

Isolated Endophytic Fungi from the Plant *Curcuma longa* and Their Potential Bioactivity—A Review

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Abstract

Endophytes (both fungi and bacteria) represent a treasure house for bioactive compounds such as anticancer, immunomodulatory, antioxidant, antiparasitic, insecticidal etc. for use in the pharmaceutical and agrochemical industries. Endophytic population is greatly influenced by climatic conditions and location where the host plant grows. Curcuma longa L. (Turmeric) is a medicinal plant belonging to the Zingiberaceae family that is usually used as spice and preservative. Traditionally it is used to treat various conditions and symptoms such as digestive disorders, arthritis, cardiovascular conditions, cancer, bacterial infections etc. In recent times, there have been different discoveries on endophytic fungi and their biological activity from C. longa. But there is no comprehensive review on endophytic fungi of C. longa. The aim of this review is to analyze the published report based on the endophytic fungi to provide for the first time an updated information about their isolation from different tissues, their biological activities including the phytochemistry of C. longa. This will lead the way to forecast the missing link for future research work.

Keywords

Curcuma longa, Endophytes, Compounds, Bioactivity

1. Introduction

Curcuma longa L. (Turmeric) is a rhizomatous herbaceous perennial plant of the

ginger family, Zingiberaceae [1]. It is a naturally grown plant in the Indian subcontinent and Southeast Asia. Turmeric has been used in Asia for thousands of years and is a major part of Ayurveda, Siddha medicine, Unani, and traditional Chinese medicine [2]. A lot of scientific works on pharmacological properties of turmeric have been reported by many scientists and researchers such as anti-inflammatory [3] [4], antiallergic [5], antiobesity [6], lipid-lowering [7], antiproliferative [8], anti-microbial [9] [10], anti-oxidant [11] [12], anti-diabetic [13], hypoglycemic [14], immunomodulating [15], insecticidal [16], anti-fungal [17], neuroprotective [18], anti-mutagenic [19], hypolipidemic [20] etc.

Endophyte, the most important integral part of plant tissues, is a progressively significant area of research in many fields because of their chemical miscellany and their ability to produce many unique secondary metabolites that can be utilized for fuel, medicine, restoration and agriculture. Endophytes are isolated from medicinal plants possess strong fungicidal, bactericidal and cytotoxic metabolites [21]. Previous studies indicate that there have been few investigations done on endophytic microbes of turmeric plant (*Curcuma longa*). Thus, exploring endophytic microbes from *Curcuma longa* increases the probability to discover novel compound which is extensive in resistance tissues. There is no review on the endophytic fungi from turmeric plants. Therefore, it is necessary to review the endophytic fungi from *Curcuma longa*. Hence, this review discusses the current research progresses on endophytic fungi from the turmeric plant, including types of endophytic fungi identified, described bioactive compounds, and biological activities of endophytes to discover the current scope of knowledge of endophytes.

2. Isolated Compounds from Curcuma longa

A total of 235 compounds with various activities were isolated and identified from the flowers, leaves, roots and rhizomes part of *Curcuma longa* which is the most phytochemically investigated plant in the world. These compounds are primarily phenolic and terpenoid compounds including diarylheptanoids (including commonly known as curcuminoids), diarylpentanoids, monoterpenes, sesquiterpenes, diterpenes, triterpenes, sterols, fatty acids and also some alkaloidal compounds. A list of isolated compounds from different groups of *C. longa* is presented in **Table 1**. Curcumin is the key phytochemical compound

Table 1. Isolated compounds from C. longa.

Sl.No	Compounds	Compound type	References
1	curcumin (curcumin I),	Diarylheptanoid	[24] [28]-[35]
	demethoxycurcumin (curcumin II),		
	1-(4-hydroxy-3-methoxyphenyl)-7-(3,4- dihydroxyphenyl)-1,6-heptadiene-3,5-dione,		
	1-(4-hydroxyphenyl)-7-(3,4-dihydroxyphenyl)- 1,6-heptadiene-3, 5-dione,		

