Endophytes from *Ginkgo biloba* and their secondary metabolites

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**Abstract**

*Ginkgo biloba* is a medicinal plant which contains abundant endophytes and various secondary metabolites. According to the literary about the information of endophytics from *Ginkgo biloba*, *Chaetomium*, *Aspergillus*, *Alternaria*, *Penicillium* and *Charobacter* were isolated from the root, stem, leaf, seed and bark of *G. biloba*. The endophytics could produce lots of phytochemicals like flavonoids, terpenoids, and other compounds. These compounds have antibacterial, antioxidation, anticoagulant, antitumoral, antimicrobial and some novel functions. This paper set forth the development of active extracts isolated from endophytes of *Ginkgo biloba* and will help to improve the resources of *Ginkgo biloba* to be used in a broader field.

**Keywords:** *Ginkgo biloba*, Chinese medical plant, Endophytes, Secondary metabolites

**Background**

*Ginkgo biloba* (*G. biloba*) is a deciduous tree belonging to the ginkgo genus, which is also known as *Gongsunshu*, etc. *G. biloba* is one of the most ancient plants on earth dating back more than 200 million years. Commonly *Ginkgo biloba* has been used as a medicinal plant and its seeds, leaves and fruits can be used for medicines with biological activities involving antibacteria, antioxidation, anticoagulant and others. However, *Ginkgo* trees grow slowly and under natural conditions they need more than 20 years from planting to fruiting, which is a restricting point for its development; while its endophytics provide physiological metabolic pathways to produce numerous novel medicinal compounds which have become a hotspot [1].

The endophytics play important roles in the process of host plant growth and systematic evolution [1, 2]. During the whole life, endophytics protect their host from infectious diseases and also help to survive in adverse environment [3]. Since the unique relationships between the host plant and associated endophytes, endophytes in *G. biloba* have been recognized as important sources of a variety of novel secondary metabolites with anticancer, antimicrobial and other biological activities [4, 5].

Secondary metabolites are the chemical bank which provides a huge quantity of diverse commercial products for human medicines. First report about endophytics is that Stierle et al. isolated *Taxomyces andreanae* from phloem of *Taxus brevifolia*, which can produce taxol and related chemicals at the concentration of 24–50 ng/L [6]. From then on, more and more endophytics from pharmaceutical plants, such as *Camptotheca acuminata* [7], pine [8] and *Taxus* plants [9–11] were isolated. As to *G. biloba*, various endophytics including *Chaetomium*, *Aspergillus*, *Alternaria*, *Penicillium* and *Charobacter* were isolated from the root, stem, leaf, seed and bark of *G. biloba*. They produce lots of phytochemicals like flavonoids, terpenoids, and other compounds [12, 13]. 50% of these isolates showed antimicrobial activities against various pathogens. Some secondary metabolites such as 2-hexenal have been involved in the plant’s defense against pests. These bioactive metabolites are attractive to developing the commercial prodrugs and agricultural/industrial production. Most importantly, as a therapeutic drug, *G. biloba* has no side effects even after long periods of use and its phytopharmaceuticals are readily accessible throughout the world. For better using endophytic and...
secondary metabolites from ginkgo trees, we summarize the data previously reported.

**Endophytes in Ginkgo biloba**
The whole plant of *G. biloba* can be used as medicine. In its root, stem, leaf, seed and bark of *Ginkgo biloba*, various endophytes have been isolated and their biological function was investigated. The conventional procedure of endophytes isolation is to wash the roots, stems or leaves of ginkgo firstly with 75% alcohol for 3 min, rinse with sterile water 3–5 times, 0.1% mercury sterilized for 2 min, rinsed with sterile water 3–5 times, cut into 0.5 cm × 0.5 cm pieces. The cutting pieces were inoculated in PDA medium at 28 °C for 4 days. After purification, ginkgo endophytes were isolated.

For the endophytic procaryotes, on the total DNA as the template, 27F(AGAGTTTGATC-CTG GGT CAG)/1492R(GGT TAC CTG TTA TTGA TATGC) as a primer, 16S rDNA was amplified. For the endophytic eukarya, ITS5 (GAAG TAAAAG TCGTACAAGG)/ITS4 (TCCTCCGCT TTA TTGA TATGC) as a primer, ITS rDNA was amplified. According to the culturing and molecular analysis between different species, the endophytes residing in *G. biloba* belong to *Chaetomium*, *Aspergillus*, *Alternaria*, *Penicillium*, *Charobacter*, etc.

**Endophytic procaryotes in Ginkgo biloba**

From the previous reports, around 50 species of endophytic procaryotes were found including *Bacillus subtilis*, *Lactobacillus* sp., *Fusobacterium* sp., *Gemella* sp., *Neisseria* sp., *Pseudomonas* sp., *Rothia* sp., *Veillonella* sp., etc. Basing on 16S RNA sequence of endophytic procaryotes from previous literatures, the phylogenetic tree was constructed in Fig. 1. Amongst these procaryotes, the community structure or compositional differences at different taxonomic levels was presented in Fig. 2.

*Sphingomonadaceae* are a family of the *Alphaproteobacteria* and most abundant in *G. biloba*. An important feature is the presence of sphingolipids in the outer membrane of the cell wall [14]. In this family, some species are phototrophic which may have high nutritional value. The phototrophic bacteria are rich in amino acids, folic acid and vitamins, especially vitamin B12, biotin and coenzyme Q. Some other species are known as the ability to degrade some aromatic compounds which has the interests for environmental remediation [11].

Other abundant species are family *Hyphomicrobiaceae*, *Burkholderiaceae*, *Methylobacteriaceae*, *Enterobacteriaceae*, *Neisseriaceae* and *Micrococcaceae*. The family *Hyphomicrobiaceae* is affiliated with *Alphaproteobacteria* and members of this family are distributed everywhere in soils, freshwater, and also under the marine. This family is highly diverse morphologically and physiologically.

Most are aerobic chemoheterotrophs and a few can grow anaerobically by denitrification or mixed-acid fermentation.

The *Methylobacteriaceae* comprises a large family of *Alphaproteobacteria* and contains three genera including *Methylobacterium*, *Microvirga*, and *Meganema*. *Methylobacterium* species are ubiquitous in the natural environment. Some species induce plant leaf and root nodule formation, and can promote plant growth by production of auxins [15]. Most of *Methylobacterium* are methylo- trophs and they can use methanol or other one-carbon compounds as energy sources to produce proteins [16]. Otherwise, in *Methylobacterium*, common fatty acids were contained especially ubiquinone Q-10, a popular dietary supplement.

Family *Enterobacteriaceae* contains a large number of genera that are biochemically and genetically related to one another. Many of them are pathogens, such as *Salmonella*, *Shigella* or *Yersinia*, because they produce endotoxins. Endotoxins reside in the cell wall and when the cell dies and the cell wall disintegrates, endotoxins are released [9].

Family *Burkholderiaceae* belongs to the order *Burkholderiales* within the class *Betaproteobacteria*. This family is characterized by the presence of ecologically extremely diverse organisms and contains truly environmental saprophytic organisms, phytopathogens, opportunistic pathogens, as well as primary pathogens for humans and animals.

Family *Neisseriaceae* and *Micrococcaceae* are widespread in soil, subterranean cave silts, sea, glacier silts, sewage, water sludge, aerial surfaces of plants, vegetables, and various animal species and are even more distantly related to the human pathogens.

**Endophytic eukarya in Ginkgo biloba**

The phylogenetic tree of endophytic eukarya (Fig. 3) was constructed basing on ITS sequence of roots and leaves of *Ginkgo biloba* from previous literatures. Amongst these endophytic eukarya, the community structure at different taxonomic levels was presented in Fig. 4.

Amongst eukarya, family *Pleosporaceae* belongs to sac fungi. The taxonomic relationship of this family to associated genera is still not determined. The classification of *Pleosporaceae* has been a challenge because of the lack of the importance of morphological characters and reference strains. From the present knowledge, the family *Pleosporaceae* includes numerous saprobic, opportunistic human and plant pathogenic taxa [17].

*Phaeosphaeriaceae* is a large and important family of fungi in the order *Pleosporales*. Species in this family have a cosmopolitan distribution, and are generally
nectrotrophic or saprobic on a wide range of plants [18]. This family includes economically important plant pathogens and previously accommodated 35 sexual and asexual genera and comprised more than 300 species with a range of morphological characters [19].

The Xylariaceae are a family of mostly small ascomycetous fungi. It is one of the most commonly encountered groups of ascomycetes and is found throughout the temperate and tropical regions of the world. They are typically found on wood, seeds, fruits, or plant leaves, some even associated with insect nests. Most decay wood and many are plant pathogens. Phylogenetic analyses suggest that there are two main lineages in this family, Hypoxyloideae and Xylarioideae [20, 21].

**Secondary metabolites of endophytics in Ginkgo biloba**

A series of compounds were obtained by fermentation, extraction, and isolation from endophytics of *G. biloba*, amongst which 115 metabolites were found in the fermentation broth of *Chaetomium* fungi, 44 metabolites were found from *Aspergillus*, 43 metabolites found in the genus *Xylaria*. The amount from these three genera accounted for 72% of the secondary metabolites from endophytic procaryotes and 21% were isolated from *Fusarium, Alternaria* and *Penicillium*. The number of metabolites of each genus is shown in Fig. 5.

Many metabolic products from *G. biloba* have strong inhibitory effects on pathogenic bacteria *Staphylococcus*
The secondary metabolites of Ginkgo, such as flavonoids and ginkgolides, are drugs or prodrugs used in the treatment of peripheral arterial diseases, neurological disorders, sclerosis of cerebral arteries, and cerebral ageing.
Secondary metabolites of Chaetomium

*Chaetomium* is the largest type of endophytic fungus from *G. biloba* and its secondary metabolites are biologically diverse. *Chaetomium globosum* is one of main endophytics. A total of 115 metabolites were isolated from the fermentation broth of *Chaetomium globosum* (see Fig. 6 and Table 1). Among them, chaetoglobosin A, chaetoglobosin C, chaetoglobosin E, chaetoglobosin G, chaetoglobosin Vb, chaetomugilin A, chaetomugilin D and ergosterol peroxide (peroxyergosterol; 5α, 8α-peroxy-(22E, 24R)-ergot-6,22-diene-3β-ol), which has been reported in many literatures, may be a research hotspot. Among these compounds, chaetomugilin A, chaetomugilin D, chaetoglobosin A and chaetoglobosin C have strong cytotoxic activity [22].

