lu Y, Zhu X, Lin Y, Liu L (2015b) Lasiodiplodins from mangrove endophytic fungus *Lasiodiplodia sp.* 318#. Natl Prod Res 1–6

Li X, Guo X, Deng Z, Yang J, Zou K (2015c) A new α-pyrone derivative from endophytic fungus *Pestalotiopsis microspora*. Rec Nat Prod 9(4):503–508

Li W, Yang X, Yang Y, Duang R, Chen G, Li X, Li Q, Qin S, Li S, Zhao L, Ding Z (2016a) Anti-phytopathogen, multi-target acetylcholinesterase inhibitory and antioxidant activities of metabolites from endophytic *Chaetomium globosum*. Nat Prod Res 30(22):2616–2619

Li G, Kusari S, Golz C, Strohmannb C, Spiteller M (2016b) Three cyclic pentapeptides and a cyclic lipopeptide produced by endophytic *Fusarium decemcellulare* LG53. R Soc Chem Adv 6:54092–54098

Lia W, Yanga X, Yanga X, Duanga R, Chena G, Lia X, Lia Q, Qina S, Lia S, Zhaoc L, Dinga Z (2016) Anti-phytopathogen, multi-target acetylcholinesterase inhibitory and antioxidant activities of metabolites from endophytic *Chaetomium globosum*. Nat Prod Res doi.org/10.1080/14786419.2015.1129328

Liang H, Xing Y, Chen J, Zhang D, Guo S, Wang C (2012) Antimicrobial activities of endophytic fungi isolated from *Ophiopogon japonicus* (Liliaceae). BMC Complement Alt Med 12(1):238–243

Liang Z, Zhang J, Zhang X, Li J, Zhang X, Zhao C (2015a) Endophytic fungus from *Sinopodophyllum emodi* (Wall.) Ying that produces Podophyllotoxin. J Chromatogr Sci. doi:10.1093/chromsci/bmv124

Liang Z, Zhang T, Zhang X, Zhang J, Zhao C (2015b) An alkaloid and a steroid from the endophytic fungus *Aspergillus fumigatus*. Molecules 20:1424–1433

Liu X, Dong M, Chen X, Jiang M, Lv X, Zhou J (2007) Antimicrobial activity of an endophytic *Xylaria sp.* YX-28 and identification of its antimicrobial compound 7-amino-4-methylcoumarin. Appl Microbiol Biotechnol 78(2):241–247

Liu D, Lia XM, Lia CS, Wang BG (2013) Nigerasterols A and B, antiproliferative sterols from the mangrove-derived endophytic fungus *Aspergillus niger* MA-132. Helv Chim Acta 96:1055–1061

Liu Y, Yang Q, Xia G, Huang H, Li H, Ma L, Lu Y, He L, Xia X, She Z (2015a) Polyketides with α-glucosidase inhibitory activity from a mangrove endophytic fungus, *Penicillium sp.* HN29-3B1. J Nat Prod 78:1816–1822

Liu Y, Chen S, Liu Z, Lu Y, Xia G, Liu H, He L, She Z (2015b) Bioactive metabolites from mangrove endophytic fungus *Aspergillus* sp. 16-5B. Mar Drugs 13:3091–3102

Liu LYH, Hu XP, Li W, Cao XY, Yang HR, Lin ST, Xu CB, Liu SX, Li CF (2016) Antimicrobial and antitumor activity and diversity of endophytic fungi from traditional Chinese medicinal plant *Cephalotaxus hainanensis*. Gen Mol Res 15(2):gmr.15028633

Lou J, Yua R, Wang Y, Mao Z, Fua L, Liu Y, Zhou L (2016) Alternariol 9-methyl ether from the endophytic fungus *Alternaria sp.* Samif01 and its bioactivities. Braz J Microbiol 47:96–101

Luo J, Liu X, Li E, Guo L, Che Y (2013) Arundinols A−C and Arundinones A and B from the plant endophytic fungus *Microsphaeropsis arundinis*. J Nat Prod 76:107–112
Luo ZP, Lin HY, Ding WB, He HL, Li YZ (2015) Phylogenetic diversity and antifungal activity of endophytic fungi associated with *Tephrosia purpurea*. Mycobiol 43(4):435–443
Ma YM, Liang XA, Zhang HC, Liu R (2016) Cytotoxic and antibiotic cyclic pentapeptide from an endophytic *Aspergillus tamarii* of *Ficus carica*. J Agric Food Chem 64(19):3789–3793
Mahapatra S, Banerjee D (2014) Evaluation of in vitro antioxidant potency of exopolysaccharide from endophytic *Fusarium solani* SD5. Int J Biol Mac 53:62–66
Mahdi T, Mohamed I, Yagi S (2014) Endophytic fungal communities associated with ethnomedicinal plants from Sudan and their antimicrobial and antioxidant prospective. J Forest Prod Industries 3(6):248–256
Mapperson RR, Kotiw M, Davis RA, Dearnaley JDW (2014) The diversity and antimicrobial activity of *Preussia sp*. endophytes isolated from Australian dry rainforests. Curr Microbiol 68:30–37
Maria GL, Sridhar KR, Raviraja NS (2005) Antimicrobial and enzyme activity of mangrove endophytic fungi of southwest coast of India. J Agr Tech 1:67–80
Mendis K, Rietveld A, Warsame M, Bosman A, Greenwood B, Wernsdorfer WH (2009) From malaria control to eradication: the WHO perspective. Tropical Med Int Health 14:802–809
Meng LHM, Zhang P, Li XM, Wang BG (2015) Penicibrocazines A–E, five new sulfide diketopiperazines from the marine-derived endophytic fungus *Penicillium brocae*. Mar Drugs 13:276–287
Metwaly AM, Kadry HA, El-Hela AA, Mohammad AE, Ma G, Cutler SJ, Ross SA (2013) Nigrosphaerin A a new isochromene derivative from the endophytic fungus *Nigrospora sphaerica*. Phytochem Lett 7:1–5
Mishra PD, Verekar S, Almeida AK, Roy SK, Jain S, Balakrishnan S, Vishwakarma S, Deshmukh SK (2013) Anti-inflammatory and anti-diabetic naphthaquinones from an endophytic fungus *Dendryphion nanum* (Nees). S. Hughes Ind J Chem 52:565–567
Mishra L, Kumar V, Singh G, Passari YAK, Gupta MK, Kumar V (2016a) Distribution and antimicrobial potential of endophytic fungi associated with ethnomedicinal plant *Melastoma malabathricum*. J Environ Biol 37(2):229–237
Mishra VK, Passari AK, Singh BP (2016b) In vitro antimycotic and biosynthetic potential of fungal endophytes associated with *Schima wallichii*. Fun Biol 367–381
Mou Y, Meng J, Fu X, Wang X, Tian J, Wang M, Peng Y, Zhou L (2013) Antimicrobial and antioxidant activities and effect of 1-hexadecene addition on Palmarumycin C2 and C3 yields in liquid culture of endophytic fungus *Berkleasmium sp.* Dzf12. Molecules 18:15587–15599
Mousa WK, Raizada MN (2013) The diversity of anti-microbial secondary metabolites produced by fungal endophytes: an interdisciplinary perspective. Front Microbiol 4:4–18
Munim A, Ramadhan MG, Soemiati A (2013) Screening of endophytic fungi from *Cassia siamea* Lamk leaves as a-glucosidase inhibitor. Int Res J Pharm 4(5):128–131
Narendran R, Kathiresan K (2016) Antimicrobial activity of crude extracts from mangrove-derived *Trichoderma sp.* against human and fish pathogens. Biocat Agri Biotechnol 6:189–194
Nath A, RaghuNatha P, Joshi SR (2012) Diversity and biological activities of endophytic fungi of *Emblica officinalis*, an ethnomedicinal plant of India. Mycobiology 40(1):8–13
Nath A, Chattopadhyay A, Joshi SR (2015) Biological activity of endophytic fungi of *Rauwolfia serpentina* Benth: an ethnomedicinal plant used in folk medicines in Northeast India. Proc Natl Acad Sci India Sect B: Biol Sci 85(1):233–240
Netala VR, Kotakadi VS, Bobbu P, Gaddam SA, Tartte V (2016) Endophytic fungal isolate mediated biosynthesis of silver nanoparticles and their free radical scavenging activity and anti microbial studies. 3. Biotech 6:132. doi:10.1007/s13205-016-0433-7
Nirmala MJ, Samundeeswari A, Sankar PD (2011) Natural plant resources in anti-cancer therapy-a review. Res Plant Biol 1(3):1–14
Nisa H, Kamili AN, Nawchoo IA, Shafi S, Shameem N, Bandh SA (2015) Fungal endophytes as prolific source of phytochemicals and other bioactive natural products: a review. Microb Pathog:1e10