	bisdemethoxycurcumin (curcumin III),		
	tetrahydroxycurcumin,		
	5-hydroxyl-1-(4-hydroxy-3-methoxyphenyl)-7- (4-hydroxyphenyl)-4,6-heptadiene-3-one,		
	5-hydroxyl-1,7-bis(4-hydroxy-3-methoxyphenyl)- 4,6-heptadiene-3-one,		
	1,7-bis(4-hydroxyphenyl)-1-heptene-3,5-dione,		
	5-hydroxyl-7-(4-hydroxy-3-methoxyphenyl)-1- (4-hydroxyphenyl)-4,6-heptadiene-3-one,		
	3-hydroxy-1,7-bis-(4-hydroxyphenyl)-6- heptene-1,5-dione,		
	1,5-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)- 7-(4-hydroxyphenyl)-4,6-heptadiene-3-one,		
	1,5-dihydroxy-1-(4-hydroxyphenyl)-7-(4-hydroxy- 3-methoxyphenyl)-4,6-heptadiene-3-one,		
	1,5-dihydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-4, 6-heptadiene-3-one,		
	1,5-dihydroxy-1,7-bis(4-hydroxyphenyl)- 4,6-heptadiene-3-one,		
	1,5-epoxy-3-carbonyl-1,7-bis(4-hydroxyphenyl)- 4,6-heptadiene,		
	Cyclocurcumin,		
	1,7-bis(4-hydroxy-3-methoxyphenyl)-1,4,6- heptatrien-3-one,		
	1,7-bis-(4-hydroxyphenyl)-1,4,6-heptatrien-3-one,		
	1,5-bis(4-hydroxyphenyl)-penta-(1E,4E)- 1,4-dien-3-one,		
	1-(4-hydroxy-3-methoxyphenyl)-5-(4-hydroxyphenyl)- 1,4-pentadiene-3-one,		
	1,5-bis(4-hydroxy-3-methoxyphenyl)-penta- (1E,4E)-1,4-dien-3-one		
2	4"-(4"'-hydroxyphenyl)-2"-oxo-3"-butenyl-3- (4'-hydroxyphenyl-3'-methoxy)-propenoate,	Phenylpropene	[28] [35] [36]
	4"-(4"'-hydroxyphenyl-3-methoxy)-2"-oxo-3"- butenyl-3-(4'-hydroxyphenyl)-propenoate,		
	calebin-A,		
	(E)-4-(4-hydroxy-3-methoxyphenyl)but-3-en-2-one,		
	(E)-ferulic acid,		
	(Z)-ferulic acid		
3	vanillic acid,	Phenolic	[35]
	vanillin		
4	p-cymene,	Monoterpenoid	[27] [38]-[44]
	m-cymene,		
	<i>a</i> -terpinene,		

Continued γ-terpinene, β -phellandrene, p-mentha-1,4(8)-diene, terpinen-4-ol, 4-terpinol, Limonene, Terpinolene, Thymol, Phellandrol, Carvacrol, (E)-carveol, *y*-terpineol, Menthol, 1,3,8-paramenthatriene, p-methylacetophenone, Piperitone, o-cymene, Carvone, p-menth-8-en-2-one, *a*-thujene, *a*-terpineol, p-cymen-8-ol, p-meth-8-en-2-one, piperitone epoxide, Sylvestrene, Menthofuran, β , β -dimethylstyrene, Camphor, Teresantalol, Benzene, 1-methyl-4-(1-methylpropyl), 2-norpinanone, borneol, bornyl acetate, (E)-chrysanthenyl acetate, (Z)-cinerone, (Z)-sabinol,

ontinuea			
	2-(2,5-dihydroxy-4-methylcyclohex-3-enyl)		
	propanoic acid,		
	camphene,		
	3-carene,		
	2-carene,		
	ascaridole,		
	α-pinene,		
	β -pinene,		
	cineole,		
	cis-ocimene,		
	citronellal,		
	geranial,		
	neral,		
	myrcene,		
	R-citronellene,		
	citronellylpentanoate,		
	nerol,		
	geraniol,		
	iso-artemisia ketone,		
	trans-ocimene,		
	linalool,		
	neryl acetate,		
	geranic acid,		
	geranyl acetate,		
	3-bornanone,		
	4,8-dimethyl-3,7-nonadien-2-ol,		
	3,4,5,6-tetramethyl-2,5-octadiene,		
	3,7-dimethyl-6-nonenal,		
	2,6-dimethyl-2,6-octadiene-1,8-diol,		
	4,5-dimethyl-2,6-octadiene		
5	ar-turmerone,	Bisabolane	[25]
	<i>a</i> -turmerone,		[26] [35]-[52]
	β -turmerone,		
2	2-methyl-6-(4-hydroxyphenyl)-2-hepten-4-one,		
	2-methyl-6-(4-hydroxy-3-methylphenyl)-2- hepten-4-one,		
2	-methoxy-5-hydroxybisabola-3,10-diene-9-one,		