Chaetomugilin A and D, both are a kind of azaphilone isolated from Chaetomium globosum and has been shown to exhibit inhibitory activity against the brine shrimp (*Artemia salina*) and Mucor miehei [22]. Chaetomugilide A isolated from *Chaetomium globosum*
TY1 has strong activity against hepatoma cell HepG-2, and the IC_{50} value is only 1.7 μmol/L [23]. Chaetoglobosin A is a Chaetomium secretion with the anticancer activity in vitro [24] and it derivates into other bilobalide compounds MBJ-0038, MBJ-0039, and MBJ-0040 [25]. Chaetoglobosin E is a cytochalasan alkaloid found in Chaetomium globosum and Chaetomium subaffine. It is a cytochalasan alkaloid, a member of indoles, a macrocycle...
and a secondary alpha-hydroxy ketone. It has a role as a Chaetomium metabolite and an antineoplastic agent.

One new cytochalasan alkaloid, chaetoglobosin V(b), together with two structurally related known compounds, chaetoglobosin V and chaetoglobosin G, were isolated from the ethyl acetate extract of a culture of the endophytic fungus Chaetomium globosum, associated with the leaves of G. biloba tree. The structures of the isolated compounds were elucidated by spectroscopic methods including 1D and 2D NMR and mass spectrometry. The absolute conformation of chaetoglobosin V(b) was established by means of electronic circular dichroism (CD) spectroscopy. The correlation between compounds was demonstrated by a biomimetic transformation of chaetoglobosin G under mild conditions in chaetoglobosins V and V(b). The isolated metabolites were tested against some phytopathogens [22].

The compound flavipin isolated from Chaetomium globosum CDW 7 has strong antioxidant activity [23]. Chaetomium globosum ZY-22 could produce two polyhydroxylated steroids [24] and two other important compounds, bilobalide, ginkgolides are to be beneficial to human health [26]. Bilobalide has neuroprotective effects [27] as well as inducing the liver enzymes CYP3A1 and 1A2 which may be partially responsible for interactions between ginkgo and other herbal medicines or pharmaceutical drugs; while ginkgolide has been investigated for its potential to reducing migraine frequency [28]. Ergosterol peroxide (5α,8α-epidioxy-22E-ergosta-6,22-dien-3β-ol) is a steroid derivative. It has been reported to

![Fig. 5](image)

**Fig. 5** a The metabolite quantity of some major endophytics in Ginkgo biloba; b the metabolite quantity of some minor endophytics in Ginkgo biloba
exhibit immune-suppressive, anti-inflammatory, antiviral, trypanocidal and antitumor activities in vitro [27].

**Secondary metabolites of Aspergillus**

*Aspergillus* is the dominant flora of endophytic fungi of *G. biloba* and was isolated from different parts of *G. biloba* which cultivated in various areas. A total of 44 metabolites were found in the fermentation broth of *Aspergillus* (see Table 2), among which 3-hydroxy-terphenyl, 4,5-dimethoxycandidusin A, prenylcandidusin C, and prenylterphenyllin were studied most popularly. For 4″-Deoxycandidusin A, 4″-deoxytripentin, 4′-deoxy-3-hydroxyrisperidone, aspergiloid A, coumarin A, and tribenzine, three articles reported about each compound, respectively. Among these metabolites, 3-hydroxy-terphenyl and 4″-deoxyxanthadinus A, 4″-deoxytripentin have strong inhibitory activity against neuraminidase [29]; 4″-deoxy-3-hydroxytripentin, 3-hydroxy-terphenyl, 4″-deoxyxanthadinus has moderate activity against human nasopharyngeal carcinoma cell KB, human gastric cancer cell SGC-7901, human colon cancer cell SW1116 and human lung cancer cell A549 [30].

**Secondary metabolites of Alternaria**

*Alternaria* is a very common fungus. It is an important pathogen for plants, human and animal diseases. It is a biological resource with great application potential as well. According to the existing literatures, 17 metabolites were isolated from the fermentation products of *Alternaria* (see Table 3). Alterperyleneol inhibits human telomerase activity (IC₅₀ = 30 μM), but altertoxin I (dihydroalterperyleneol), a structurally related compound, did not affect activity at 1 mM. Moreover, alterperyleneol and altertoxin I show phytotoxic and antifungal activity [31].

In these metabolites, botulinum toxin and botulinum toxin II have strong cytotoxic activity. When the concentration is 10 μg/mL, the mortality rate of brine shrimp is 68.9% and 73.6%, respectively [32]. *Alternaria* No. 28 could produce cytotoxic metabolites which have inhibitory potential against some different protein kinases [7].

**Secondary metabolites of Penicillium**

*Penicillium* is widely distributed in nature and generally has a strong biological activity. According to the existing literatures, 17 secondary metabolites were found from the fermentation products of *Penicillium* sp. in *G. biloba* (Table 4), and some metabolites were biologically active. The compound arcacic acid is isolated from the fermentation broth of *Penicillium commune*, which has antibacterial activity and has inhibition activities on 12 kinds of plant pathogens, especially has strong inhibitory activity against *Bacillus licheniformis* and *Sclerotinia sclerotiorum*, and the IC₅₀ values are only 39.28 mg/L and 60.62 mg/L [33].

The compounds adenosine, deoxyadenosine and adenine which were isolated from the fermentation product of *Penicillium* sp. YY-20 have a strong scavenging capacity for DPPH free radical [34]. Wu isolated *Penicillium cataractum* SYPF 7131 from 58 endophytic fungi obtained from the leaves, stems and roots of *G. biloba*. 

![Figure 6](https://example.com/fig6.png)

*Fig. 6* The quantity of different kinds of metabolites from Chaetomium
Table 1  Secondary metabolites of Chaetomium in Ginkgo biloba

| No. | Metabolites                                                  | CAS number | Molecular structure | Endophytes         | Application                          | References |
|-----|-------------------------------------------------------------|------------|---------------------|--------------------|--------------------------------------|------------|
| 1   | (22E, 24R)-ergosta-7,22-diene-3β,5α,6β-triol/cerevisterol  | 516-37-0   |                     | Chaetomium globosum | [33]                                 |            |
| 2   | (22E, 24R)-ergosta-7,22-diene-3β,5α,6β,9α-tetraol          | 88191-06-4 |                     | Chaetomium globosum | [44]                                 |            |
| 3   | (7Z,11E)-7,11-Hexadecadien-1-yl acetate                    | 53042-79-8 |                     | Chaetomium globosum | Pesticide                           | [45]       |
| 4   | (E,E)-2,4-Decadienal                                       | 25152-84-5 |                     | Chaetomium globosum | Food additive; fragrance            | [45]       |
| 5   | (Z)-9-Hexadecenoic acid, methyl ester                      | 1120-25-8  |                     | Chaetomium globosum | [45]                                 |            |
| 6   | (Z,Z)-9,12-Octadecadienoic acid                           | 60-33-3    |                     | Chaetomium globosum | Biosynthesis of prostaglandins and cell membranes | [45]       |
| 7   | 1-(3-Acetyl-2,2-dimethylcyclopropyl)-2-methyl-1-propanone  | 77142-84-8 |                     | Chaetomium globosum | T16                                 | [49]       |
| 8   | 1-(3-Methoxy-2-pyrazinyl)-2-methyl-1-propanone             | 98618-81-6 |                     | Chaetomium globosum | T16                                 | [46]       |
| 9   | 1,3-Dioxolane, 2-methoxy                                   | 19693-75-5 |                     | Chaetomium globosum | T16                                 | [46]       |
| 10  | 1-Eicosene                                                 | 3452-07-1  |                     | Chaetomium globosum | T16                                 | [45]       |
| 11  | 1-Trimethylsilyl methanol                                  | 3219-63-4  |                     | Chaetomium globosum | T16                                 | [46]       |
| 12  | 2,3,4-Trimethyl-5,7-dihydroxy-2,3-dihydrobenzofuran       | 1824584-79-3 |                   | Chaetomium globosum | [47]                                 |            |
| 13  | 2,4,5-Trimethyl-1,3-dioxolane                              | 3299-32-9  |                     | Chaetomium globosum | T16                                 | [46]       |
| 14  | 2,4-Decadienal                                             | 2363-88-4  |                     | Chaetomium globosum | Food additive | [20, 21] |
| No. | Metabolites                                      | CAS number | Molecular structure | Endophytes                  | Application                                                      | References |
|-----|-------------------------------------------------|------------|---------------------|-----------------------------|------------------------------------------------------------------|------------|
| 15  | 2′-O-Methyladenosine                           | 2140-79-6  | ![Molecule](image)  | Chaetomium globosum        | Inhibition of vaccinia virus growth                                | [47]       |
| 16  | 2′-Deoxyadenosine                              | 958-09-8   | ![Molecule](image)  | **Chaetomium globosum**    | Anti-tumor and antiviral nucleoside drugs (cladribine)            | [44]       |
| 17  | 20-Dihydrochaetoglobosin A                    | 149560-98-5| ![Molecule](image)  | **Chaetomium globosum**    |                                                                   | [47]       |
| 18  | 21 Methoxy-Chaetoglobosin F                   |            | ![Molecule](image)  | **Chaetomium globosum**    |                                                                   | [47]       |
| 19  | 2-Cyclohexyl-hex-5-en-2-ol                     | 959261-17-7| ![Molecule](image)  | **Chaetomium globosum**    | T16                                                               | [46]       |
| 19  | 2-Ethyl-5-propylphenol                        | 72386-20-0 | ![Molecule](image)  | **Chaetomium globosum**    | T16                                                               | [46]       |
| 20  | 2-Methyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one | 31272-04-5 | ![Molecule](image)  | **Chaetomium globosum**    | T16                                                               | [46]       |
| 21  | 2-Octyl-cyclopropaneoctanal                   | 56196-06-6 | ![Molecule](image)  | **Chaetomium globosum**    | No16                                                              | [45]       |
| 22  | 3,4-Dihydroxyphenyl acetic acid               | 102-32-9   | ![Molecule](image)  | **Chaetomium globosum**    |                                                                   | [47]       |
| 23  | 3-Methylorsellinic acid                       | 4707-46-4  | ![Molecule](image)  | **Chaetomium globosum**    | Neuroprotective Activity                                          | [46]       |
| 24  | 4-Aminophenylacetic acid/p-aminophenylacetic acid/4-aminophenylacetic acid | 1197-55-3 | ![Molecule](image)  | **Chaetomium globosum**    | Anti-inflammatory Inhibition colitis                              | [47]       |
| 25  | 4-Methyl-1-hepten-5-one                       | 26118-97-8 | ![Molecule](image)  | **Chaetomium globosum**    |                                                                   | [46]       |
| No. | Metabolites                                           | CAS number       | Molecular structure | Endophytes         | Application                                                                 | References |
|-----|------------------------------------------------------|------------------|--------------------|--------------------|-----------------------------------------------------------------------------|------------|
| 26  | 5-(hydroxymethyl)-1H-pyrrole-2-carbaldehyde         | 67350-50-9       | ![Structure](image) | Chaetomium globosum | Hapten, produces advanced glycation end-products (AGEs)                      | [47]       |
| 27  | 5′-Epichaetovirdin A                                 | 1308671-17-1     | ![Structure](image) | Chaetomium globosum | No. 12                                                                      | [45]       |
| 28  | 5′-Deoxy-5′-methylamino-adenosine                    | No cas no.       | ![Structure](image) | Chaetomium globosum |                                                                             | [47]       |
| 29  | 9(11)-dehydroergosterol peroxide                    | 86363-50-0       | ![Structure](image) | Chaetomium globosum | ZY-22                                                                       | [44]       |
| 30  | 9,12-Octadecadien-1-ol                              | 1577-52-2        | ![Structure](image) | Chaetomium globosum | No. 16                                                                       | [45]       |
| 31  | Acetaldehyde, diethyl acetal                         | 105-57-7         | ![Structure](image) | Chaetomium globosum | T16                                                                          | [46]       |
| 32  | Adenosine                                            | 58-61-7          | ![Structure](image) | Chaetomium globosum | ZY-22                                                                        | [46]       |
| 33  | Allantoin                                            | 97-59-6          | ![Structure](image) | Chaetomium globosum |                                                                             | [48]       |
| 34  | alpha-Methylstyrene                                  | 98-83-9          | ![Structure](image) | Chaetomium globosum |                                                                             | [48]       |
| 35  | Anthranilic acid                                     | 118-92-3         | ![Structure](image) | Chaetomium globosum | MX-0510                                                                      | [33]       |
| 36  | Benzeneacetic acid                                   | 103-82-2         | ![Structure](image) | Chaetomium globosum | No. 16                                                                       | [45]       |
| 37  | Benzeneacetic acid, methyl ester                     | 101-41-7         | ![Structure](image) | Chaetomium globosum | No. 16                                                                       | [45]       |
| 38  | Benzeneethanol/phenylethyl alcohol                   | 60-12-8          | ![Structure](image) | Chaetomium globosum |                                                                             | [45]       |
### Table 1 (continued)