Nishanthi R, Gowrie RU, Chathurdevi G (2016) An evaluation of potential bioactive metabolites of endophytic fungi isolated from medicinal plant. Eur J Pharm Res 3(4):450–458

Nongalleima KH, Dey A, Deb L, Singh CB, Thongam B, Devi HS, Devi SI (2013) Endophytic fungus isolated from *Zingiber zerumbet* (L.) Sm. inhibits free radicals and cyclooxygenase activity. Int J Pharm Tech Res 5:301–307

Nur A, Muh Danial R (2015) Isolation and characterization of endophytic fungi from medicinal plant, buah makassar (Makassar fruit: *Brucea javanica*). J Chem Pharma Res 7(1):757–762

Ogbonna AI, Onwuliri FC, Ogbonna CIC (2015) Growth response and amylolytic activity of two *Aspergillus* sp. isolated from *Artemisia annua* L. plantation soils. J Acad Ind Res 3(10):456–462

Ola ARB, Debbab A, Aly AH, Mandi A, Zerfass I, Hamacher A, Kassack MU, Brötz-Oesterhelt HB, Kurtan T, Proksch P (2014) Absolute configuration and antibiotic activity of neosartorin from the endophytic fungus *Aspergillus fumigatiaffinis*. Tetrahedron Lett 55:1020–1023

Orachaipunlap K, Suwannasai N, Whalley AJS, Phosri C, Sihanonth P (2016) Biological activities of endophytic *Xylaria* sp. isolated from tropical forest in Chaiyaphum province, Thailand. Biol Chem Res 3:200–208

Orlandelli RC, Pamphile J (2012) Diversity of endophytic fungal community associated with *Piper hispidum* (Piperaceae) leaves. Genet Mol Res 11(2):1575–1585

Orlandelli RC, da Silva MLC, Vasconcelos AFD, Almeidaa IV, Vicentini VEP, Prietoc A, Hernandezc MDD, Azevedo JL, Pamphilea JA (2017) (1→3,1→6)-d-glucans produced by *Diaporthe* sp. endophytes: purification, chemical characterization and antiproliferative activity against MCF-7 and HepG2-C3A cells. Int J Biol Macromol 94:431–437

Ortega HE, Shen YY, Dyke KT, Ríos N, Cubilla-Ríos L (2014) Polyhydroxylated macrolide isolated from the endophytic fungus *Pestalotiopsis mangiferae*. Tetrahedron Lett 55:2642–2645

Packiaraj R, Jeyakumar S, Ayyappan N, Adhirajan N, Premkumar G, Rajarathinam K, Muthuramkumar S (2016) Antimicrobial and cytotoxic activities of endophytic fungus *Colletotrichum gloeosporioides* isolated from endemic tree *Cinnamomum malabatrum*. Stud Fungi 1(1):104–113

Palanichamy P, Thangavel A, Maruthamuthu M (2014) Ethyl acetate extraction of antibacterial compounds of endophytic fungi isolated from medicinal plants. Chem Sci Rev Lett 3(10):178–182

Pan F, Liu ZQ, Chen Q, Xu YW, Hou K, Wu W (2016) Endophytic fungus strain 28 isolated from *Houttuynia cordata* possesses wide-spectrum antifungal activity. Braz J Microbiol 47:480–448

Park JH, Choi GJ, Lee HB (2005) Griseofulvin from *Xylaria sp.* strain F0010, an endophytic fungus of *Abies holophylla* and its antifungal activity against plant pathogenic fungi. J Microbiol Biotechnol 15:112–117

Park YH, Chung JY, Ahn DJ, Kwon TR, Lee SK, Bae I, Yun HK, Bae H (2015) Screening and characterization of endophytic fungi of *Panax ginseng* Meyer for biocontrol activity against ginseng pathogens. Biol Control 91:71–81

Parthasarathya R, Sathiyabama M (2015) Lovastatin producing endophytic fungus isolated from a medicinal plant *Solanum xanthocarpum*. Natl Prod Res. doi:10.1080/14786419.2015.1016938

Patel C, Yadav S, Rahi S, Dave A (2013) Studies on biodiversity of fungal endophytes of indigenous monocotaceous and dicotaceous plants and evaluation of their enzymatic potentialities. Int J Scientific Res Publications 7(3):2250–3153

Patil MP, Patil RH, Patil SG, Maheshwari VL (2014) Endophytic mycoflora of Indian medicinal plant, *Terminalia arjuna* and their biological activities. Int J Biotechnol Wellness Ind 3:53–61

Patil MG, Pagare J, Patil SN, Sidhu AK (2015a) Extracellular enzymatic activities of endophytic fungi isolated from various medicinal plants. Int J Curr Microbiol App Sci 4(3):1035–1042

Patil MP, Patil RH, Maheshwari VL (2015b) Biological activities and identification of bioactive metabolite from Endophytic *Aspergillus flavus* L7 isolated from *Aegle marmelos*. Curr Microbiol 71(1):39–48

Pavithra N, Sathish L, Babu N, Venkatarathanamma V, Pushpalatha H, Reddy GB, Ananda K (2014) Evaluation of α-amylase, α-glucosidase and aldose reductase inhibitors in ethyl acetate extracts of endophytic fungi isolated from antidiabetic medicinal plants. Int J Pharm Sci Res 5(12):5334–5341