2-methyl-6-(4-formylphenyl)-2-hepten-4-one,

5-hydroxyl-ar-turmerone,

4-methylene-5-hydroxybisabola-2,10-diene-9-one,

ar-curcumene,

ar-turmerol,

bisabola-3,10-diene-2-one,

bisabolone,

4, 5-dihydroxybisabola-2,10-diene,

4-hydroxybisabola-2,10-diene-9-one,

4-methoxy-5-hydroxy-bisabola-2,10-diene-9-one,

bisacurone,

bisacurone A,

bisacurone B,

bisacurone C,

bisabolone-9-one,

bisacumol,

turmeronol A,

turmeronol B,

a-oxobisabolene,

a-zingiberene,

xanthorrhizol,

zingerone,

dehydrozingerone,

(Z)-*a*-atlantone,

(E)-*a*-atlantone,

 β -bisabolene,

(6S,7R)-bisabolene,

γ-bisabolene,

 γ -curcumene,

 β -curcumene,

a-curcumene,

 β -sesquiphellandrene,

(Z)-γ-atlantone,

(E)- γ -atlantone,

(6S)-2-methyl-6-[(1R,5S)-(4-methene-5hydroxyl-2-cyclohexen)-2-hepten-4-one,

curcuphenol,

curlone,

	curculonone C,		
	curculonone D,		
	curculonone B,		
	curculonone A, 2, 5-dihydroxybisabola-3, 10-diene,		
	(6R)-[(1R)-1,5-dimethylhex-4-enyl]-3- methylcyclohex-2-en-1-one,		
	β -atlantone,2,8-epoxy-5-hydroxybisabola- 3,10-diene-9-one,		
	<i>a</i> -bisabolol,		
	dihydro-ar-turmerone,		
	dehydrocurcumene		
6	(4S,5S)-germacrone-4,5-epoxide,	Germacrane	[39] [40] [49]
	dehydrocurdione,		
	germacrene D,		
	germacrone,		
	germacrone-13-al,		
	β-germacene		
7	1,10-dehydro-10-deoxy-9-oxozedoarondiol,	Guaiane	[35] [49]
	curcumenol,		
	epiprocurcumenol,		
	isoprocurcumenol,		
	zedoaronediol,		
	procurcumadiol,		
	procurcumenol		
8	naphthalene,1,2,3,4,4a,5,6,8a-octahydro-4a,8- dimethyl-2-(1-methylethylidene),	Selinane	[38] [41]
	a-selinene,		
	juniper camphor,		
	corymbolone		
9	a-santalol,	Santalane	[38]
	<i>a</i> -santalene,		
	β -santalene		
10	(E)-caryophyllene,	Caryophyllane	[38] [43]
	caryophyllene oxide		
11	β -elemene,	Elemane	[38] [41]
	γ-elemene		
12	acoradiene	Acorane	[38]
13	aristolene	Aristolene	[38]
14	(Z)- <i>a</i> -bergamotene	Bergamotane	[43]

15	curcumenone	Carabrane	[49]
16	di-epi-cedrene	Cedrane	[38]
17	himachalene	Himachalene	[38]
18	(E)-sesquisabinene hydrate	Sesquisabinane	[43]
19	bicyclo [7.2.0] undecane,10,10-dimethyl-2,6-bis(methylene),	Sesquiterpene	[35] [37] [38 [39] [40] [42 [43] [51] [53
	10,10-dimethyl-2,6-bis(methylene),		
	γ-gurjunen epoxide,		
	1-epi-cubenol,		
	cubebene,		
	7-epi-sesquithujene,		
	caryophyllene,		
	6 <i>a</i> -hydroxycurcumanolide A,		
	curcumanolide A,		
	curcumanolide B,		
	curcumin L,		
	<i>a</i> -humulene,		
	12-oxabicyclo [9.1.0]dodeca-3,7-diene,		
	1,5,5,8-tetramethyl,		
	adoxal,		
	2,6,10-dodecatrien-1-ol,		
	3,7,11-trimethyl,		
	(E,E)- <i>a</i> -farnesene,		
	5,9-undecadien-2-one,		
	6,10-dimethyl-, (Z),		
	hxadecane-1,2-diol,		
	nerolidal,		
	(Z)-β-farnesene,		
	nerolidyl propionate		
20	Phytol,	Diterpenoid	[38] [41]
	(E,E,E)-3,7,11,15-tetramethylhexadeca- 1,3,6,10,14-pentaene,		
	2,6,11,15-tetramethyl-hexadeca-2,6,8,10,14-pentaene,		
	1,6,10,14-hexadecatetraen-3-ol,		
	3,7,11,15-tetramethyl-,(E,E)		
21	hopenone I,	Triterpenoid	[54]
	hop-17(21)-en-3β-ol,		
	hop-17(21)-en-3 β -yl acetate		