| No. | Metabolites                     | CAS number     | Molecular structure | Endophytes        | Application | References |
|-----|---------------------------------|----------------|---------------------|-------------------|-------------|------------|
| 39  | Butyraldehyde, 4-phenyl         | 18328-11-5     | ![Molecule](#)      | Chaetomium globosum | T16         | [46]       |
| 40  | Cerebroside B                   | 88642-46-0     | ![Molecule](#)      | Chaetomium globosum | ZY-22       | [46]       |
| 41  | Cerebroside C                   | 98677-33-9     | ![Molecule](#)      | Chaetomium globosum | ZY-22       | [46]       |
| 42  | Chaetoglobosin A                | 50335-03-0     | ![Molecule](#)      | Chaetomium globosum |             | [44, 49]  |
| 43  | Chaetoglobosin B                | 50335-04-1     | ![Molecule](#)      | Chaetomium globosum | CDW7        | [48]       |
| 44  | Chaetoglobosin C                | 50645-76-6     | ![Molecule](#)      | Chaetomium globosum |             | [26, 28]  |
| 45  | Chaetoglobosin D                | 55945-73-8     | ![Molecule](#)      | Chaetomium globosum |             | [49]       |
| 46  | Chaetoglobosin E                | 55945-74-9     | ![Molecule](#)      | Chaetomium globosum | (CDW7)      | [49]       |
| 47  | Chaetoglobosin F                | 55945-75-0     | ![Molecule](#)      | Chaetomium globosum | (CDW7)      | [47]       |
| 48  | Chaetoglobosin Fa               | 1599426-06-8   | ![Molecule](#)      | Chaetomium globosum |             | [47]       |
| No. | Metabolites       | CAS number         | Molecular structure | Endophytes          | Application | References |
|-----|-------------------|--------------------|---------------------|---------------------|-------------|------------|
| 49  | Chaetoglobosin Fex| 149457-95-4        |                     | Chaetomium globosum |             | [47]       |
| 50  | Chaetoglobosin G  | 65773-98-0         |                     | Chaetomium globosum (NM0066) |             | [47]       |
| 51  | Chaetoglobosin R  | 777939-30-7        |                     | Chaetomium globosum |             | [49]       |
| 52  | Chaetoglobosin V  | 1399682-37-1       |                     | Chaetomium globosum |             | [47]       |
| 53  | Chaetoglobosin Vb | 1399690-75-5       |                     | Chaetomium globosum (CDW7) |             | [48]       |
| 54  | Chaetoglobosin Y  | 1608108-89-9       |                     | Chaetomium globosum |             | [48]       |
| 55  | Chaetomugilide A  | 1418138-71-2       |                     | Chaetomium globosum |             | [45, 47]  |
| 56  | Chaetomugilide B  | 1433976-48-7       |                     | Chaetomium globosum |             | [45]       |
| 57  | Chaetomugilide C  | 1418138-70-1       |                     | Chaetomium globosum |             | [45, 47]  |
| 58  | Chaetomugilin A   | 1041640-66-7       |                     | Chaetomium globosum |             | [45]       |
| No. | Metabolites       | CAS number       | Molecular structure | Endophytes        | Application | References |
|-----|-------------------|------------------|---------------------|-------------------|-------------|------------|
| 59  | Chaetomugilin D   | 1098081-38-9     |                     | Chaetomium globosum |             | [25]       |
| 60  | Chaetomugilin I   | 1187848-00-5     |                     | Chaetomium globosum |             | [25]       |
| 61  | Chaetomugilin J   | 1187848-01-6     |                     | Chaetomium globosum |             | [25]       |
| 62  | Chaetomugilin O   | 1187848-06-1     |                     | Chaetomium globosum |             | [25]       |
| 63  | Chaetomugilin Q   | 1319729-85-5     |                     | Chaetomium globosum |             | [25]       |
| 64  | Chaetomugilin S   | 1399093-77-6     |                     | Chaetomium globosum |             | [25]       |
| 65  | Chaetoviridin C   | 128230-02-4      |                     | Chaetomium globosum |             | [15]       |
| 66  | Chaetoviridin D   | 128230-04-6      |                     | Chaetomium globosum |             | [33]       |
| 67  | Chaetoviridin E   | 1178875-15-4     |                     | Chaetomium globosum |             | [33]       |
| 68  | Cyclo-(Phe-Gly)   | 5037-75-2        |                     | Chaetomium globosum |             | [33]       |
| No. | Metabolites                                           | CAS number | Molecular structure | Endophytes          | Application                                                                 | References |
|-----|------------------------------------------------------|------------|---------------------|---------------------|----------------------------------------------------------------------------|------------|
| 69  | Cyclopentadecane                                     | 295-48-7   | ![Molecule](image1) | Chaetomium globosum No.16 |                                                                       | [45]       |
| 70  | Dimethyl phthalate                                   | 131-11-3   | ![Molecule](image2) | Chaetomium globosum No.16 | Used in plastics, insect repellents, safety glass, and lacquer coatings | [45]       |
| 71  | Epimwskorwnone A                                     | 1073-96-7  | ![Molecule](image3) | Chaetomium globosum |                                                                       | [33]       |
| 72  | Ergosta-4 6,8,22-tetraen-3-one/ergosta-4,6,8,22-tetraen-3-one | 194721-75-0 | ![Molecule](image4) | Chaetomium globosum (ZY-22) |                                                                       | [33]       |
| 73  | Ergosterol                                            | 57-87-4    | ![Molecule](image5) | Chaetomium globosum | Formation of vitamin D2                                                   | [49]       |
| 74  | Ergosterol peroxide 6a,8a-epi-dioxo-(22E,24R)-ergosta-6,22-dien-3β-ol | 2061-64-5 | ![Molecule](image6) | Chaetomium globosum | An antineoplastic agent, an antimycobacterial drug and a trypanocidal drug | [33]       |
| 75  | Ethanoic acid                                         | 64-19-7    | ![Molecule](image7) | Chaetomium globosum T16 | Food additive, and in petroleum production                                | [46]       |
| 76  | Ethyl 13-methyl-tetradecanoate                        | 64317-63-1 | ![Molecule](image8) | Chaetomium globosum No.16 |                                                                       | [45]       |
| 77  | Ethyl 2-heptenoate                                    | 2351-88-4  | ![Molecule](image9) | Chaetomium globosum T16 |                                                                       | [45]       |
| No. | Metabolites                                             | CAS number | Molecular structure | Endophytes               | Application                                         | References |
|-----|--------------------------------------------------------|------------|---------------------|--------------------------|-----------------------------------------------------|------------|
| 78  | Ethylidene acetate                                     | 542-10-9   | ![structure](image)  | Chaetomium globosum      | T16                                                  | [45]       |
| 79  | flavipin (1,2-benzenedicarboxaldehyde-3,4,5-trihydroxy-6-methyl) | 483-53-4   | ![structure](image)  | Chaetomium globosum      | CDW7, Antioxidant fungicides                         | [22]       |
| 80  | Fumigaclavine B                                        | 6879-93-2  | ![structure](image)  | Chaetomium globosum      |                                                      | [47]       |
| 81  | Fumitremorgin C                                        | 118974-02-0| ![structure](image)  | Chaetomium globosum      | (NM0066), A mycotoxin and a breast cancer resistance protein inhibitor | [33]       |
| 82  | Gliotoxin                                              | 67-99-2    | ![structure](image)  | Chaetomium globosum      | (NM0066), A mycotoxin, an immunosuppressive agent, an protein farnesyltransferase inhibitor, a proteasome inhibitor and an antifungal agent | [33]       |
| 83  | Globosterol                                             | 1193319-70-8| ![structure](image) | Chaetomium globosum      | ZY-22                                               | [44]       |
| 84  | Glycerol formal                                        | 5464-28-8  | ![structure](image)  | Chaetomium globosum      | T16                                                  | [46]       |
| 85  | Hexadecane                                             | 544-76-3   | ![structure](image)  | Chaetomium globosum      |                                                      | [45]       |
| 86  | Hexadecanoic acid, ethyl ester                        | 628-97-7   | ![structure](image)  | Chaetomium globosum      | No. 16, Used as a solvent and an ingredient in gasoline and diesel and jet fuels | [45]       |
| 87  | Hexadecanoic acid, methyl ester                       | 112-39-0   | ![structure](image)  | Chaetomium globosum      | No. 16, Used as softener, lubricant, food additive  | [45]       |
| 88  | Indole-3-carboxylic acid                              | 771-50-6   | ![structure](image)  | Chaetomium globosum      | ZY-22, Used for synthesis of to rise tron and antiviral drugs | [33]       |
| 89  | Indole-3-acetic acid                                   | 87-51-4    | ![structure](image)  | Chaetomium globosum      |                                                      | [33]       |
| 90  | Isopentyl alcohol, acetate                            | 123-92-2   | ![structure](image)  | Chaetomium globosum      | T16, Used as a solvent and preparation of a variety of flavor food flavor | [22]       |
| No. | Metabolites                  | CAS number | Molecular structure | Endophytes               | Application                                                                 | References |
|-----|------------------------------|------------|---------------------|--------------------------|------------------------------------------------------------------------------|------------|
| 91  | Lactic acid                 | 50-21-5    | ![Molecular structure](image) | Chaetomium globosum T16   | Used to make some plasticizers, adhesives, pharmaceuticals and salts, used in the leather tanning industry and as a solvent | [46]       |
| 92  | Lactic acid, 2-methyl-ethyl ester | 80-55-7   | ![Molecular structure](image) | Chaetomium globosum T16   |                                                                                | [46]       |
| 93  | Maltol                      | 118-71-8   | ![Molecular structure](image) | Chaetomium globosum MX-0510 | Food additive                                                               | [33]       |
| 94  | Mannitol                    | 87-78-5    | ![Molecular structure](image) | Chaetomium globosum       | Used as an osmotic diuretic                                                  | [33]       |
| 95  | Methyl 13-methyltetradecanoate | 5129-59-9 | ![Molecular structure](image) | Chaetomium globosum No. 16 |                                                                                | [45]       |
| 96  | Methyl 9,12-heptadecadienoate | 15620-59-4 | ![Molecular structure](image) | Chaetomium globosum No. 16 |                                                                                | [45]       |
| 97  | Methyl vinylcarbinol         | 598-32-3   | ![Molecular structure](image) | Chaetomium globosum       | Food additive                                                               | [46]       |
| 98  | Methylthiogliotoxin         | 74149-38-5 | ![Molecular structure](image) | Chaetomium globosum (NM0066) |                                                                                | [33]       |
| 99  | o-Coumaric acid             | 583-17-5   | ![Molecular structure](image) | Chaetomium globosum ZY-22 | An antioxidant and is believed to reduce the risk of stomach cancer by reducing the formation of carcinogenic nitrosamines | [33]       |
| 100 | Octanoic acid, methyl ester | 111-11-5   | ![Molecular structure](image) | Chaetomium globosum No. 16 | Food additive                                                               | [45]       |