Pawle GA, Singh SK (2014) Antioxidant potential of endophytic fungus *Colletotrichum* spesies isolated from *Polygala elongata*. Int J Pharm Biol Sci 5(3):313–319

Phongpaichit S, Rungjindamai N, Rukachaisirikul V, Sakayaroj J (2006) Antimicrobial activity in cultures of endophytic fungi isolated from *Garcinia* species. FEMS Immunol Med Microbiol 48(3):367–372

Pimentel MR, Molina G, Dionisio AP, Marostica Junior MR, Pastore GM (2011) The use of endophytes to obtain bioactive compounds and their application in biotransformation process. Biotechnol Res Int. doi:10.4061/2011/576286

Pinheiro EAA, Carvalho JM, Dos Santos DCP, Feitosa ADO, Marinho PSB, Guilhon GMSB, de Souza ADL, da Silva FMA, Marinho AMR (2013) Antibacterial activity of alkaloids produced by endophytic fungus *Aspergillus sp.* EJC08 isolated from medical plant *Bauhinia guianensis*. Natl Prod Res 27:1633–1638

Polonio JC, Almeida TT, Garcia A, Mariucci GEG, Azevedo JL, Rhoden SA, Pamphile JA (2015) Biotechnological prospecting of foliar endophytic fungi of guaco (*Mikania glomerata* Spreng.) with antibacterial and antagonistic activity against phytopathogens. Gen Mol Res 14(3):7297–7309

Pompeng P, Sommit D, Sriubolmas N, Ngamrojanavanich N, Matsubara K, Pudhom K (2013) Antiangiogenetic effects of anthranoids from *Alternaria sp*., an endophytic fungus in a Thai medicinal plant *Erythrina variegata*. Phytomedicine 20(10):918–922

Prabavathy D, Valli NC (2013) Antimicrobial and antidiabetic activity of an endophytic fungi isolated from *Adathoda beddomei*. Int J Pharm Pharm Sci 5(3):780–783

Prabpai S, Wiyakrutta S, Sriubolmas A, Kongsaeree P (2015) Antimycobacterial dihydronaphthalenone from the endophytic fungus *Nodulisporium sp.* of *Antidesma ghaesembilla*. Phytochem Lett 13:375–378

Prabukumar S, Rajkuberan C, Ravindran K, Sivaramakrishnan S (2015) Isolation and characterization of endophytic fungi from medicinal plant *Crescentia cujete* and their antibacterial, antioxidant and anticancer properties. Int J Pharm Pharm Sci 7(11):316–321

Pretsch A, Nagl M, Schwendinger K, Kreiseder B, Wiederstein M, Pretsch D, Genov M, Hollaus M, Zinssmeister D, Debbab A, Hundsberger H, Eger A, Proksch P, Wiesner C (2014) Antimicrobial and anti-inflammatory activities of endophytic fungi *Talaromyces wortmannii* extracts against acne-inducing bacteria. PLoS One 9(6):e97929

Pugazhenthiran N, Anandan S, Kathiravan G, Prakash NKU, Crawford S, Kumar AM (2009) Microbial synthesis of silver nanoparticles by *Bacillus sp*. J Nanopart Res 11(7):1811–1815

Pulici M, Sugawara F, Koshino H, Uzawa J, Yoshida S, Lobkovsky E, Clardy J (1996) Pestalotiopsins A and B: new caryophyllenes from an endophytic fungus of *Taxus brevifolia*. J Org Chem 61(6):2122–2124

Purwantini I, Mustofab W, Asmah R (2015) Isolation of endophytic fungi from *Artemisia annua*, and identification of their antimicrobial compound using bioautography method. Int J Pharm Pharm Sci 7(12):95–99

Qadri M, Johri S, Shah BA, Khajuria A, Sidiq T, Lattoo SK, Abdin MA, Qadri SR (2013) Identification and bioactive potential of endophytic fungi isolated from selected plants of the Western Himalayas. Springer Plus 2:8

Qadri M, Rajput R, Abdin MZ, Vishwakarma RA, Hassan SR (2014) Diversity, molecular phylogeny, and bioactive potential of fungal endophytes associated with the Himalayan Blue Pine (*Pinus wallichiana*). Microb Ecol 67:877–887

Qi X, Wang E, Xing M, Zhao W, Chen X (2012) Rhizosphere and non-rhizosphere bacterial community composition of the wild medicinal plant *Rumexpatientia*. World J Microbiol Biotechnol 28(5):2257–2265

Qian Y, Yu H, He D, Yang H, Wang W, Wan X, Wang L (2013) Biosynthesis of silver nanoparticles by the endophytic fungus *Epicoccum nigrum* and their activity against pathogenic fungi. Bioprocess Biosyst Eng 36(11):1613–1619

Qin JC, Zhang YM, Gao JM, Bai MS, Yang SX, Laatsch H, Zhang AL (2009) Bioactive metabolites produced by *Chaetomium globosum* an endophyte isolated from *Ginkgo biloba*. Bioorg Med Chem Lett 19:1572–1574

Rabha AJ, Naglot A, Sharma GD, Gogoi HK, Veer V (2014) In vitro evaluation of antagonism of endophytic *Colletotrichum gloeosporioides* against potent fungal pathogens of *Camellia sinensis*. Ind J Microbiol 54(3):302–309

Raj KG, Manikandan R, Arulvasu C, Pandi M (2015) Anti-proliferative effect of fungal taxol extracted from *Cladosporium oxysporum* against human pathogenic bacteria and human colon cancer cell line HCT 15. Spectrochim Acta Part A: Mol Biomol Spectrosc 138:667–674

Raja HA, Kaur A, El-Elimat T, Figueroa M, Kumar R, Deep G, Agarwal R, Faethd SH, Cecha NB, Oberlies NH (2015) Phylogenetic and chemical diversity of fungal endophytes isolated from *Silybum marianum* (L) Gaertn. (milk thistle). Mycology 6(1):8–27

Rajeshwari S, Umamaheswari S, Prasanth AD, Rajamanikandan KP (2016) Bioactive potential of endophytic fungi *Aspergillus flavus* (SS03) against clinical isolates. Int J Pharm Pharm Sci 8(9):37–40

Rajput DK, Chanyal S, Agrawal PK (2016) Optimization of protease production by endophytic fungus, *Alternaria alternata* isolated from gymnosperm tree- *Cupressus torulosa*. World J Pharm Pharm Sci 5(7):1034–1054

Rajulu MBG, Thirunavukkarasu N, Babu AG, Aggarwal A, Suryanarayanana TS, Reddy MS (2013) Endophytic xylariaceae from the forests of Western Ghats, Southern India: distribution and biological activities. Mycology 4(1):29–37

Rakshith D, Santosh P, Satish S (2013) Isolation and characterization of antimicrobial metabolite producing endophytic *Phomopsis sp*. from *Ficus pumila* Linn. (Moraceae). Int J Chem Anal Sci 4:156–160