22	β -sitosterol,	Steroid	[35] [38]
	stigmasterol,		
	gitoxigenin,		
	20-oxopregn-16-en-12-yl acetate		
23	linoleic acid,	Fatty acid	[41]
	8,11-Octadecadienoic acid,		
	methyl ester,		
	palmitic acid (n-hexadecanoic acid),		
	oleic acid,		
	stearic acid		
24	curcuma-J,	Miscellaneous	[38] [50] [55]
	2-(2'-methyl-1'-propenyl)-4,6- dimethyl-7-hydroxyquinoline,		
	2,3,5-trimethylfuran,		
	(1,2,3-trimethyl-cyclopent-2-enyl)-methanol,		
	dicumyl peroxide,		
	1-(3-cyclopentylpropyl)-2,4-dimethy-benzene,		
	1,4-dimethyl-2-(2-methylpropyl)-benzene,		
	2,2'-oxybis [octahydro-7,8,8-trimethyl- 4,7-methanobenzofuran,		
	cyclohexylformate,		
	methyleugenol,		
	3,3,5-trimethyl-cyclohexanol acetate,		
	2,4-dimethyl-8-oxabicyclo [3.2.1]oct-6-en-3-one,		
	2,6-dimethyl-6-(4-methyl-3-pentenyl)-2- cyclohexene-1-carboxaldehyde,		
	bicyclo [3.3.1]nonan-9-one,		
	2,4-dimethyl-3-nitro-(exo),		
	2,2,4-trimethyl-3-(3,8,12,16-tetramethyl-heptadeca- 3,7,11,15-tetraenyl)-cyclohexanol,		
	pyrazolo [1,5-a]pyridine,		
	3,3a,4,7-tetrahydro-3,3-dimethyl-, (3aS)		

responsible for many of turmeric's eccentric properties and bright yellow colouring. Curcumin has been shown to reveal antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, and anticancer activities and thus, has a potential against various malignant diseases, diabetes, allergies, arthritis, Alzheimer's disease, and other chronic illnesses [22]. Ar-turmerone and curlone have antimutagenic activity [2] [23] whereas sodium curcuminate has anti-inflammatory activity [2]. The structures of some bioactive compounds from *C. longa* are given in **Table 2**.