| 101 | Pentadecane                 | 629-62-9   | ![Molecular structure](image) | Chaetomium globosum No. 16 | Used as a solvent and in some household pesticides                           | [45]       |
| 102 | Pentadecanoic acid, methyl ester | 7132-64-1 | ![Molecular structure](image) | Chaetomium globosum No. 16 | Fuels and fuel additives, intermediates, pesticide                           | [45]       |
| 103 | p-Hydroxybenzoic acid       | 99-96-7    | ![Molecular structure](image) | Chaetomium globosum       | Used as preservatives, fungicides                                           | [33]       |
| 104 | Pseurotin A                 | 58523-30-1 | ![Molecular structure](image) | Chaetomium globosum (NM0066) | An azaspiro compound, an oxaspiro compound and a lactam                       | [33]       |
| No. | Metabolites                        | CAS number | Molecular structure | Endophytes                      | Application                                                                 | References |
|-----|-----------------------------------|------------|---------------------|---------------------------------|-----------------------------------------------------------------------------|------------|
| 105 | Quercetin                         | 117-39-5   | ![Molecular structure](image) | Chaetomium globosum GCZX015     | Combined with chemotherapeutic drugs, produces anti-inflammatory and anti-allergy effects | [33]       |
| 106 | Squalene                          | 111-02-4   | ![Molecular structure](image) | Chaetomium globosum (NM0066)    | Investigated as an adjunctive cancer therapy, also used as cosmetics and dietary supplement | [33]       |
| 107 | S-Tetrachloroethane               | 79-34-5    | ![Molecular structure](image) | Chaetomium globosum T16         | Used to make paint, varnish and rust removers, as a solvent and as an ingredient in pesticides | [45]       |
| 108 | Succinic acid                     | 110-15-6   | ![Molecular structure](image) | Chaetomium globosum             | A radiation protective agent, an anti-ulcer drug                             | [33]       |
| 109 | Tetradecane                       | 629-59-4   | ![Molecular structure](image) | Chaetomium globosum No.16       | Used as a solvent and some pesticide sprays                                   | [45]       |
| 110 | Thymine                           | 65-71-4    | ![Molecular structure](image) | Chaetomium globosum ZY-22       | A pyrimidine nucleobase and a pyrimidine                                     | [33]       |
| 111 | Tridecane                         | 629-50-5   | ![Molecular structure](image) | Chaetomium globosum No.16       | Used as a solvent and as an ingredient in gasoline and diesel and jet fuel    | [45]       |
| 112 | Triethylene glycol monomethyl ether acetate | 3610-27-3 | ![Molecular structure](image) | Chaetomium globosum T16         | Use in the body to help synthesis of many enzymes, and the biosynthesis of polysaccharides and the transportation of sugars containing aldehydes | [46]       |
| 113 | Uracil                            | 66-22-8    | ![Molecular structure](image) | Chaetomium globosum ZY-22       | Use in the body to help synthesis of many enzymes, and the biosynthesis of polysaccharides and the transportation of sugars containing aldehydes | [49]       |
| 114 | α-Guaiene                         | 3691-12-1  | ![Molecular structure](image) | Chaetomium globosum No.16       |                                                                              | [45]       |
| No. | Metabolites                                      | CAS number         | Molecular structure                  | Endophytes     | Application                                                                 | References |
|-----|-------------------------------------------------|--------------------|--------------------------------------|----------------|----------------------------------------------------------------------------|------------|
| 1   | 3-Hydroxyterphenyllin                           | 66163-76-6         | ![Molecular structure](image1)       | Aspergillus sp. | Induces apoptosis and S phase arrest in human ovarian carcinoma cells      | [28, 50]   |
| 2   | 4″-Deoxycandidusin A                            | 1354549-88-4       | ![Molecular structure](image2)       | Aspergillus sp. |                                                                           | [51, 52]   |
| 3   | 4″-Deoxyterphenyllin                            | 59904-04-0         | ![Molecular structure](image3)       | Aspergillus sp. |                                                                           | [50]       |
| 4   | 4,5-Dimethoxycandidusin A/3,4-dimethoxycandidus A | 1354549-89-5       | ![Molecular structure](image4)       | Aspergillus sp. |                                                                           | [50, 52]   |
| 5   | 4″-Deoxy-3-hydroxyterphenyllin                  | 1296205-84-9       | ![Molecular structure](image5)       | Aspergillus sp. |                                                                           | [50, 52]   |
| 6   | 4″-Deoxy-5″-desmethyl-terphenyllin              | 1354549-87-3       | ![Molecular structure](image6)       | Aspergillus sp. |                                                                           | [50]       |
| 7   | 4″-Deoxyprenylterphenyllin                     | 959124-87-9        | ![Molecular structure](image7)       | Aspergillus sp. IFB-YXS | Potential anticancer lead molecules                        | [50]       |
| 8   | 4-Hydroxy-3-(3″-methyl-2″-butenyl) benzoic acid | 1138-41-6          | ![Molecular structure](image8)       | Aspergillus sp. YXf3 | Show potent inhibition of HLE                                         | [50]       |
| 9   | 5″-Desmethylterphenyllin                       | 1299485-87-2       | ![Molecular structure](image9)       | Aspergillus sp. | An alpha-glucosidase inhibitor                                             | [50]       |
| 10  | Alternariol                                     | 641-38-3           | ![Molecular structure](image10)      | Aspergillus sp. YXf3 | An cholinesterase inhibitor and a mycotoxin                          | [52]       |
| No. | Metabolites                                | CAS number | Molecular structure | Endophytes       | Application                  | References |
|-----|--------------------------------------------|------------|---------------------|------------------|------------------------------|------------|
| 11  | Alternariol monomethyl ether/ alternariol-4-methyl ether | 23452-05-3 | ![Molecular Structure](image1) | Aspergillus sp. YXf3 | An antifungal agent          | [52]       |
| 12  | Aspergiloid A                              | 1354549-91-9 | ![Molecular Structure](image2) | Aspergillus sp.   |                              | [50]       |
| 13  | Aspergiloid B                              | 1354549-92-0 | ![Molecular Structure](image3) | Aspergillus sp.   |                              | [50]       |
| 14  | Aspergiloid C                              | 1354549-93-1 | ![Molecular Structure](image4) | Aspergillus sp.   |                              | [50]       |
| 15  | Aspergiloid D                              | 1354549-94-2 | ![Molecular Structure](image5) | Aspergillus sp.   |                              | [50]       |
| 16  | Aspergiloid E                              | 1579256-33-9 | ![Molecular Structure](image6) | Aspergillus sp. YXf3 |                              | [52]       |
| 17  | Aspergiloid F                              | 1579256-35-1 | ![Molecular Structure](image7) | Aspergillus sp. YXf3 |                              | [52]       |
| 18  | Aspergiloid G                              | 1579256-37-3 | ![Molecular Structure](image8) | Aspergillus sp. YXf3 |                              | [52]       |
| No. | Metabolites          | CAS number  | Molecular structure | Endophytes          | Application                                           | References |
|-----|---------------------|-------------|---------------------|---------------------|------------------------------------------------------|------------|
| 19  | Aspergiloid H       | 1579256-39-5| ![Molecular structure](image) | Aspergillus sp. YXf3 | Anti-cancer and inhibition of plant pathogens        | [52]       |
| 20  | Aspergiloid I       | 1887750-59-5| ![Molecular structure](image) | Aspergillus sp. YXf3 | Anti-cancer and inhibition of plant pathogens        | [50]       |
| 21  | Candidusin A        | 81474-59-1  | ![Molecular structure](image) | Aspergillus sp.     |                                                       | [50]       |
| 22  | Candidusin C/4'-methoxycandidusin A | 267007-58-9 | ![Molecular structure](image) | Aspergillus sp.     |                                                       | [50]       |
| 23  | Chlorflavonin       | 23363-64-6  | ![Molecular structure](image) | Aspergillus sp. (strain no. YXf3) | An antifungal agent | [50]       |
| 24  | Chlorflavonin A     | 1443055-96-6| ![Molecular structure](image) | Aspergillus sp. (strain no. YXf3) | An antifungal agent | [50]       |
| 25  | Cyclo-(L-Leu-L-Trp) | 15136-34-2  | ![Molecular structure](image) | Aspergillus sp. YXf3 |                                                       | [50]       |
| 26  | Ginkgolide B        | 15291-77-7  | ![Molecular structure](image) | Aspergillus fumigatus var. fumigatus FG 05 | Ginkgolide B protects human umbilical vein endothelial cells against xenobiotic injuries via PXR activation | [52]       |
| 27  | Ginkgolide C        | 15291-76-6  | ![Molecular structure](image) | Aspergillus sp.     |                                                       | [32]       |
| 28  | Prenylcandidusin B  | 1297472-19-5| ![Molecular structure](image) | Aspergillus sp. IFB-YXS | An antineoplastic agent | [53]       |
| 29  | Prenylcandidusin C  | 1297472-20-8| ![Molecular structure](image) | Aspergillus sp.     | An antineoplastic agent | [53]       |
| 30  | Prenylterphenyllin  | 959124-85-7 | ![Molecular structure](image) | Aspergillus sp.     | Exhibits cytotoxic activity, an antineoplastic agent | [53]       |
| No. | Metabolites                  | CAS number     | Molecular structure | Endophytes          | Application                                      | References |
|-----|------------------------------|----------------|---------------------|---------------------|--------------------------------------------------|------------|
| 31  | Prenylterphenyllin B         | 1297472-16-2   |                     | Aspergillus sp. IFB-YXS | Exhibits cytotoxic activity, an antineoplastic agent | [53]       |
| 32  | Sphaeropsidin A              | 38991-80-9     |                     | Aspergillus sp. YXf3 | Larvicidal and biting deterrents against *Aedes aegypti* | [50]       |
| 33  | Sphaeropsidin B              | 39022-38-3     |                     | Aspergillus sp. YXf3 |                                                  | [50]       |
| 34  | Terphenolide                 | 1354549-90-8   |                     | Aspergillus sp.      |                                                  | [50]       |
| 35  | Terphenyllin                 | 52452-60-5     |                     | Aspergillus sp.      | A mycotoxin                                      | [50]       |
| 36  | Tereinol                     | 669073-67-0    |                     | Aspergillus sp. YXf3 |                                                  | [31]       |
| 37  | Xanthoascin                  | 61391-08-0     |                     | Aspergillus sp. IFB-YXS |                                              | [53]       |
| 38  | Prenylterphenyllin D         | 2079979-59-0   |                     | Aspergillus sp. IFB-YXS | Antibacterial activities, anti-phytopathogenic activities | [31]       |
| 39  | Prenylterphenyllin E         | 2079979-60-3   |                     | Aspergillus sp. IFB-YXS | Antibacterial activities, anti-phytopathogenic activities | [31]       |
| 40  | 2′-O-Methylprenylterphenyllin| 2079979-61-4   |                     | Aspergillus sp. IFB-YXS | Antibacterial activities, anti-phytopathogenic activities | [31]       |
Table 2 (continued)