Ramesha A, Srinivas C (2014) Antimicrobial activity and phytochemical analysis of crude extracts of endophytic fungi isolated from *Plumeria acuminata* L. and *Plumeria obtusifolia* L. Eur J Exp Biol 4(2):35–43

Rao HCY, Santosh P, Rakshith D, Satish S (2015a) Molecular characterization of an endophytic *Phomopsis liquidambaris* CBR-15 from *Cryptolepis buchanani* Roem. and impact of culture media on biosynthesis of antimicrobial metabolites. 3. Biotech 5(2):165–173

Rao HCY, Bakera S, Rakshitha D, Satisha S (2015b) Molecular profiling and antimicrobial potential of endophytic *Gliomastix polychroma* CLB32 inhabiting *Combretum latifolium* Blume. Mycology 6:176–181

Ratnaweera PB, Williams DE, de Silva ED, Wijesundera RLC, Dalisay DS, Andersen RJ (2014) Helvolic acid, an antibacterial nortriterpenoid from a fungal endophyte, *Xylaria sp*. of orchid *Anoectochilus setaceus* endemic to Sri Lanka. Mycology 5(1):23–28

Ratnaweera PB, Williams DE, Patrick BO, de Silva ED, Andersen RJ (2015a) Solanioic acid, an antibacterial degraded steroid produced in culture by the fungus *Rhizoctonia* solani isolated from tubers of the medicinal plant *Cyperus rotundus*. Org Lett 17:2074–2077. doi:10.1021/acs.orglett.5b00596

Ratnaweera PB, de Silva ED, Williams DE, Andersen RJ (2015b) Antimicrobial activities of endophytic fungi obtained from the arid zone invasive plant *Opuntia dillenii* and the isolation of equisetin, from endophytic *Fusarium sp*. BMC Complement Altern Med 15:220. doi:10.1186/s12906-015-0722-4

Ratnaweera PB, de Silva ED, Wijesundera RLC, Andersen RJ (2016) Antimicrobial constituents of *Hypocrea virens*, an endophyte of the mangrove-associate plant *Premna serratifolia L.* J Nat Sci 44(1):43–51

Raviraja NS, Maria GL, Sridhar KR (2006) Antimicrobial evaluation of endophytic fungi inhabiting medicinal plants of the western Ghats of India. Eng Life Sci 6(5):515–520

Ravnikar M, Tercelj M, Janes D, Strukelj B, Kreft S (2015) Antibacterial activity of endophytic fungi isolated from conifer needles. Afr J Biotechnol 14(10):867–871

Razavi M, Salahinejad E, Fahmy M, Yazdimamaghani M, Vashaee D, Tayebi L (2015) Green chemical and biological synthesis of nanoparticles and their biomedical applications. In: Green processes for nanotechnology. Springer International Publishing, pp 207–235

Rekha D, Shivanna MB (2014) Diversity, antimicrobial and antioxidant activities of fungal endophytes in *Cynodon dactylon* (L.) Pers. and *Dactyloctenium aegyptium* (L.) P. Beauv. Int J Curr Microbiol Appl Sci 3(8):573–591

Ren Y, Strobel GA, Graff JC, Jutila M, Park SG, Gosh S, Teplow D, Condron M, Pang E, Hess WM, Moore E (2008) Colutellin A, an immunosuppressive peptide from *Colletotrichum dematium*. Microbiology 154(7):1973–1979
Rhoden SA, Garcia A, Bongiorno VA, Azevedo JL, Pamphile JA (2012) Antimicrobial activity of crude extracts of endophytic fungi isolated from medicinal plant *Trichilia elegans* A. Juss J Appl Pharm Sci 2:57–59
Ronsberg D, Debbab A, Mandi A, Vasylyeva V, Bohler P, Stork B, Engelke L, Hamacher A, Sawadogo R, Diederich M, Wray V, Lin W, Kassack MU, Janiak C, Scheu S, Wesselborg S, Kurta T, Aly AH, Proksch P (2013) Pro-apoptotic and immunostimulatory tetrahydroxanthone dimers from the endophytic fungus *Phomopsis longicolla*. J Org Chem 78(24):12409–12425
Rosaline I, Agastian P (2013) Glucosidase inhibitory activity and in vitro free radical scavenging activity of ethyl acetate extracts of endophytes isolated from the root of *Catharanthus roseus*. Int J Pharm Bio Sci 4(2):1246–1258
Ruma K, Kumar S, Prakash HS (2013) Antioxidant, anti-inflammatory, antimicrobial and cytotoxic properties of fungal endophytes from *Garcinia* species. Int J Pharm Pharm Sci 5(3):889–897
Ruma K, Kumar S, Kini KR, Prakash HS (2015) Genetic diversity and antimicrobial activity of endophytic *Myrothecium spp*. isolated from *Calophyllum apetalum* and *Garcinia Morella*. Mol Biol Rep 42:1533–1543
Sadananda TS, Govindappa M, Ramachandra YL (2013) Antibacterial activity of *Viscum album* endophytic fungal lectin. Int J Biol Pharm Res 4(12):1033–1042
Sadrati N, Daoud H, Zerroug A, Dahamna S, Bouharat S (2013) Screening of antimicrobial and antioxidant secondary metabolites from endophytic fungi isolated from wheat (*Triticum durum*). J Plant Prot Res 53(2):128–136
Sajitha N, Vasuki S, Suja M (2014) Antibacterial and antioxidant activities of l-glutaminase from seaweed endophytic fungi *Penicillium citrinum*. World J Pharma Phar Sci 3(4):682–695
Salini G, Madhusoodhanan A, Joseph A, Mohan A, Navya RK, Nair VV (2015) Antibacterial and antioxidant potential of endophytic fungi isolated from mangroves. Der Pharmacia Lett 7(12):53–57
Samaga PV, Rai VR (2014) Diversity and bioactivity of endophytic fungi from *Nothapodyte foetida* (Wt.) sleumer and *Hypericum mysorense* heyne. In: Microbial diversity and biotechnology in food security. Springer India, pp 91–102
Samaga PV, Rai VR, Rai KML (2014) *Bionectria ochroleuca* NOTL33—an endophytic fungus from *Nothapodytes foetida* producing antimicrobial and free radical scavenging metabolites. Ann Microbiol 64(1):275–285
Sandhu SS, Kumar S, Aharwal RP, Chaturvedi S (2014) Anti-bacterial potential of endophytic fungi isolated from *Saraca indica*. J Biol Chem Sci 1(1):24–34
Santiago C, Fitchett C, Murno MHG, Jalil J, Santhanam J (2012) Cytotoxic and antifungal activities of 5-Hydroxyramulosin, a compound produced by an endophytic fungus isolated from *Cinnamomum mollisimum*. Evid Based Complement Altern Med. doi:10.1155/2012/689310
Santiago C, Sun L, Munro MHG, Santhanam J (2014) Polyketide and benzopyran compounds of an endophytic fungus isolated from *Cinnamomum mollissimum*: biological activity and structure. Asian Pac J Trop Biomed 4(8):627–632
Santos IPD, Silva LCND, Silva MVD, Araujo JMD, Silva Cavalcanti MD, Menezes Lima VLD (2015) Antibacterial activity of endophytic fungi from leaves of *Indigofera suffruticosa* Miller (Fabaceae). Front Microbiol 6: doi:10.3389/fmicb.2015.00350
Saxena S, Meshram V, Kapoor N (2015) *Muscodor tigerii* sp. nov.-Volatile antibiotic producing endophytic fungus from the Northeastern Himalayas. Ann Microbiol 65:47–57
Schaible GA, Strobel GA, Mends MT, Geary B, Sears J (2015) Characterization of an endophytic *Gloeosporium sp*. and its novel bioactivity with “Synergistans”. Microb Ecol 70:41–50
Schlaeppi K, Bulgarelli D (2015) The plant microbiome at work. Mol Plant-Microbe Interact 28:212–217
Selim KA, El-Beih AA, AbdEl-Rahman TM, El-Diwany AI (2012) Biology of endophytic fungi. Curr Res Environ Appl Mycol 2:31–82