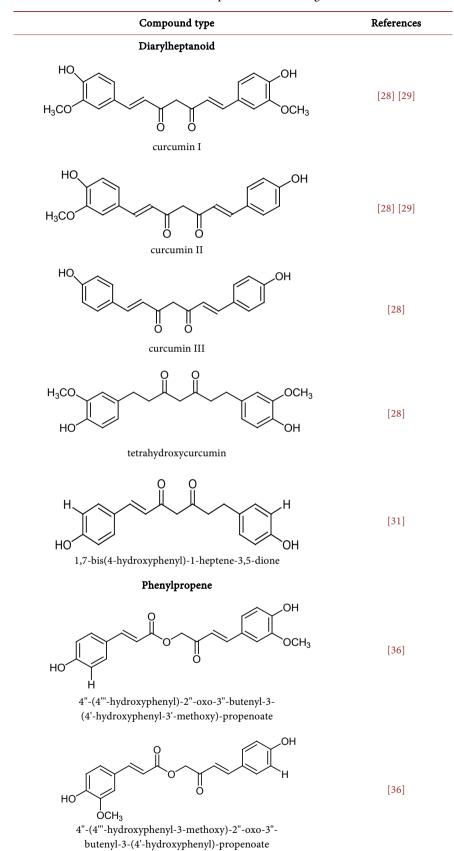
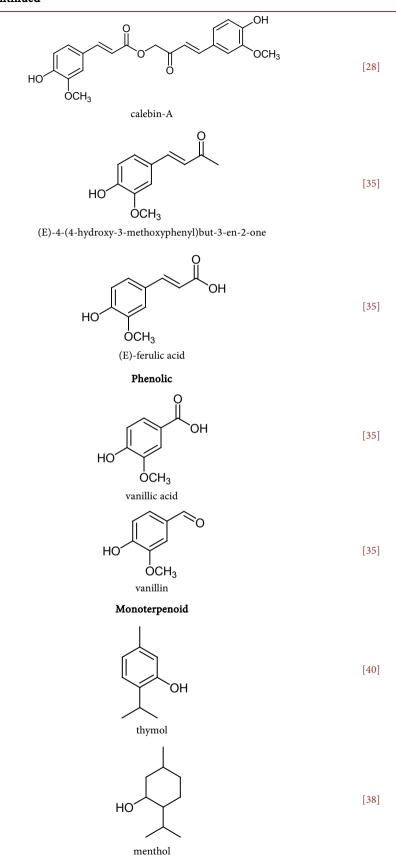
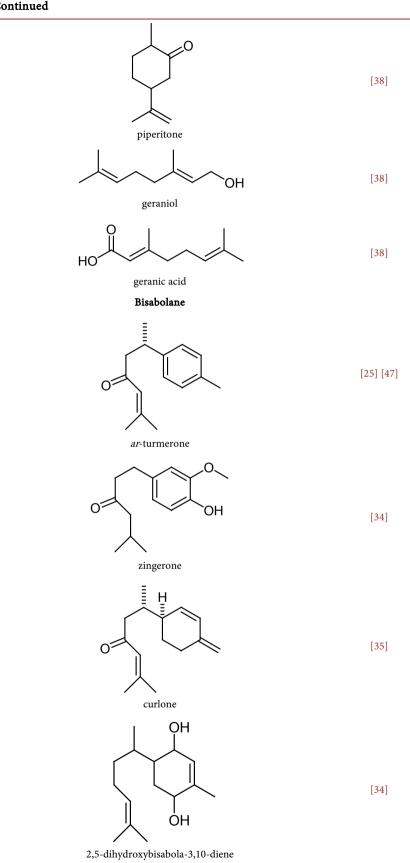
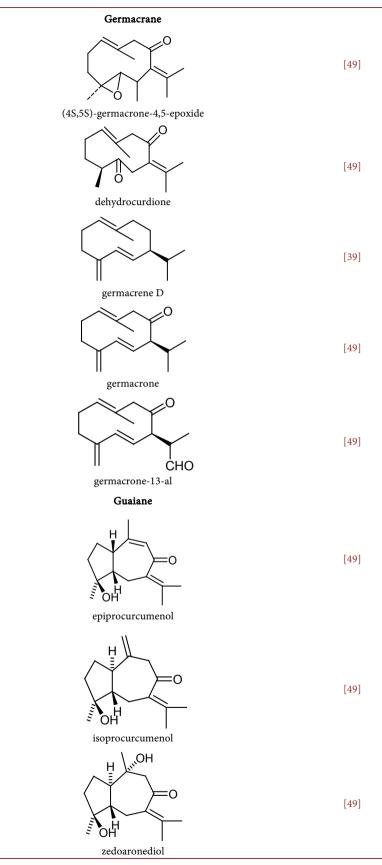


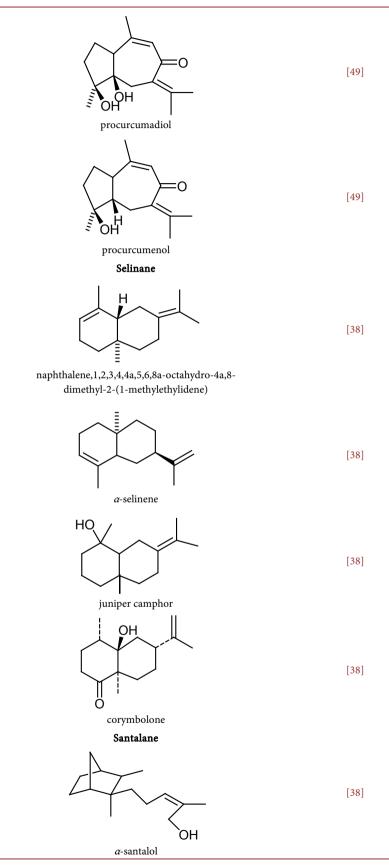
Table 2. Structures of some bioactive compounds from C. longa.