| No. | Metabolites                                      | CAS number | Molecular structure | Endophytes   | Application | References |
|-----|--------------------------------------------------|------------|---------------------|--------------|-------------|------------|
| 41  | 4-O-Methylprenylterphenyllin                     | 2079979-62-5 | ![Molecular Structure](image) | Aspergillus sp. IFB-YXS |            | [31]       |
| 42  | [1,1′,4′,1″-Terphenyl]-4,4″-dil, 2″,3″,5″-trimethoxy-(9CI) | 59914-89-5 | ![Molecular Structure](image) | Aspergillus sp. IFB-YXS |            | [31]       |
| 43  | [1,1′,4′,1″-Terphenyl]-2″,4″-dil,3″,4,6″-trimethoxy-(9CI) | 59903-93-4 | ![Molecular Structure](image) | Aspergillus sp. IFB-YXS |            | [31]       |
| 44  | [1,1′,4′,1″-Terphenyl]-2″,4-dil,3″,4,6″-trimethoxy-(9CI) | 59903-92-3 | ![Molecular Structure](image) | Aspergillus sp. IFB-YXS |            | [31]       |
| No. | Metabolites                              | CAS number | Molecular structure | Endophytes         | Application                                      | References |
|-----|-----------------------------------------|------------|---------------------|--------------------|--------------------------------------------------|------------|
| 1   | (22E,24R)-ergosta-7,22-diene-3β,5α,6β-triol/cerevisterol | 516-37-0   | ![Molecular structure](image1) | Alternaria tenuissima SY-P-07 | SY-P-07 [29]                                       | [29]       |
| 2   | (2R,3R)-3,5,7,3',5'-pentahydroxyflavane | 87592-94-7 | ![Molecular structure](image2) | Alternaria tenuissima SY-P-07 | SY-P-07 [29]                                       | [29]       |
| 3   | 3β,5α,9α-Trihydroxy-(22E,24R)-ergosta-7,22-dien-6-one | 88191-14-4 | ![Molecular structure](image3) | Alternaria tenuissima SY-P-07 | SY-P-07 [29]                                       | [29]       |
| 4   | 6-Epi-stemphytriol                       | 1262797-65-8 | ![Molecular structure](image4) | Alternaria tenuissima SY-P-07 | SY-P-07 [29]                                       | [29]       |
| 5   | 7-Epi-8-hydroxyaltertoxin I             | 1262797-64-7 | ![Molecular structure](image5) | Alternaria tenuissima SY-P-07 | SY-P-07 [29]                                       | [29]       |
| 6   | Alternariol                             | 641-38-3   | ![Molecular structure](image6) | Alternaria No. 28 | An cholinesterase inhibitor                      | [29]       |
| 7   | Alternariol monomethyl ether/alternariol-4-methyl ether | 23452-05-3 | ![Molecular structure](image7) | Alternaria No. 28 | An antifungal agent                               | [29]       |
| 8   | Alterperylenol                          | 88899-62-1 | ![Molecular structure](image8) | Alternaria tenuissima |                                                 | [45]       |
| 9   | Altertoxin I (dihydroalterperylenol)    | 56258-32-3 | ![Molecular structure](image9) | Alternaria sp.      |                                                 | [29]       |
| 10  | Ergosta-4,6,8,22-tetraen-3-one/ergosta-4,6,8,22-tetraen-3-one | 194721-75-0 | ![Molecular structure](image10) | Alternaria No. 28 |                                                 | [29]       |
| 11  | Ergosterol                              | 57-87-4    | ![Molecular structure](image11) | Alternaria sp.      | Formation of vitamin D2                          | [29]       |
| No. | Metabolites       | CAS number   | Molecular structure | Endophytes                  | Application                                                                 | References |
|-----|------------------|--------------|---------------------|-----------------------------|------------------------------------------------------------------------------|------------|
| 12  | Flazin           | 100041-05-2  |                     | *Alternaria tenuissima* SY-P-07  |                                                                              | [47]       |
| 13  | Solanapyrone G   | 220924-51-6  |                     | *Alternaria tenuissima* SY-P-07  |                                                                              | [47]       |
| 14  | Stemphypanylenol | 102694-33-7  |                     | *Alternaria tenuissima* SY-P-07  | An antifungal agent                                                          | [47]       |
| 15  | Tenuazonic acid  | 610-88-8     |                     | *Alternaria* No. 28           | An antibiotic with antiviral and antineoplastic, also as a mycotoxin          | [29]       |
| 16  | Vivotoxin II     | 1261267-71-3 |                     | *Alternaria* No. 28           |                                                                              | [29]       |
| No. | Metabolites                                      | CAS number  | Molecular structure | Endophytes               | Application                                                                 | References |
|-----|-------------------------------------------------|-------------|---------------------|--------------------------|----------------------------------------------------------------------------|------------|
| 1   | 2′-Deoxyuridine/uracil deoxyriboside            | 951-78-0    | ![Structure](image1) | *Penicillium* sp. YY-25  | Antimetabolite                                                              | [29]       |
| 2   | 3-Methylorsellinic acid                         | 4707-46-4   | ![Structure](image2) | *Penicillium* No. 97     | Antibacterial activity                                                     | [29]       |
| 3   | 3-Methylpiperazine-25-dione                     | 6062-46-0   | ![Structure](image3) | *Penicillium* sp. YY-24  |                                                                          | [29]       |
| 4   | Adenine                                         | 73-24-5     | ![Structure](image4) | *Penicillium* sp. YY-22  | Dietary supplement                                                         | [29]       |
| 5   | Adenosine                                       | 58-61-7     | ![Structure](image5) | *Penicillium* sp. YY-20  | Analgesic, antiarrhythmic                                                 | [29]       |
| 6   | Anthranilamide                                  | 88-68-6     | ![Structure](image6) | *Penicillium* No. 97     | Fluorescent dyes                                                          | [54]       |
| 7   | Anthranilic acid                                | 118-92-3    | ![Structure](image7) | *Penicillium* No. 97     | Anticonvulsants                                                           | [55]       |
| 8   | Cyclopaldic acid                                | 477-99-6    | ![Structure](image8) | *Penicillium commune* (TMSF169) |                                                                            | [56]       |
| 9   | Ferulic acid                                    | 1135-24-6   | ![Structure](image9) | *Penicillium* No. 97     | Free radical scavengers, anti-inflammatory agents, antihypertensive agents, anticoagulants | [55]       |
| 10  | Fructigenine A                                  | 144606-96-2 | ![Structure](image10) | *Penicillium* No. 97     | Inhibits the growth of leukemia cells                                     | [55]       |
| No. | Metabolites                          | CAS number | Molecular structure | Endophytes        | Application                                                                 | References |
|-----|-------------------------------------|------------|---------------------|-------------------|-----------------------------------------------------------------------------|------------|
| 11  | Indole-3-acetic acid                | 87-51-4    |                     | **Penicillium** No. 97 | Used for preventing, destroying or mitigating pests                        | [55]       |
| 12  | Methyl β-D-ribofuranoside           | 7473-45-2  |                     | **Penicillium** sp. YY-21 | Used to synthesize novel alpha-amino acid esters against herpes simplex virus 1 (hsv-1) and hepatitis B virus | [29]       |
| 13  | Orsellinic acid                     | 480-64-8   |                     | **Penicillium** No. 97 |                                                                             | [29]       |
| 14  | p-Hydroxybenzoic acid               | 99-96-7    |                     | **Penicillium** No. 97 |                                                                             | [55]       |
| 15  | β-sitosterol                         | 83-46-5    |                     | **Penicillium** No. 97 | Hypolipidemic agents                                                        | [55]       |
| 16  | Quercetin glycoside (orange pigment) | 3520-72-7  |                     | **Penicillium** sp. |                                                                             | [34]       |
| No. | Metabolites | CAS number | Molecular structure | Endophytes  | Application                                                                                                                                                                                                 | References |
|-----|-------------|------------|--------------------|-------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| 1   | 7-Amino-4-methylcoumarin | 26093-31-2 | ![Molecular structure](image) | Xylaria sp. YX-28 | A fluorescent dye used to stain biological specimens                                                                 | [57]        |
| 2   | Pentadecane | 629-62-9   | ![Molecular structure](image) | Xylaria sp. YX-28 | Treatment of plantar keratosis with medicinal plant in diabetic patients                                                                                                                                   | [57]        |
| 3   | Quercetin   | 117-39-5   | ![Molecular structure](image) | Xylaria Colletotrichum | Chemotherapy induced oral mucositis; treatment of erosive and atrophic oral lichen planus; chronic obstructive pulmonary disease; gastroesophageal reflux disease | [57]        |
| 4   | Tetradecane | 629-59-4   | ![Molecular structure](image) | Xylaria sp.YX-28 |                                                                                                                                                                                                              | [57]        |
| 5   | Tridecane   | 629-50-5   | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                                                                                                                                                              | [57]        |
| 6   | Dibutyl phthalate | 84-74-2 | ![Molecular structure](image) | Xylaria sp. YX-28 | Against the larval trombiculid mite; preventing scrub typhus of topical application in troops                                                                                                           | [57]        |
| 7   | 1,3-Diphenyl-2-pyrazoline | 2538-52-5 | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                                                                                                                                                              | [57]        |
| 8   | 1-Acetyl-1,2,3,4-tetrahydropyridine | 19615-27-1 | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                                                                                                                                                              | [57]        |
| 9   | ZZ-7,11-Hexadecadien-1-ol | 53963-06-7 | ![Molecular structure](image) | Xylaria sp.YX-28 | Prevention of angina pectoris due to coronary artery disease; short-term reduction of intraocular pressure                                                                                                    | [57]        |
| 10  | Isosorbide  | 652-67-5   | ![Molecular structure](image) | Xylaria sp. YX-28 | Prevention of angina pectoris due to coronary artery disease; short-term reduction of intraocular pressure                                                                                                    | [57]        |
| 11  | Dimethoxy-phenol | 91-10-1 | ![Molecular structure](image) | Xylaria sp.YX-28 | Food Flavoring Agents                                                                                                                                                                                     | [57]        |
| 12  | 1-hydroxymethyl-1,2,3,4-tetrahydro-naphthalen-2-ol | 872824-43-6 | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                                                                                                                                                              | [57]        |
| 13  | (1,4-Dimethylpent-2-enyl)benzene | 951288-80-5 | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                                                                                                                                                              | [57]        |
| 14  | 2,4-Bis(1,1-dimethylethyl)phenol | 96-76-4 | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                                                                                                                                                              | [57]        |
| 15  | 3-Phenyl-4-methyl-isoxazol-5(4)-one | 875244-90-9 | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                                                                                                                                                              | [57]        |
### Table 5 (continued)

