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EDITED BY
Peng Zhang,
Tobacco Research Institute (CAAS), China

REVIEWED BY
Dong-Lin Zhao,
Tobacco Research Institute (CAAS), China
Guo-Bo Xu,
Guizhou Medical University, China

*CORRESPONDENCE
Dong Wang
dwang@cdutcm.edu.cn
Yun Deng
dengyun@cdutcm.edu.cn

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Research advances in the structures and biological activities of secondary metabolites from *Talaromyces*

Li-Rong Lei, Lei-Qiang Gong, Meng-Ying Jin, Rui Wang, Ran Liu, Jing Gao, Meng-Dan Liu, Li Huang, Guang-Zhi Wang, Dong Wang* and Yun Deng*

State Key Laboratory of Characteristic Chinese Medicine Resource of Southwest China, School of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu, China

The genus *Talaromyces* belongs to the phylum Ascomycota of the kingdom Fungi. Studies have shown that *Talaromyces* species yield many kinds of secondary metabolites, including esters, terpenes, steroids, alkaloids, polyketides, and anthraquinones, some of which have biological activities such as anti-inflammatory, bacteriostatic, and antitumor activities. The chemical constituents of fungi belonging to the genus *Talaromyces* that have been studied by researchers over the past several years, as well as their biological activities, are reviewed here to provide a reference for the development of high-value natural products and innovative uses of these resources.

KEYWORDS

***Talaromyces*, secondary metabolite, biological activity, polyketides, terpenoids, nitrogen compounds**

Introduction

As new diseases have emerged in recent years in response to environmental changes, the search for new sources to develop effective and safe drugs cannot be delayed. Natural resources offer the potential to find new structural classes with unique bioactivities for disease treatment. Endophytic fungi represent a rich source of bioactive metabolites (Uzma et al., 2018). The genus *Talaromyces* is widely distributed in soil, plants, sponges, and foods. Recent findings have demonstrated that *Talaromyces* are very abundant in marine environments (Nicoletti and Vinale, 2018). This may be due to the fact that the ocean itself is rich in species resources. Moreover, the extreme living conditions of the oceans have led marine microorganisms to develop more specific metabolic patterns and *Talaromyces* can produce a number of structurally diverse active substances. Their metabolites have a wide range of biological activities, such as anti-inflammatory meroterpenoids, thioester-containing benzoate derivatives that exhibit significant α-glucosidase inhibitory activity and oxaphenalenone dimers with broad antibacterial activity. In this paper, we will summarize and describe the research on the secondary metabolites of *Talaromyces* species

and their biological activities over the past several years, to provide a reference for subsequent research on *Talaromyces*, and to provide an outlook on the problems in the isolation and analysis of fungal secondary metabolites and the prospect of *Talaromyces* species. The current problems in the isolation and analysis of fungal secondary metabolites are summarized and the prospects of their utilization are provided.

Research status of *Talaromyces* species

Talaromyces belongs to the fungal phylum, ascomycete subphylum, ascomycetes, sporangia, and fungal family, which are widely distributed in sponges, plants, and soil. The colonies started out yellow and slowly turned gray-green over the course of a week. The middle of the back is yellow, and the edges are white (Figure 1). *Talaromyces* has various species (Figure 2). *T. marneffei*, *T. funiculosum*, and *T. purpureogenus* are the most studied strains at present. In addition, new strains, such as *T. rubrifaciens*, *T. australis*, *T. kendrickii*, *T. veerkampii*, *T. fuscoviridis*, and *T. stellenboschiensi* were isolated and purified (Visagie et al., 2015; Luo et al., 2016), and the corresponding chemical constituents were studied, which greatly enriched the species of chemical constituents of the fungi. The secondary metabolites of *Talaromyces* are rich in species, have novel structures and have good biological activity, which provides a basis for the development and application of endophytes. At present, the compounds isolated from the secondary metabolites of *Talaromyces* include esters, terpenoids and steroids, alkaloids, polyketones, anthraquinones and others, and most of them have good biological activities such as anti-inflammatory, antibacterial and antitumor activities.

Related studies have shown that *Talaromyces* species have great potential in agriculture, food, cosmetics, medicine, and environmental protection. In the field of agriculture, *Talaromyces* species can inhibit pathological changes in crops and promote crop growth. *T. tratensis* can be used as a biological control agent to control brown spot and dirty panicle diseases in rice (Dethoup et al., 2018). The secondary metabolites in *T. tratensis*, such as glucanase, can effectively treat rot disease that affects the yield of cucumbers and tomatoes (Halo et al., 2019). *T. flavus* not only promotes the growth of cotton and potatoes (Naraghi et al., 2012) but also produces an enzyme that plays an important role in resisting plant diseases for their strong capacity of degrading chitin (Xian et al., 2011). Most *Talaromyces* species can produce a red pigment (Frisvad et al., 2013; Venkatachalam et al., 2018), which can be used as a natural colorant in cosmetics and foods. The thermostable enzyme produced in *T. emersonii* can effectively improve bread quality with respect to hardness, staling, and loaf