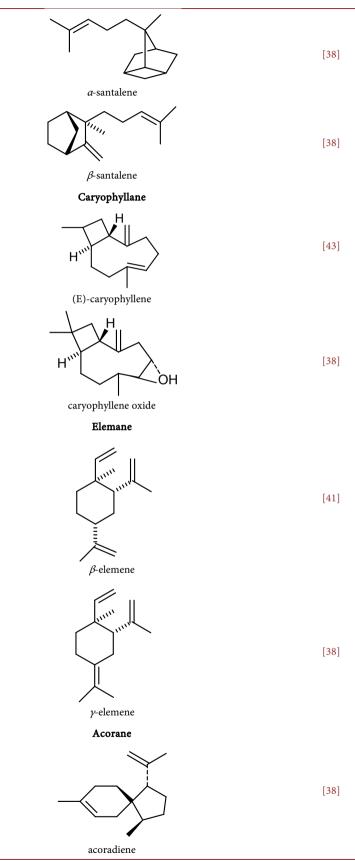


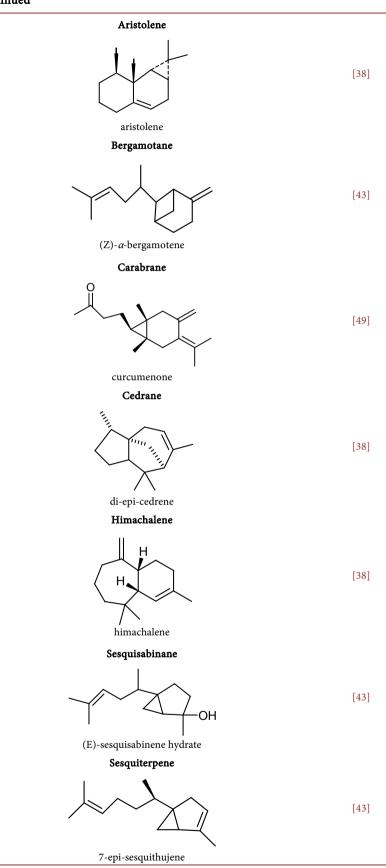




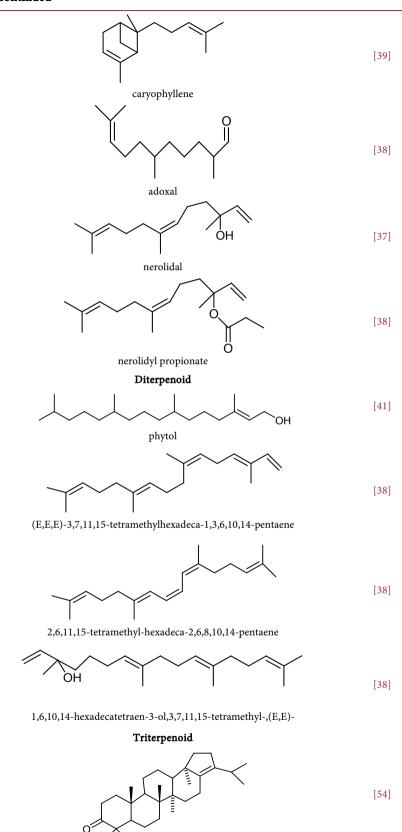






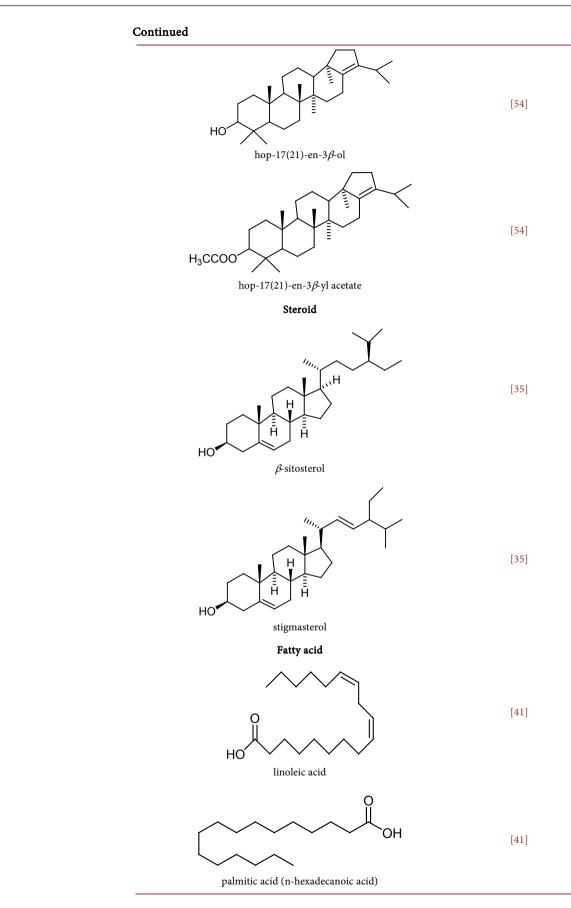




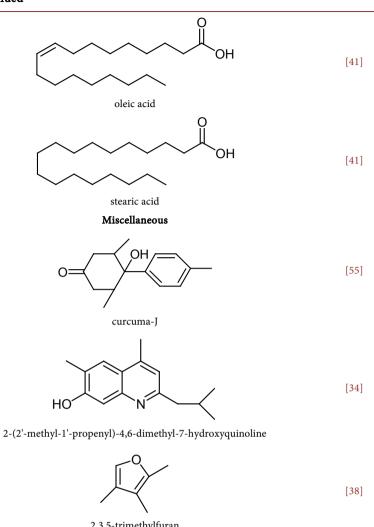


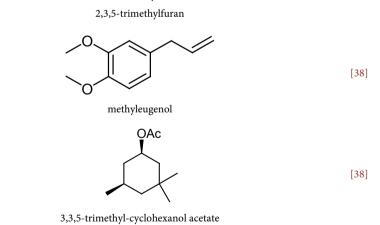
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3. Isolated Endophytic Fungi from Curcuma longa

Endophytic fungi *Fusarium nivale*, *Fusarium solani*, *Doratomyces stemonitis*, *Penicillium*, *Diaphorte sp.* were isolated from *Curcuma longa* [56] [57] [58]. Various studies have been identified the prospective of endophytic fungi from this plant as antioxidant, antidiabetic, anti-microbial and antitumor [62] [63]

[64] [65] [66]. Therefore, in this section, endophytic fungi from different parts of *C. longa* is reviewed and presented in **Table 3**.

3.1. Endophytic Fungi of Rhizome

From the rhizome of *C. longa* several endophytic fungi have been isolated [62]. Exactly 207 endophytic fungi were found to be isolated in one of the study that belongs to the seven genera namely, *Acremonium, Aspergillus, Exophiala, Fusa-rium, Penicillium, Phoma,* and *Stachybotrys.* Among the species *F. solani, F. delphinoides, F. verticillioides* and *A. versicolor, A. venenatus* bearing the genus of *Fusarium sp.* and *Aspergillus sp.* were recovered from rhizomes of *C. longa.