Selim KA, Ahmed A, Abdel-Rahman TM, El-Diwany AI (2014) Biological evaluation of endophytic fungus, *Chaetomium globosum* JN711454, as potential candidate for improving drug discovery. Cell Biochem Biophys 68(1):67–82

Sharma N, Barooah M (2015) Plant growth promoting endophytic fungi isolated from tea (*Camellia sinensis*) shrubs of Assam, India. App Ecol Environ Res 13(3):877–891

Sharma R, Vijaya Kumar BS (2013) Isolation characterization and antioxidant potential of endophytic fungi of *Ocimum sanctum* Linn. (Lamiaceae). Ind J Appl Res 3(7):5–10

Sharma T, Kaul S, Dhar MK (2015) Diversity of culturable bacterial endophytes of saffron in Kashmir, India. Springer Plus 4(1):1–13

Shentu X, Zhan X, Ma Z, Yu X, Zhang C (2014) Antifungal activity of metabolites of the endophytic fungus *Trichoderma brevicompactum* from garlic. Braz J Microbiol 45(1):248–254

Shweta S, Gurumurthy BR, Ravikanth G, Ramanan US, Shivanna MB (2013) Endophytic fungi from *Miquelia dentata* Bedd. produce the anticancer alkaloid, camptothecine. Phytomedicine 20(3):337–342

Silva-Hughes AF, Wedge DE, Cantrell CL, Carvalhoa CR, Panb Z, Moraes M, Madoxxe VL, Rosaa LH (2015) Diversity and antifungal activity of the endophytic fungi associated with the native medicinal cactus *Opuntia humifusa* (Cactaceae) from the United States. Microbiol Res 175:67–77

Singh B, Kaur A (2016) Antidiabetic potential of a peptide isolated from an endophytic *Aspergillus awamori*. J App Microbiol 120:301–311. doi:10.1111/jam.12998

Singh B, Thakur A, Kaur S, Chadha BS, Kaur A (2012) Acetylcholinesterase inhibitory potential and insecticidal activity of an endophytic *Alternaria sp.* from *Ricinus communis*. Appl Biochem Biotechnol 168(5):991–1002

Singh D, Rathod V, Ninganagouda S, Hiremath J, Singh AK, Mathew J (2014). Optimization and characterization of silver nanoparticle by endophytic fungi *Penicillium sp.* isolated from *Curcuma longa* (Turmeric) and application studies against MDR *E. coli* and *S. aureus*. Bioinorg. Chem. Appl. Article ID 408021, 8 pages doi.org/10.1155/2014/408021

Singh AK, Rathod V, Dattu Singh SN, Kulkarni P, Mathew J, Ul Haq M (2015a) Bioactive silver nanoparticles from endophytic fungus *Fusarium sp.* isolated from an ethanomedicinal plant *Withania somnifera* (Ashwagandha) and its antibacterial activity. Int J Nanomater Bios 5(1):15–19

Singh B, Kaur T, Kaur S, Manhas RK, Kaur A (2015b) An alpha-glucosidase inhibitor from an endophytic *Cladosporium sp*. with potential as a biocontrol agent. Appl Biochem Biotechnol 175:2020–2034. doi:10.1007/s12010-014-1325-0

Singh SK, Verma M, Ranjan A, Singh RK (2016) Antibacterial activity and preliminary phytochemical screening of endophytic fugal extract of *Rauvolfia serpentine*. The Open Conf Proceed J 7:104–113

Siriwardane AMDA, Kumar NS, Jayasinghe L, Fujimoto Y (2015) Chemical investigation of metabolites produced by an endophytic *Aspergillus* sp. isolated from *Limonia acidissima*. Nat Prod Res 29(14):1384–1387

Soltani J, Moghaddam MSH (2014) Antiproliferative, antifungal, and antibacterial activities of endophytic *Alternaria* sp. from Cupressaceae. Curr Microbiol 69:349–356

Song YC, Huang WY, Sun C, Wang FW, Tan RX (2005) Characterization of Graphislactone A as the antioxidant and free radical scavenging substance from the culture of *Cephalosporium sp.* IFB-E001, an endophytic fungus in *Trachelospermum jasminoides*. Biol Pharm Bull 28(3):506–509

Sowparthani K (2016) In vitro phytochemical analysis, high performance liquid chromatography, and antibacterial activity of endophytic fungi *Pestalotiopsis* sp. isolated from *Acalypha indica*. Asian J Pharm Clin Res 9(4):101–103

Srinivas RP, Nigam A, Aruna J, Alam A, Ishara L, Chamith YH, Chikkaswamy BK (2015) Antimicrobial activity in cultures of endophytic fungi isolated in some medicinal plant species. Int J Adv Res IT Engg 4(2):1–24

Srivastava A, Anandrao RK (2015) Antimicrobial potential of fungal endophytes isolated from leaves of *Prosopis juliflora* (sw.) Dc. An important weed. Int J Pharm Pharm Sci 7(12):128–136