| No. | Metabolites                                         | CAS number | Molecular structure | Endophytes  | Application                                                                 | References |
|-----|-----------------------------------------------------|------------|---------------------|-------------|-----------------------------------------------------------------------------|------------|
| 16  | 3,4-Dihydro-8-hydroxy-3-methyl-isocoumarin          | 1200-93-7  | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                 | [57]       |
| 17  | [(3-butenylthio)-2-nitroethyl]-benzene             | 128869-50-1| ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                 | [57]       |
| 18  | Pentadecanoic acid, methyl ester                    | 7132-64-1  | ![Molecular structure](image) | Xylaria sp. YX-28 | pesticide                                                                   | [57]       |
| 19  | 14-Octadecenal                                      | 56554-89-3 | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                 | [57]       |
| 20  | E-11,13-Dimethyl-12-tetradecen-1-ol acetate        | 400037-00-5| ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                 | [57]       |
| 21  | Hexadecanoic acid, methyl ester                     | 112-39-0   | ![Molecular structure](image) | Xylaria sp. YX-28 | Food flavoring agents                                                        | [57]       |
| 22  | n-Hexadecanoic acid                                | 57-10-3    | ![Molecular structure](image) | Xylaria sp. YX-28 | Inhibits HIV-1 infection; a potential candidate for specifically attack multiple myeloma cells | [57]       |
| 23  | 2-Undecenal                                         | 2463-77-6  | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                 | [57]       |
| 24  | Hexadecanoic acid, 14-methyl-methyl ester          | 2490-49-5  | ![Molecular structure](image) | Xylaria sp. YX-28 |                                                                 | [57]       |
| 25  | 9,12-Octadecadienoic acid(ZZ)-methyl ester         | 112-63-0   | ![Molecular structure](image) | Xylaria sp. YX-28 | Flavoring agent or adjuvant                                                 | [57]       |
| 26  | 9-Octadecenoic acid (Z)-methyl ester               | 112-62-9   | ![Molecular structure](image) | Xylaria sp. YX-28 | Solvents                                                                   | [57]       |
| 27  | 3,7,11-trimethyl-2,6,10-Dodecatrien-1-ol           | 4602-84-0  | ![Molecular structure](image) | Xylaria sp. YX-28 | Inhibits proliferation and induces apoptosis of tumour-derived but not non-transformed cell lines | [57]       |
| 28  | 9,12-Octadecadienoic acid (ZZ)                     | 2197-37-7  | ![Molecular structure](image) | Xylaria sp. YX-28 | Treats the prevention of preeclampsia;                                     | [57]       |
| 29  | 9-Octadecanamide (Z)                               | 3322-62-1  | ![Molecular structure](image) | Xylaria sp. YX-28 | Induce drowsiness or sleep or to reduce psychological excitement or anxiety | [57]       |
| 30  | Pentadecanoic acid,2-hydroxymethyl ester          | 98863-01-5 | ![Molecular structure](image) | Xylaria sp. YX-28 | Emulsifier                                                                 | [57]       |
| 31  | Ferruginol                                          | 514-62-5   | ![Molecular structure](image) | Xylaria sp. YX-28 | An antineoplastic agent; antibacterial agent; protective agent              | [57]       |
| 32  | 9,12-Octadecadienoic acid(ZZ)-2-hydroxy-1-(hydroxy methyl)ethyl ester | 544-35-4 | ![Molecular structure](image) | Xylaria sp. YX-28 | Flavoring agents                                                            | [57]       |
| 33  | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester | 23470-00-0 | ![Molecular structure](image) | Xylaria sp. YX-28 | Lipid maps classification                                                   | [57]       |
Table 5 (continued)