* The rest of the genera were isolated as single species. From them, *Exophiala lecanii* the fungal endophyte was isolated for the first time from the rhizome of *C. longa* [59]. Another investigation reported 31 endophytic fungi from the rhizome of *C. longa* [60]. In most studies of endophytic fungi, the sterile mycelia fungi are reported as mycelia-sterile. Unlike those one mycelia-sterile was identified as *Phaeosphaeria ammophilae* from rhizome by Eris *et al.*, [61]. One of the genus *Eurotium sp.* was also noted from the healthy rhizomes of *C. longa* [63].

3.2. Endophytic Fungi of Leaf

A total of 6 endophytic fungi have been isolated from leaves of *C. longa* through a study [64]. Another study carried by Eris *et al.*, have isolated one fungus *Dal-dinia eschscholzii* from leaf of *C. longa* [61].

Genus	Identified by	Plant tissue	References
Acremonium sp.	ITS-5.8s r-DNA analysis	Rh	[59]
Aspergillus versicolor and Aspergillus venenatus	ITS-5.8s r-DNA analysis	Rh	[59]
Exophiala lecanii	ITS-5.8s r-DNA analysis	Rh	[59]
Fusarium Solani, Fusarium proliferatum, Fusarium oxysporum	ITS-5.8s r-DNA analysis	Rh, S, Fl, In	[59] [60] [61]
Trichoderma harzianum, Trichoderma atroviride, Trichoderma asperellum	ITS-5.8s r-DNA analysis	Rh	[60]
Penicillium citrinum	ITS-5.8s r-DNA analysis	Rh	[59]
Phoma herbarum	ITS-5.8s r-DNA analysis	Rh	[59]
Stachybotrys sp.	ITS-5.8s r-DNA analysis	Rh	[59]
Pestalopsis microspora	ITS-5.8s r-DNA analysis	Rh	[60]
Phaeosphaeria ammophilae	ITS-5.8s r-DNA analysis	Rh	[61]
Daldinia eschscholzii	ITS-5.8s r-DNA analysis	L	[61]
Arthrobotrys foliicola	ITS-5.8s r-DNA analysis	R	[61]
Drechslera kusanoi	ITS-5.8s r-DNA analysis	In	[61]

 Table 3. Endophytic fungi from different parts of turmeric plant.