Stepniewska Z, Kuznair A (2013) Endophytic microorganisms- promising applications in bioremediation of greenhouse gases. Appl Microbiol Biotechnol 97:9589–9596
Strobel GA (2003) Endophytes as sources of bioactive products. Microb Infect 5:535–544
Strobel G, Daisy B, Castillo B, Harper J (2004) Natural products from endophytic microorganisms. J Nat Prod 67:257–268
Su J, Yang M (2015) Huperzine A production by *Paecilomyces tenuis* YS-13, an endophytic fungus isolated from *Huperzia serrata*. Nat Prod Res 29(11):1035–1041
Sun X, Kong X, Gao H, Zhu T, Wu G, Gu Q, Li D (2013) Two new meroterpenoids produced by the endophytic fungus *Penicillium sp.* SXH-65. Arch Pharm Res 37(8):978–982
Sundram S (2013) First report: isolation of endophytic *Trichoderma* from oil palm (*Elaeis guineensis* Jacq.) and their in vitro antagonistic assessment on *Ganoderma boninense*. J Oil Palm Res 25(3):368–372
Sunitha VH, Devi DN, Srinivas C (2013) Extracellular enzymatic activity of endophytic fungal strains isolated from medicinal plants. World J Agric Sci 9(1):01–09
Sunkar S, Nachiyar CV (2013) Endophytic fungi mediated extracellular silver nanoparticles as effective antibacterial agents. Int J Pharm Pharm Sci 5(2):95–100
Supaphon P, Phongpaichit S, Rukachaisirikul V, Sakayaroj J (2013) Antimicrobial potential of endophytic fungi derived from three seagrass species: *Cymodocea serrulata, Halophila ovalis* and *Thalassia hemprichii*. PLoS One 8(8):72520. doi:10.1371/journal.pone.0072520
Swarnalatha Y, Bhaswati S, Lokeswara CY (2015) Bioactive compound analysis and antioxidant activity of endophytic bacterial extract from *Adhathoda beddomei*. Asian J Pharm Clin Res 8(1):70–72
Syed S, Qadri M, Riyaz-Ul-Hassan S, Johri S (2013) A novel exocellulase from an endophytic fungal strain DEF1. Int J Res Pharma Biomed Sci 4(2):573–577
Talontsi FM, Dittrich B, Schuffler A, Sun H, Laatsch H (2013) Epicoccolides: antimicrobial and antifungal polyketides from an endophytic fungus *Epicoccum* sp. associated with *Theobroma cacao*. European J Org Chem 15:3174–3180
Talontsi FM, Lamshöft M, Douanla-Meli C, Kouam SF, Spiteller M (2014) Antiplasmodial and cytotoxic dibenzofurans from *Preussia* sp. harboured in *Enantia chlorantha*. Fitoterapia 93:233–238
Tanney JB, McMullin DR, Green BD, Miller JD, Seifert KA (2016) Production of antifungal and antiinsectan metabolites by the *Picea* endophyte *Diaporthe maritima* sp. nov. Fungal Biol 120(11):1448–1457
Tapwal A, Pradhan S, Chandra S, Rashmi S (2016) Antimycotic activity and phytochemical screening of fungal endophytes associated with *Santalum album*. Nusantara Biosci 8(1):14–17
Taware R, Abnave P, Patil D, Rajamohananan PR, Raja R, Soundararajan G, Ahmad A (2014) Isolation, purification and characterization of Trichothecinol-a produced by endophytic fungus *Trichothecium sp.* and its antifungal, anticancer and antimetastatic activities. Sustain Chem process 2(1):1–9
Tayung K, Barik BP, Jha DK, Deka DC (2011) Identification and characterization of antimicrobial metabolite from an endophytic fungus, *Fusarium solani* isolated from bark of Himalayan yew. Mycosphere 2:203–213
Teiten MH, Mack F, Debbab A, Aly AH, Dicato M, Proksch P, Diederich M (2013) Anticancer effect of altersolanol A, a metabolite produced by the endophytic fungus *Stemphylium globuliferum*, mediated by its pro-apoptotic and anti-invasive potential via the inhibition of NF-κB activity. Bioorg Med Chem Lett 21(13):3850–3858
Tejesvi MV, Kini KR, Prakash HS, Subbiah V, Shetty HS (2007) Genetic diversity and antifungal activity of species of *Pestalotiopsis* isolated as endophytes from medicinal plants. Fungal Divers 24:37–54
Tejesvi HMV, Segura DRS, Schnorr KM, Sandvang D, Mattila S, Olsen PB, Neve S, Kruse T, Kristensen HH, Pirttila AM (2013) An antimicrobial peptide from endophytic *Fusarium tricinctum* of *Rhododendron tomentosum*. Fungal Divers 60:153–159
Tenguria RK, Firodiya A (2013) Diversity of endophytic fungi in leaves of glycine max (L.) merr. from central region of Madhya Pradesh. World J Pharm Pharm Sci 2:5928–5934

Thakur JP, Haider R, Singh DK, Kumar BS, Vasudev PG, Luqman S, Kalra A, Saikia D, Negi AS (2015) Bioactive isochromenone isolated from *Aspergillus fumigatus*, endophytic fungus from *Bacopa monnieri*. Microbiol Res 6:5800

Tolulope R, Adeyemi A, Erute M, Abiodun T (2015) Isolation and screening of endophytic fungi from three plants used in traditional medicine in Nigeria for antimicrobial activity. Int J Green Pharm 9(1):58

Tonial F, Maia BH, Gomes-Figueiredo JA, Sobottka AM, Bertol CD, Nepel A, Savi DC, Vicente VA, Gomes RR, Glienke C (2016) Influence of culturing conditions on bioprospecting and the antimicrobial potential of endophytic fungi from *Schinus terebinthifolius*. Curr Microbiol 72:173–183

Tuppad DS, Shishupala S (2014) Evaluation of endophytic fungi from *Butea monosperma* for antimicrobial and enzyme activity. J Med Plants Stud 2(4):38–45

Turner TR, James EK, Poole PS (2013) The plant microbiome. Genome Biol 14:209. doi:10.1186/gb-2013-14-6-209

Umashankar T, Govindappa M, Ramachandra YL (2014) In vitro antioxidant and antimicrobial activity of partially purified coumarins from fungal endophytes of *Crotalaria pallida*. Int J Curr Micobiol App Sci 3(8):58–72

Ushasri R, Anusha R (2015) In vitro anti-diabetic activity of ethanolic and acetone extracts of endophytic fungi *Syncephalastrum racemosum* isolated from the seaweed *Gracilaria corticata* by alpha-amylase inhibition assay method. Int J Curr Microbiol App Sci 4(1):254–259

Verma VC, Singh SK, Solanki R, Prakash S (2011) Biofabrication of anisotropic gold nanotriangles using extract of endophytic *Aspergillus clavatus* as a dual functional reductant and stabilizer. Nanoscale Res Lett 6:16

Verma SK, Gond SK, Mishra A, Sharma VK, Kumar J, Singh DK, Kumar A, Goutam J, Kharwar RN (2014) Impact of environmental variables on the isolation, diversity and antibacterial activity of endophytic fungal communities from *Madhuca indica* Gmel. at different locations in India. Ann Microbiol 64:721–734

Vieira ML, Johann S, Hughes FM, Rosa CA, Rosa LH (2014) The diversity and antimicrobial activity of endophytic fungi associated with medicinal plant *Baccharis trimera* (Asteraceae) from the Brazilian savannah. Can J Microbiol 60(12):847–856

Vijayan S, Koilaparambil D, George TK, Shaikmoideen JM (2016) Antibacterial and cytotoxicity studies of silver nanoparticles synthesized by endophytic *Fusarium solani* isolated from *Withania somnifera* (L.) J Water Environ Nanotechnol 1(2):91–103