| No. | Metabolites                              | CAS number | Molecular structure | Endophytes | Application | References |
|-----|------------------------------------------|------------|---------------------|------------|-------------|------------|
| 34  | Bis(2-ethylhexyl)phthalate               | 117-81-7   |                     | Xylaria sp. YX-28 |             | [57]       |
| 35  | 5,6,8,9,10,11-Hexahydrobenz[a]anthracene | 67064-61-3 |                     | Xylaria sp. YX-28 |             | [57]       |
| 36  | 1,2,3,4-Tetrahydro-Triphenylene         | 5981-10-2  |                     | Xylaria sp. YX-28 |             | [57]       |
Table 6  Secondary metabolite of Fusarium in Ginkgo biloba

| No. | Metabolites                  | CAS number | Molecular structure | Endophytes               | Application                                                                                   | References |
|-----|------------------------------|------------|---------------------|--------------------------|-----------------------------------------------------------------------------------------------|------------|
| 1   | Adenosine                    | 58-61-7    | ![Molecular structure](image) | Fusarium solani GBT07 GBT07 | Terminate paroxysmal supraventricular tachycardia; terminating stable and narrow-complex supraventricular tachycardias; adjunct to thallous chloride TI 201 myocardial perfusion scintigraphy and vagal maneuvers and clinical assessment | [11]       |
| 2   | Benzeneethanol/Phenylethyl alcohol | 60-12-8   | ![Molecular structure](image) | Fusarium sp. G1024       | Anti-infective agents, local disinfectants, preservatives, pharmaceutical                        | [11]       |
| 3   | Enniatin B                   | 917-13-5   | ![Molecular structure](image) | Fusarium sp.              |                                                                                               | [58]       |
| 4   | Ginkgolide B                 | 15291-77-7 | ![Molecular structure](image) | Fusarium oxysporum        |                                                                                               | [59, 60]   |
| 5   | Hexadecane                   | 544-76-3   | ![Molecular structure](image) | Fusarium sp. G1024       |                                                                                               | [11]       |
| 6   | Kaempferide                  | 491-54-3   | ![Molecular structure](image) | Fusarium solani           | An antihypertensive agent                                                                      | [61]       |
| 7   | Kaempferol                   | 520-18-3   | ![Molecular structure](image) | Fusarium oxysporum        | A possible cancer treatment; antibacterial agent                                               | [61]       |
| 8   | Quercetin                    | 117-39-5   | ![Molecular structure](image) | Fusarium oxysporum        |                                                                                               | [57]       |
| 9   | Rutin                        | 153-18-4   | ![Molecular structure](image) | Fusarium oxysporum        | A role as an antioxidant; anti-allergic; anti-inflammatory; antiproliferative; and anticarcinogenic properties | [61]       |
| 10  | Soyasapogenol B              | 595-15-3   | ![Molecular structure](image) | Fusarium oxysporum Schlecht GB-1(3) |                                                                                               | [61]       |
| 11  | Tetradecane                  | 629-59-4   | ![Molecular structure](image) | Fusarium sp. G1024       |                                                                                               | [11]       |
| 12  | β-Sitosterol                 | 83-46-5    | ![Molecular structure](image) | Fusarium oxysporum Schlecht GB-1(3) | As anticholesteremic drug, antioxidant, treats hyperlipidemia                                  | [61]       |
| No. | Metabolites                        | CAS number | Molecular structure | Endophytes      | Application                                                                 | References |
|-----|-----------------------------------|------------|---------------------|-----------------|-----------------------------------------------------------------------------|------------|
| 13  | Isorhamnetin                      | 480-19-3   | ![Structure](structure13.png) | Fusarium sp     | Warning; (tyrosinase inhibitor; an anticoagulant)                           | [62]       |
| 14  | Decane                            | 124-18-5   | ![Structure](structure14.png) | Fusarium sp G1024 |                                                                               | [11]       |
| 15  | 2-Ethyl-1-hexanol                 | 104-76-7   | ![Structure](structure15.png) | Fusarium sp G1024 |                                                                               | [11]       |
| 16  | 2-Butanol,3,3'-oxybis-4-ethylphenol | 123-07-9  | ![Structure](structure16.png) | Fusarium sp G1024 | Flavoring Agents                                                            | [11]       |
| 17  | Dodecane                          | 112-40-3   | ![Structure](structure17.png) | Fusarium sp G1024 | Increase the risk of neoplasms in humans or animals                        | [11]       |
| 18  | 1,2-benzisothiazole               | 272-16-2   | ![Structure](structure18.png) | Fusarium sp G1024 |                                                                               | [11]       |
| 19  | 4-Ethyl-2-methoxyphenol           | 2785-89-9  | ![Structure](structure19.png) | Fusarium sp G1024 | Flavoring agents                                                            | [11]       |
| 20  | p-Nitroacetophenone               | 100-19-6   | ![Structure](structure20.png) | Fusarium sp G1024 | Potentiate the effectiveness of radiation therapy in destroying unwanted cells | [11]       |
| 21  | 2,3,5,6-Tetramethyl-p-benzoquinone | 527-17-3  | ![Structure](structure21.png) | Fusarium sp G1024 | product quinones duroquinone                                                | [11]       |
| 22  | Eicosane                          | 112-95-8   | ![Structure](structure22.png) | Fusarium sp G1024 | Flavoring Agents                                                            | [11]       |
| 23  | 1,2-Benzenedicarboxylic acid bis(2-methylpropyl)ester | 88-99-3 | ![Structure](structure23.png) | Fusarium sp G1024 |                                                                               | [11]       |
| 24  | Dibutyl phthalate                 | 84-74-2    | ![Structure](structure24.png) | Fusarium sp G1024 | Against the larval trombiculid mite; preventing scrub typhus of topical application in troops | [11]       |
| No. | Metabolites                                  | CAS number   | Molecular structure                                                                 | Endophytes                  | Application                                                                                                           | References |
|-----|---------------------------------------------|--------------|-------------------------------------------------------------------------------------|-----------------------------|-----------------------------------------------------------------------------------------------------------------------|------------|
| 1   | 2-(Hydroxymethylthio)ethanol                | 876503-58-1  | ![Molecular structure](image1)                                                       | *Colletotrichum sp.* NTB-2  | Platelet aggregation inhibitor, an alpha-glucosidase inhibitor, an antineoplastic agent                               | [63]       |
| 2   | Apigenin-8-C,β-di-glucopyranoside           | 3681-93-4    | ![Molecular structure](image2)                                                       | *Colletotrichum sp.*       |                                                                                                                      | [63, 64]   |
| 3   | 6-Ethoxyl-2,4-amide lactone                |              | ![Molecular structure](image3)                                                       | *Bacillus amyloliquefaciens* CGMCC 5569 |                                                                                                                      | [64]       |
| 4   | 6-Hydroxybutyl-2,4-amide lactone            |              | ![Molecular structure](image4)                                                       | *Bacillus amyloliquefaciens* CGMCC 5569 |                                                                                                                      | [64]       |
| 5   | 6-Hydroxypropyl-2,4-amide lactone           |              | ![Molecular structure](image5)                                                       | *Bacillus amyloliquefaciens* CGMCC 5569 |                                                                                                                      | [64]       |
| 6   | Biuret                                      | 108-19-0     | ![Molecular structure](image6)                                                       | *Bacillus amyloliquefaciens* CGMCC 5569 | Used for preventing, destroying or mitigating pests                                                                   | [64]       |
| 7   | Ginkgolide B                               | 15291-77-7   | ![Molecular structure](image7)                                                       | *Oospora wallr.* G10       | Fibrinolytic agents                                                                                                   | [65]       |
| 8   | 2'-Deoxyuridine/uracil deoxyriboside       | 951-78-0     | ![Molecular structure](image8)                                                       | Unidentified                | Antimetabolites                                                                                                      | [65]       |
| 9   | 3-Methylpiperazine-2,5-dione               | 6062-46-0    | ![Molecular structure](image9)                                                       | Unidentified                |                                                                                                                      | [65]       |
| 10  | Adenine                                    | 73-24-5      | ![Molecular structure](image10)                                                      | Unidentified                |                                                                                                                      | [65]       |
| 11  | Adenine deoxyriboside                      |              | ![Molecular structure](image11)                                                      | Unidentified                |                                                                                                                      | [65]       |
| 12  | Adenosine                                  | 58-61-7      | ![Molecular structure](image12)                                                      | Unidentified                | Used as an initial treatment for the termination of paroxysmal Supraventricular tachycardia                           | [65]       |
| No. | Metabolites | CAS number | Molecular structure | Endophytes | Application | References |
|-----|-------------|------------|---------------------|------------|-------------|------------|
| 13  | Quercetin   | 117-39-5   | ![Molecular Structure](image) | Stemphylium sp. | Antioxidants | [37, 66] |
|     |             |            |                     | Actinomyces |             |            |
|     |             |            |                     | Nodulisporium hyalosporum |             | [67] |
|     |             |            |                     | Schizophyllum commune Fr. |             |            |
|     |             |            |                     | Fusella Sacc |             | [37] |
|     |             |            |                     | Alternaria sp |             |            |
|     |             |            |                     | Sphacelia sp. |             |            |
|     |             |            |                     | Anpelomyces humuli |             |            |
|     |             |            |                     | Phoma glomerate |             | [30, 61] |
|     |             |            |                     | Trichothecium |             | [53] |
|     |             |            |                     | Mucor circinelloides |             | [40] |
|     |             |            |                     | Sphaeropsis sp. |             | [68] |
|     |             |            |                     | B301 |             |            |
| 14  | Kaempferol  | 520-18-3   | ![Molecular Structure](image) | Fusella Sacc | As a selective estrogen receptor modulator | [66] |
|     |             |            |                     | Alternaria sp |             |            |
|     |             |            |                     | Gibberella sp. |             |            |
|     |             |            |                     | Sphacelia sp. |             |            |
|     |             |            |                     | Dematium Pers |             |            |
|     |             |            |                     | Trichothecium |             | [53] |
|     |             |            |                     | Sphaeropsis sp. |             | [68] |
| 15  | Cerebroside B | 88642-46-0 | ![Molecular Structure](image) | Phyllosticta sp. | An antimicrobial compound | [20, 21] |
|     |             |            |                     | TP78, (GenBank ID: KC445736) |             |            |
| 16  | Cerebroside C | 98677-33-9 | ![Molecular Structure](image) | Phyllosticta sp. | Increases tolerance to chilling injury and alters lipid composition in wheat roots | [20, 21] |
|     |             |            |                     | TP78 (GenBank ID: KC445736) |             |            |
| 17  | Enniatin B1 | 19914-20-6 | ![Molecular Structure](image) | Tuberculariaceae F1-3 | Fusarium mycotoxins | [69] |
| 18  | Enniatin D  | 19893-21-1 | ![Molecular Structure](image) | Tuberculariaceae sp. F1-3 | Inhibition of Botrytis cinerea spore germination | [69] |
| 19  | Benzeneethanol/Phenylethyl alcohol | 60-12-8 | ![Molecular Structure](image) | Muscodor albus strain GBA | Anti-bacterial agents and antioxidants. Anti-Infective Agents | [69] |
| No. | Metabolites       | CAS number | Molecular structure | Endophytes                  | Application                                      | References |
|-----|------------------|------------|---------------------|-----------------------------|--------------------------------------------------|------------|
| 20  | Ginkgolide C     | 15291-76-6 | ![Molecular Structure](image1) | *Gloeosporium; Tolura; Phacodium* | Reduced lipid accumulation and suppresses adipogenesis | [32]       |
| 21  | Kaempferide      | 491-54-3   | ![Molecular Structure](image2) | *Phoma glomerata*           | Reverse bacterial resistance to amoxicillin in AREC | [61]       |
|     |                  |            |                     | *Anpelomyces humuli*        |                                                  |            |
| 22  | Rutin            | 153-18-4   | ![Molecular Structure](image3) | *Mucor circinelloides GF521* | Used therapeutically to decrease capillary fragility | [61]       |
|     |                  |            |                     | *Nodulisporium hyalosporum*  |                                                  |            |
|     |                  |            |                     | *Nodulisporium* sp. A21     | Used to treat the infection caused by *candida albicans* and *cryptococcus neoformans* | [55]       |
|     |                  |            |                     | *Sphacelothrix*              | Prevents endothelial dysfunction, superoxide production, *isorhamnetin* appears to be a potent drug against esophageal cancer | [62]       |
| 23  | Sporothriolide   | 154799-92-5| ![Molecular Structure](image4) | *Plantactinospora* sp. NEAU-gxj3 |                                                  | [68]       |
| 24  | Iisorhamnetin    | 480-19-3   | ![Molecular Structure](image5) | *Stemphylium* sp. *Alternaria* sp. *Gibberella* sp. *Trichotecium* |                                                   |            |
|     |                  |            |                     | *sphaeropsis*                |                                                  |            |
| 25  | Antibiotic U-62162 | 82516-67-4 | ![Molecular Structure](image6) | *Plantactinospora* sp. NEAU-gxj3 | Inhibited the growth of Gram-positive bacteria | [20, 21]  |
| 26  | Salternamide C   | 1662688-81-4| ![Molecular Structure](image7) | *sphaeropsis*                |                                                  | [68]       |
| 27  | Abscisic acid    | 21293-29-8 | ![Molecular Structure](image8) | *Phoma betae*                | Plant Growth Regulator                            | [69]       |
| 28  | Taxol            | 33069-62-4 | ![Molecular Structure](image9) | *Phomopsis* sp. 2 strain BKH 30 (BSL No. 72) | An antineoplastic agent, tubulin modulators       | [70]       |
| 29  | Acetic acid, methyl ester | 79-20-9 | ![Molecular Structure](image10) | *Muscodoralbus* strain GBA |                                                  | [69]       |
| No. | Metabolites                                      | CAS number | Molecular structure | Endophytes            | Application                                                                 | References |
|-----|-------------------------------------------------|------------|---------------------|-----------------------|-----------------------------------------------------------------------------|------------|
| 30  | 2-Butanone                                       | 78-93-3    |                     | *M. albus* strain GBA | Polar aprotic solvent                                                      | [69]       |
| 31  | Acetic acid, 2-methylpropyl ester                | 110-19-0   |                     | *M. albus* strain GBA | An antifungal agent                                                         | [71]       |
| 32  | 1-Propanol, 2-methyl                             | 78-83-1    |                     | *M. albus* strain GBA | Possesses nicotine-like synaptotropic actions on the nervous systems       | [71]       |
| 33  | 1-Butanol, 3-methylacetate                      | 123-92-2   |                     | *M. albus* strain GBA |                                                                             | [71]       |
| 34  | Cyclohexane-1-methyl-4-methylene                 | 2808-80-2  |                     | *M. albus* strain GBA |                                                                             | [69]       |
| 35  | 2,3-Dimethyl-3-isopropyl-cyclopentene            | 73331-73-4 |                     | *M. albus* strain GBA |                                                                             | [69]       |
| 36  | 1-Butanol, 3-methyl                              | 123-51-3   |                     | *M. albus* strain GBA |                                                                             | [69]       |
| 37  | Pynolidine                                       | 123-75-1   |                     | *M. albus* strain GBA |                                                                             | [72]       |
| 38  | Germacrene B                                     | 15423-57-1 |                     | *M. albus* strain GBA |                                                                             | [72]       |
| 39  | α-Sinensal                                       | 17909-77-2 |                     | *M. albus* strain GBA |                                                                             | [69]       |
| 40  | Propanoic acid, 2-methyl                         | 79-31-2    |                     | *M. albus* strain GBA |                                                                             | [73]       |
| 41  | trans-caryophyllene                              | 87-44-5    |                     | *M. albus* strain GBA | Anti-inflammatory agents                                                    | [73]       |
| 42  | 4-Piperidinone, 1-methyl                         | 1445-73-4  |                     | *M. albus* strain GBA |                                                                             | [73]       |
| 43  | Acetic acid, 2-phenylethyl ester                 | 103-45-7   |                     | *M. albus* strain GBA |                                                                             | [73]       |
| 44  | (−)-Vitrene                                       | 90250-82-1 |                     | *M. albus* strain GBA |                                                                             | [73]       |
This strain displayed the strongest antibacterial activity [35].