Rh = Rhizome, S = Stem, Fl = Flower, In = Inflorescence, L = Leaf, R = Root.

3.3. Endophytic Fungi of Stem

Several endophytic fungi from fresh stem of *C. longa* have been isolated [62]. The endophytic fungus *Fusarium proliferatum* was isolated from stems of healthy *C. longa* collected in Indonesia [61].

3.4. Endophytic Fungi of Root

The endophytic fungus *Arthrobotrys foliicola* was isolated from the roots of *C. longa* [61]. Some endophytic fungi have also been isolated from roots of *C. longa* [62].

3.5. Endophytic Fungi of other Parts

Some endophytic fungi from tubers and young tubers of *C. longa* have been isolated [62]. Eris *et al.*, have isolated *Fusarium verticillioides* and *Phanerochaete chrysosporium* from the flowers of *C. longa* of which the later fungus is reported as mycelia-sterile. The group also isolated *Cochliobolus kusanoi* and *Fusarium proliferatum* from the inflorescence part of the plant. *Cochliobolus kusanoi* is the teleomorph stage of *Drechslera kusanoi* [61].

4. Reported Bioactivity on Endophytic Fungi Isolated from Turmeric Plant

4.1. Antioxidant Activity

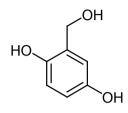
44 endophytic fungi from several parts of turmeric plant were investigated by a research group Bustanussalam *et al.*, for their antioxidant bioactive compounds. They observed both filtrate and biomass ethylacetate extracts of endophytic fungi have antioxidant activity. On the basis of DPPH free radical scavenging method filtrate extracts gave higher antioxidant activity than biomass extracts. Due to presence of fatty acids, biomass extracts are less active as antioxidant. Filtrate extracts contain many secondary metabolites that may act as protection for the endophytic fungi of host plant [62].

4.2. Anticancer Activity

A study carried out by Ratih *et al.*, have shown inhibitory activity of 4 isolates of endophytic fungi towards human breast cancer MCF-7 cell line [65]. Endophytic fungus *Eurotium sp.* was isolated from rhizomes of *C. longa* by Ruby and Raghunath and it is utilized for the production of anticancer enzyme asparaginase for the first time [63]. The enzyme is considered to participate in major role in the asparaginase metabolism of the cells. It's a likely therapeutic agent for acute lymphocytic leukemia, acute lymphoblastic leukemia and chronic myelogenous leukemia also reported to be an effective antilymphoma agent in humans.

4.3. Antifungal Activity

Suruchi *et al.*, have separated endophytic fungi from *C. longa* for antifungal activity. The group reported the active constituent Gentisyl alcohol which is an anti-phytopathogenic molecule from fungal isolate *P. herbarum*. The purified compound showed antagonistic activity against *C. gloeosporioides* causing leaf spot of turmeric and could, therefore, be explored as a biocontrol agent for the host-specific phytopathogen [59]. Similarly, Vinayarani and Prakash have isolated *T. harzianum* from the rhizome of turmeric and they concluded that this can be exploited as a potential biocontrol agent for suppressing rhizome rot and leaf blight diseases in turmeric [60].



Structure of Gentisyl alcohol

4.4. Antibacterial Activity

Endophytic fungi could be a promising source for antibacterial bioactive agents. A study carried out by Sharmila *et al.*, found that the endophytic fungus *Chaetomium sp.* isolated from *C. longa* exhibited protruding antibacterial activity against three different human pathogenic bacteria such as *Proteus sp.*, *Pseudomonas sp.* and *Staphylococcus aureus* [66].

5. Conclusion

Till today, the chemical composition of *C. longa* has thoroughly been investigated and a number of different active substances have been identified, which exhibit a wide range of medicinal value. But, very few structures of bioactive compounds are characterized and identified from endophytic fungi of *C. longa*. Most of the investigations are restricted to the level of fungal identification and bioactivity assay. But, endophytic fungi, producer of a wide array of secondary bioactive metabolites with their peculiar potential compounds, namely, antioxidant, antibacterial, antifungal, anticancer, etc., are the ideal targets for further drug discovery. These leads may play a major role in the recovery of infectious, inflammatory and also certain kinds of cancer diseases. So, extensive research is necessary in the area of endophytic fungi isolation and characterization of the compounds from *C. longa*.

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