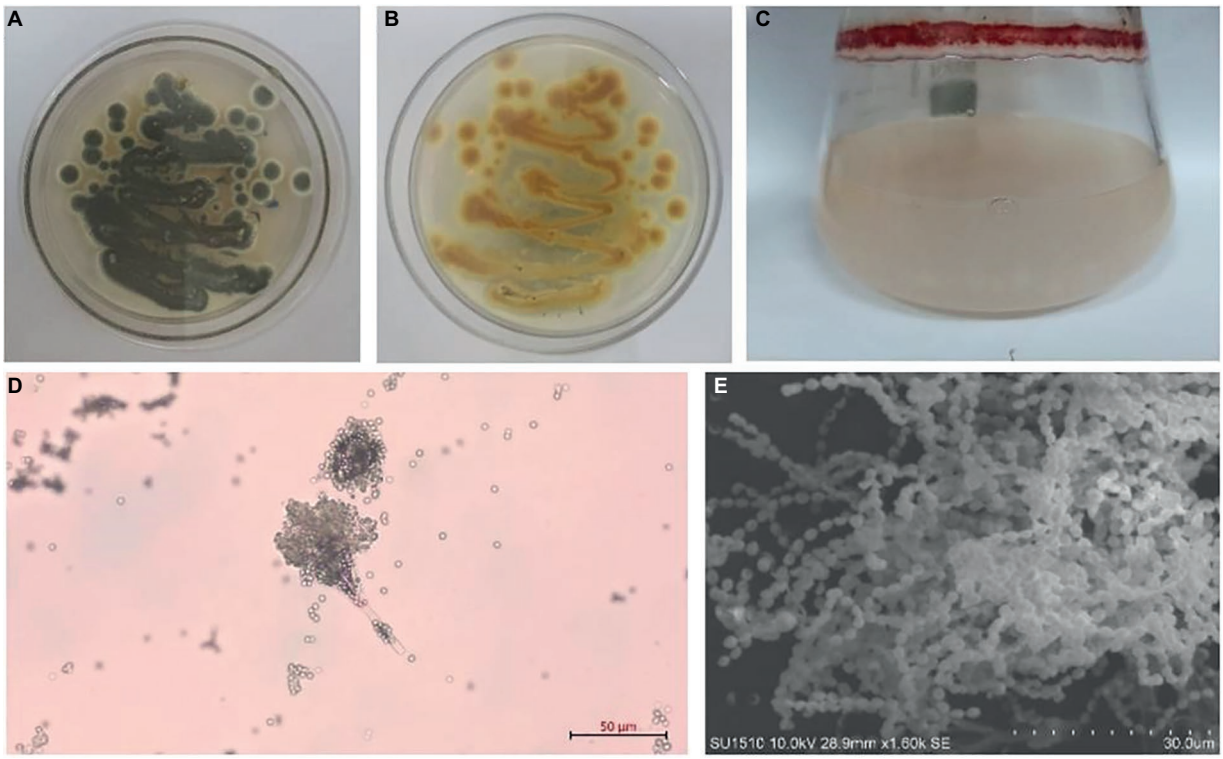

FIGURE 1
Talaromyces amestolkiae (CBS 365.48) *in vitro*. **(A,B)** Growth of *T. amestolkiae* on M1 semisolid medium at 30°C after 7 d and **(C)** in liquid M1 medium at 30°C after 7 d; **(D)** conidia, scale bar=10 µm; **(E)** *T. amestolkiae*, SEM.

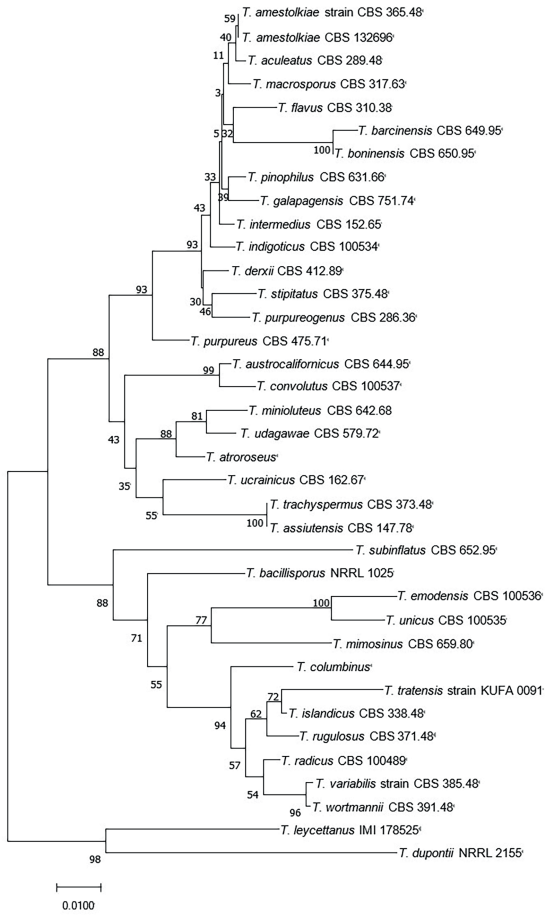

FIGURE 2
Neighbor-joining tree of *T. amestolkiae* (CBS 365.48) based on ITS rDNA.