Secondary metabolites of Xylaria
43 kinds of compounds were isolated from the fermentation products of Xylaria in Ginkgo biloba (Table 5), in which the compound 7-amino-4-methylcoumarin was isolated from the fermentation product of Xylaria sp. YX-28 [36]. It has antibacterial activity and also has strong inhibitory activity against 13 kinds of human susceptible pathogens, which is significantly higher than the positive controls ampicillin, gentamicin and tetracycline.

Secondary metabolites of Fusarum
Fusarium is one of the dominant bacteria, which can be isolated from different parts of Ginkgo cultivated in various areas. According to the literatures, 25 kinds of compounds were isolated from the fermentation products of Fusarium (Table 6). Since Fusarium of G. biloba can produce ginkgolides B, it can be used as a new source of ginkgolides B [37]. Some studies have shown that Fusarium oxysporum GF521 can produce rutin and kaempferol, and the total flavonoids production of endophytic fungi is 21.10 ± 1.30 mg/L, which indicates that Fusarium genus also have a high ability of producing flavonoids [37].

Secondary metabolites of other genus
53 compounds were isolated from the fermentation products of other genus in G. biloba (Table 7), some of which can also produce other valuable compounds. From the endophytic Muscodor albus GBA, 19 kinds of volatile components can be separated [24], which normally have a strong ecological effect. Some volatile components can inhibit the pathogenic microorganisms and enhance the disease resistance of plants. Bacillus amyloliquefaciens can produce 8 kinds of compounds [35, 37] which have some biological activities. Two compounds, apigenin-8-C-glucoside and 2-(Hydroxymethylthio) ethanol, were isolated from Colletotrichum sp. NTB-2, in which apigenin-8-C-glucoside has strong inhibitory activity against Bacillus subtilis, Salmonella typhimurium and Pseudomonas cepacia [38]. Moreover, Colletotrichum sp. could produce flavones which exhibited potent anti-cancer, anti-HIV [39] and antioxidant activities [40].

In recent years, some new ginkgo endophytes and secondary metabolites have been discovered. Guo et al. [20, 21] discovered a new amide compound from Plantactinospora sp. NEAU-gxj3, Cao et al. [22] found the metabolite sporothriolide from the Nodulisporium of G. biloba, which has anti-phytopathogenic activity.

Application of secondary metabolites from Ginkgo biloba
Following the discovery by Schwabe of Germany that Ginkgo biloba contains active ingredients—ginkgo flavonoids and ginkgolides for the prevention and treatment of cardiovascular, cerebrovascular and neurological diseases, the researches about ginkgo has become more popular. Germany and France were the first countries in the world to develop ginkgo leaf products. In the mid-1970s, they first developed Ginkgo biloba leaves for the treatment of cardiovascular diseases. Since then, there are more than 50 kinds of ginkgo products on the market.

In the application, Ginkgo can be used with the extracts. Some examples, a substance EGb 761 extracted from Ginkgo biloba has shown to be effective against Noise-induced hearing loss (NIHL) in an animal model. This substance is assumed to protect the cochlea from hair cell loss after intensive noise exposure by reducing reactive oxygen species (ROS). Further effects of EGb 761 on the cellular and systemic levels of the nervous system make it a promising candidate not only for protection against NIHL but also for its secondary comorbidities like tinnitus [41]; One Ginkgo biloba extract (GbE) was used as a nontoxic natural reducing and stabilizing agent for preparing cyto compatible graphene. The as-prepared GbE-reduced graphene oxide (Gb-rGO) showed significant biocompatibility with cancer cells. Addition of GbE makes rGO producing procedure cost-effective and green. This method could be used for various biomedical applications, such as tissue engineering, drug delivery, biosensing, and molecular imaging [42].

Some application has been using a part of the plant. Another example, Ginkgo tea is a kind of health food produced from Ginkgo biloba leaves. Two kinds of glycosidase were used to improve the flavor of Ginkgo tea, and three kinds of bioactivities were selected to investigate the health care function of the tea infusion [43].

The Ginkgo preparation mainly includes capsules, tablets, granules, tea bags. Capsules and tablets are most popular in the formulation of the product. Recently, new preparation like shampoo, facial cleanser and hair moisturizer have been introduced in cosmetics applications. Most of the ginkgo products on the market are registered as health foods and a few are registered as over-the-counter drugs.

In many existing products, especially in the medicines, 24% of total flavonoids and 6% of ginkgolides are the basic quality requirements for Ginkgo biloba extracts. Some famous manufacturers proposed higher standards. They appended ginkgolides A, B, C, J and biloba lactone as the quality indicators and generally required the content of ginkgolides A, B, C, J greater than 2.5%, the content of biloba lactone greater than 2.6%.
On the basis of data about the endophytes and secondary metabolites in G. biloba, the catalogue is diverse in terms of structural complexity and lots of them have promising biological activities, which have the potential to be a source of new pharmaceutical agents which have a constant, critical need to combat cancers, viral infections, infectious diseases, and autoimmune disorders. There is also a growing need to fight insect-borne diseases of both animals and plants as climatological changes provide conditions conducive to more intensive outbreaks of these events. The fight against any disease is a dynamic equilibrium between advances in chemotherapy and natural selection in infectious or invasive agents. If the scientific community is to maintain parity in this never-ending struggle, then new sources of novel, bioactive chemotherapeutic agents must be found.

It appears that the mechanism by which endophytes produce secondary metabolites that mimic those produced by their host plants is far from clear. Even though efforts to unravel the pathway genes in the endophytes, it has failed to detect critical genes corresponding to those existing in plants, our understanding of the mechanisms associated with the development of different diseases increases, our ability to use this knowledge to select for ever more potent and selective compounds should increase commensurately. Endophytes of G. biloba will continue to provide a fertile arena for these quests.

Prospects
With human aging process is accelerating, it has been common pursuit for a healthy and high-quality living. Since Ginkgo biloba preparations have a worldwide reputation as natural medicines and healthy products, Ginkgo development and the prospects are attractive. In the United States, Ginkgo biloba extracts have been on the list of imported drugs. Ginkgo products on the market are almost all products of American companies, and few products have been seen in Europe. At present, the European market is basically occupied by French and German products. Most of the Ginkgo extracts on the US market are produced by Japan and South Korea, a small portion is purchased from China.

Although comparing with the developed countries, China market is not competitive and too weak to take the risks, the potential of China’s Ginkgo development is still worth looking forward to. China is the birthplace and main producing area of the world’s Ginkgo. Many excellent Ginkgo germplasm resources are valuable treasures for China. With the sharp increase in Ginkgo resources and products output in China, the market has become more concerned at present (Fig. 7). At present, the Ginkgo products in China have low added-value and quality. In the development of ginkgo industry in China, it is necessary to increase the quality standardization and to improve the scientific research efforts and the production technology of Ginkgo preparations. It deserves to initiate new and technological products on flavonoids, bilobalide, polyisoprene, etc. Especially some new application in other industries should be explored, such as supplying in cytocompatible graphene preparation.

Chinese people have a tradition to have Ginkgo preparation as healthy products. China’s population accounts for about a quarter of the world’s total population. Therefore, the Ginkgo products in China should have more concerns on the domestic market and at the same time expand the international market with high-quality and featured products.

Abbreviations
G. biloba: Ginkgo biloba; CD: electronic circular dichroism; Gb-rGO: gbE-reduced graphene oxide; NIHL: noise-induced hearing loss; ROS: reactive oxygen species.

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Authors’ contributions
ZY and YT drafted the manuscript and prepared tables and figures. FH and HZ contributed to revisions of the manuscript. All authors read and approved the final manuscript.
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