Vinodhini D, Agastian P (2013) Berberine production by endophytic fungus *Fusarium solani* from *Coscinium fenestratum*. Int J Biol Pharm Res 4:1239–1245

Wang LW, Xu BG, Wang JY, Su ZZ, Lin FC, Zhang CL, Kubicek CP (2012a) Bioactive metabolites from *Phoma* species, an endophytic fungus from the Chinese medicinal plant *Arisaema erubescens*. Appl Microbiol Biotechnol 93(3):1231–1239

Wang Y, Xu L, Ren W, Zhao D, Zhu Y, Wu X (2012b) Bioactive metabolites from *Chaetomium globosum* L18, an endophytic fungus in the medicinal plant *Curcuma wenyujin*. Phytomedicine 19(3):364–368

Wang WX, Kusari S, Sezgin S, Lamshöft M, Kusari P, Kayser O, Spiteller M (2015) Hexacyclopeptides secreted by an endophytic fungus *Fusarium solani* N06 act as crosstalk molecules in *Narcissus tazetta*. Appl Microbiol Biotechnol 99(18):7651–7662

Wang WX, Kusari S, Laatsch H, Golz C, Kusari P, Strohmann C, Kayser O, Spiteller M (2016a) Antibacterial azaphilones from an endophytic fungus, *Colletotrichum sp* BS4. J Nat Prod 79:704–710. doi:10.1021/acs.jnatprod.5b00436

Wang Y, Lai Z, Li XX, Yan RM, Zhang ZB, Yang HL, Zhu D (2016b) Isolation, diversity and acetylcholinesterase inhibitory activity of the culturable endophytic fungi harboured in *Huperzia serrata* from Jinggang Mountain, China. World J Microbiol Biotechnol 32:20. doi:10.1007/s11274-015-1966-3

Wei B, Yang ZD, Chen XW, Zhou SY, Yu HT, Sun JY, Yao X, Wang YG, Xue HY (2016) Colletotrilactam A–D, novel lactams from *Colletotrichum gloeosporioides* GT-7, a fungal endophyte of *Uncaria rhynchophylla*. Fitoterapia 113:158–163

Wijeratne EMK, He H, Franzblau SG, Hoffman AM, Gunatilaka AAL (2013) Phomapyrrolidones A−C, antitubercular alkaloids from the endophytic fungus *Phoma sp*. NRRL 46751. J Nat Prod 76:1860–1865

Wu LS, Hu CL, Han T, Zheng CJ, Ma XQ, Rahman K, Qin LP (2013a) Cytotoxic metabolites from *Perenniporia tephropora*, an endophytic fungus from *Taxus chinensis* var. mairei. Appl Microbiol Biotechnol 97:305–315

Wu H, Yang HY, You XL, Li YH (2013b) Diversity of endophytic fungi from roots of *Panax ginseng* and their saponin yield capacities. Springer Plus 2:107

Xia G, Li J, Li H, Long Y, Lin S, Lu Y, He L, Lin Y, Liu L, She Z (2014) Alterporriol-type dimers from the mangrove endophytic fungus, *Alternaria* sp. (sk11), and their mptpb inhibitions. Mar Drugs 12:2953–2969

Xia X, Kim S, Bang S, Lee HJ, Liu C, Park CI, Shim HC (2015) Barceloneic acid C, a new polyketide from an endophytic fungus *Phoma sp*. JS752 and its antibacterial activities. J Antibiot 68(2):139–141

Xiao J, Zhang Q, Gao YQ, Tang JJ, Zhang AL, Gao JM (2014a) Secondary metabolites from the endophytic *Botryosphaeria dothidea* of *Melia azedarach* and their antifungal, antibacterial, antioxidant, and cytotoxic activities. J Agric Food Chem 62:3584–3590

Xiao J, Zhang Q, Gao YQ, Shi XW, Gao JM (2014b) Antifungal and antibacterial metabolites from an endophytic *Aspergillus* sp. associated with *Melia azedarach*. Nat Prod Res 28:1388–1392

Xiao Z, Lin S, Tan C, Lu Y, He L, Huang X, She Z (2015) Asperlones A and B, dinaphthalenone derivatives from a mangrove endophytic fungus *Aspergillus* sp. (2015) Mar. Drugs 13:366–378

Xu L, Wang J, Zhao J, Li P, Shan T, Wang J, Li X, Zhou L (2010) Beauvericin from the endophytic fungus, *Fusarium redolens*, isolated from *Dioscorea zingiberensis* and its antibacterial activity. Natl Prod Commun 5:811–814

Xu YM, Espinosa-Artiles P, Liu MX, Arnold AE, Gunatlilaka AL (2013) Secoemestrin D, a cytotoxic epitetrathiodioxopiperizine, and emericellenes A–E, five sesterterpenoids from *Emericella sp*. AST0036, a fungal endophyte of *Astragalus lentiginosus*. J Nat Prod 76(12):2330–2336

Yadav M, Yadav A, Kumar S, Yadav JP (2016) Spatial and seasonal influences on culturable endophytic mycobiota associated with different tissues of *Eugenia jambolana* Lam. and their antibacterial activity against MDR strains. BMC Microbiol 16:–44

Yang XL, Li ZZ (2013) New spiral γ-lactone enantiomers from the plant endophytic fungus *Pestalotiopsis foedan*. Molecules 18(2):2236–2242

Yang J, Huang R, Qiu SX, She Z, Lin Y (2013) A new isobenzofuranone from the mangrove endophytic fungus *Penicillium sp.* (ZH58). Natl Prod Res 27(20):1902–1905

Yang Y, Zhao H, Barrero RA, Zhang B, Sun G, Wilson IW, Xie F, Walker KD, Parks JW, Bruce R, Guo G, Chen L, Zhang Y, Huang X, Tang Q, Liu H, Bellgard MI, Qiu D, Lai J, Hoffman A (2014a) Genome sequencing and analysis of the paclitaxel-producing endophytic fungus *Penicillium aurantiogriseum* NRRL 62431. BMC Genomics 15(1):1–14

Yang Z, Bao L, Yin Y, Ding G, Ge M, Chen D, Qian X (2014b) Pyrenocines N–O: two novel pyrones from *Colletotrichum* sp. HCCB03289. J Antibiot 67:791–793

Yang HR, Hu XP, Jiang CJ, Qi J, Wu YC, Li W, Zeng YJ, Li CF, Liu SX (2015) Diversity and antimicrobial activity of endophytic fungi isolated from *Cephalotaxus hainanensis* Li, a well-known medicinal plant in China. App Micrbiol 61(5):484–490

Ye Y, XiaoY ML, Li H, Xie Z, Wang M, Ma H, Tang H, Liu J (2013) Flavipin in *Chaetomium globosum* CDW7, an endophytic fungus from *Ginkgo biloba*, contributes to antioxidant activity. Appl Microbiol Biotechnol 97:7131–7139

Yin OCJ, Ibrahim D, Lee CC (2015) Bioactive compounds from *Aspergillus terreus* MP15, an endophytic fungus isolated from *Swietenia macrophylla* leaf. Malaysian J Med Biol Res 2(3):262–271

Ying YM, Shan WG, Zhang LW, Zhan ZJ (2013) Ceriponols A–K, tremulane sesquitepenes from *Ceriporia lacerate* HS-ZJUT-C13A, a fungal endophyte of *Huperzia serrata*. Phytochemistry 95:360–367

You X, Feng S, Luo S, Cong D, Yu Z, Yang Z, Zhang J (2013) Studies on a rhein-producing endophytic fungus isolated from *Rheum palmatum* L. Fitoterapia 85:161–168

Yuan Y, Tian JM, Xiao J, Shao Q, Gao JM (2013) Bioactive metabolites isolated from *Penicillium* sp. YY-20, the endophytic fungus from *Ginkgo biloba*. Nat Prod Res 28(4):278–281

Zaferanloo B, Bhattacharjee S, Ghorbani MM, Mahon PJ, Palombo EA (2014a) Amylase production by *Preussia minima*, a fungus of endophytic origin: optimization of fermentation conditions and analysis of fungal secretome by LC-MS. BMC Microbiol 14(1):55–66

Zaferanloo B, Quang TD, Daumoo S, Ghorbani MM, Mahon PJ, Palombo EA (2014b) Optimization of protease production by endophytic fungus, *Alternaria alternata*, isolated from an Australian Native plant. World J Microbiol Biotechnol 30(6):1755–1762

Zaher AM, Moharram AM, Davis R, Panizzi P, Makboul MA, Calderon AI (2015a) Characterisation of the metabolites of an antibacterial endophyte *Botryodiplodia theobromae* Pat. of *Dracaena draco* L. by LC–MS/MS. Natl Prod Res 29(24):2275–2281

Zaher AM, Makboul MA, Moharram AM, Calderon BLT (2015b) A new enniatin antibiotic from the endophyte *Fusarium tricinctum* Corda. J Antibiot 68:197–200

Zeng Y, Wang H, Kamdem RST, Orfali RS, Dai H, Makhloufi G, Janiak C, Liu Z, Proksch P (2016) A new cyclohexapeptide, penitropeptide and a new polyketide, penitropone from the endophytic fungus *Penicillium tropicum*. Tetrahedron Lett 57:2998–3001

Zhang YW, Thompson R, Zhang H, Xu H (2011) APP processing in Alzheimer's disease. Mol Brain 4(1):3

Zhang H, Xiong Y, Zhao H, Yi Y, Zhang C, Yu C, Xu C (2013a) An antimicrobial compound from the endophytic fungus *Phoma sp.* isolated from the medicinal plant *Taraxacum mongolicum*. J. Taiwan Inst Chem E 44:177–181

Zhang D, Ge H, Xie D, Chen R, Zou JH, Tao X, Dai J (2013b) Periconiasins A-C, new cytotoxic cytochalasans with an unprecedented 9/6/5 tricyclic ring system from endophytic fungus *Periconia sp*. Org Lett 15(7):1674–1677

Zhang W, Xu L, Yang L, Huang Y, Li S, Shen Y (2014) Phomopsidone A, a novel depsidone metabolite from the mangrove endophytic fungus *Phomopsis sp.* A123. Fitoterapia 96:146–151

Zhang W, Wei W, Shi J, Chen C, Zhao G, Jiao R, Tan R (2015a) Natural phenolic metabolites from endophytic *Aspergillus sp*. IFB-YXS with antimicrobial activity. Bioorg Med Chem Lett 25:2698–2701

Zhang FF, Wang FZ, Zheng YC, Liu HY, Zhang XQ, Wu SS (2015b) Isolation and characterzation of endophytic huperzine A producing fungi from *Phlegmariurus phlegmaria*. Microbiology 84(5):701–709

Zhang H, Ruan C, Bai X, Zhang M, Zhu S, Jiang Y (2016a) Isolation and identification of the antimicrobial agent beauvericin from the endophytic *Fusarium oxysporum* 5–19 with NMR and ESI-MS/MS. BioMed Res Int. doi.org/10.1155/2016/1084670

Zhang H, Sun X, Xu C (2016b) Antimicrobial activity of endophytic fungus *Fusarium* sp. isolated from medicinal honeysuckle plant. Arch Biol Sci 68(1):25–30

Zhao JT, Fu YJ, Luo M, Zu YG, Wang W, Zhao CJ, Gu CB (2012a) Endophytic fungi from pigeon pea [*Cajanus cajan* (L.) Mill sp.] produce antioxidant Cajaninstilbene acid. J Agric Food Chem 60:4314–4319

Zhao JH, Zhang YL, Wang LW, Wang JY, Zhang CL (2012b) Bioactive secondary metabolites from *Nigrospora sp*. LLGLM003, an endophytic fungus of the medicinal plant *Moringa oleifera* Lam. World J Microbiol Biotechnol 28(5):2107–2112

Zhao J, Li C, Wang W, Zhao C, Luo M, Mu F, Yao M (2013) *Hypocrea lixii*, novel endophytic fungi producing anticancer agent cajanol, isolated from pigeon pea (*Cajanus cajan* [L.] Millsp.) J Appl Microbiol 115(1):102–113

Zheng L, Ma L, Zheng L (2014) In vitro α-glucosidase inhibitory activity of endophytic *Alternaria* sp. S8 isolated from *Morus alba*. Planta Med 80 – P1N17 doi: 10.1055/s-0034-1394607

Zheng YK, Miao CP, Chen HH, Huang FF, Xia YM, Chen YV, Zhao LX (2016) Endophytic fungi harbored in *Panax notoginseng*: diversity and potential as biological control agents against host plant pathogens of root-rot disease. Ginseng Res1–8

Zhou F, Kurtan TK, Yang XH, Mandi A, Geng MY, Ye BP, Scafati OT, Guo YW (2014a) Penibruguieramine A, a novel pyrrolizidine alkaloid from the endophytic fungus *Penicillium sp*. GD6 associated with Chinese mangrove *Bruguiera gymnorrhiza*. Org Lett 16:1390–1393

Zhou XM, Zheng CJ, Song XP, Han CR, Chen WH, Chen GY (2014b) Antibacterial a-pyrone derivatives from a mangrove-derived fungus *Stemphylium sp.* 33231 from the South China sea. J Antibiot 67:401–403

Zhou M, Lou J, Li YK, Wang YD, Zhou K, Ji BK, Dong W, Gao XM, Du G, Hu QF (2015) Versicolols A and B two new prenylated isocoumarins from endophytic fungus *Aspergillus versicolor* and their cytotoxic activity. Arch Pharmacal Res 1–5

Zilla MK, Qadri M, Pathania A, Strobel GA, Nalli YN, Kumar S, Guru SK, Bhushan S, Singh SK, Vishwakarma RA, Riyaz-Ul-Hassan S, Ali A (2013) Bioactive metabolites from an endophytic *Cryptosporiopsis* sp. inhabiting *Clidemia hirta*. Phytochemistry 95:291–297