volume (Waters et al., 2010). An aspartic protease from *T. leycettanus* has strong proteolytic activity and improves the clarity of fruit juice (Guo et al., 2019). *Talaromyces* species can produce many other bioactive secondary metabolites, and these compounds have been found to have antibacterial, anti-inflammatory, antitumor, antioxidant, nematocidal, and other effects in medical research. Secondary metabolites from an Australian Marine Tunicate-Associated Fungus *Talaromyces* sp. (CMB-TU011) exhibit certain antibacterial activities (Dewapriya et al., 2018). GH3 β-glucosidases from *T. amestolkiae* expressed in *Pichia pastoris* can transglycosylate phenolic molecules, and the resulting transglycosylation products can improve the biological activity of the original aglycones against breast cancer cells (Méndez-Líter et al., 2019). Talaraculones from a strain of *T. aculeatus* can inhibit the activity of α-glucosidase and can be used to prevent the progression of type II diabetes, as well as for the early treatment of type II diabetes (Ren et al., 2017). In the field of environmental protection, biosorption by microorganisms has been proven to be an effective technique for removing heavy metals from wastewater. A biological adsorbent formed by combining *T. amestolkiae* with a specific chitosan sponge can effectively remove trace heavy metals or high concentrations of lead from industrial wastewater (Wang et al., 2019). *Talaromyces* sp. KM-31 can remove arsenic from heavily polluted wastewater and can thus be employed in bioremediation strategies (Nam et al., 2019).

According to the classification of the chemical components, this paper will summarize and explain research carried out on secondary metabolites from *Talaromyces* species and their biological activities over the past 10 years with the aim of providing references for follow-up studies of *Talaromyces*, at the same time, the problems existing in the separation and analysis of fungal secondary metabolites and the prospect of *Talaromyces* species, as well as summarizing existing problems in the separation and analysis of fungal secondary metabolites and prospects for the use of secondary metabolites from *Talaromyces* species.

Studies on the chemical constituents and activity of *Talaromyces*

Ester-based compounds

Esters

Esters are chemical compounds derived by reacting an oxoacid with a hydroxyl compound such as an alcohol or phenol (Sparkman et al., 2011). Dinapinones AB1 and AB2 (**1** and **2**), dinapinones AC1 and AC2 (**3** and **4**), dinapinones AD1 and AD2 (**5** and **6**), and dinapinones AE1 and AE2 (**7** and **8**; Figure 3), which were isolated from the fermentation broth of *T. pinophilus* FKI-3864 in 2013 (Kawaguchi et al., 2013), were identified and characterized as ester derivatives. These dinaphthoquinones have the same backbone of aryl dihydronaphthoquinone and consist of one monapinone A and one different monapinone in a heterodimer. Compound **2** had a strong inhibitory effect on triacylglycerol synthesis in intact mammalian cells, with an IC_{50} value of 1.17 μM.

Seventeen new polyesters were isolated from the fermentation products of the wetland soil-derived fungus *T. flavus*, namely, talapolyesters A–F (**9**–**12**, **22** and **24**), 15G256ν (**13**), 15G256ν-me (**14**), 15G256π (**15**), 15G256β-2 (**16**), 15G256α-2 (**17**), 15G256α-2-me (**18**), 15G256ι (**19**), 15G256β (**20**), 15G256α (**21**), 15G256α-1 (**23**) (Figure 4), and 15G256ω (**25**) (He et al., 2014b). All macrocyclic polyesters (**19**–**25**) were cytotoxic to HL-60, SMMC-7721, A-549, MCF-7, and SW480 tumor cells, while linear polyesters (**9**–**18**) were inactive with IC_{50} > 40 mM compared to cisplatin. This suggests that a macrocyclic structure is required for cytotoxicity. Among them, **20** and **25** showed significant cytotoxic activity against MCF-7 cell lines with IC_{50} of 3.27 and 4.32 μM, respectively. The cytotoxic activity of 15G256 polyester was systematically investigated for the first time and a tight conformational relationship is presented.

Talaromycolides A–C (**26**–**28**), rubralide C (**29**), sclerotinin A (**30**), alternariol (**31**), and penicillide (**32**) were obtained from the

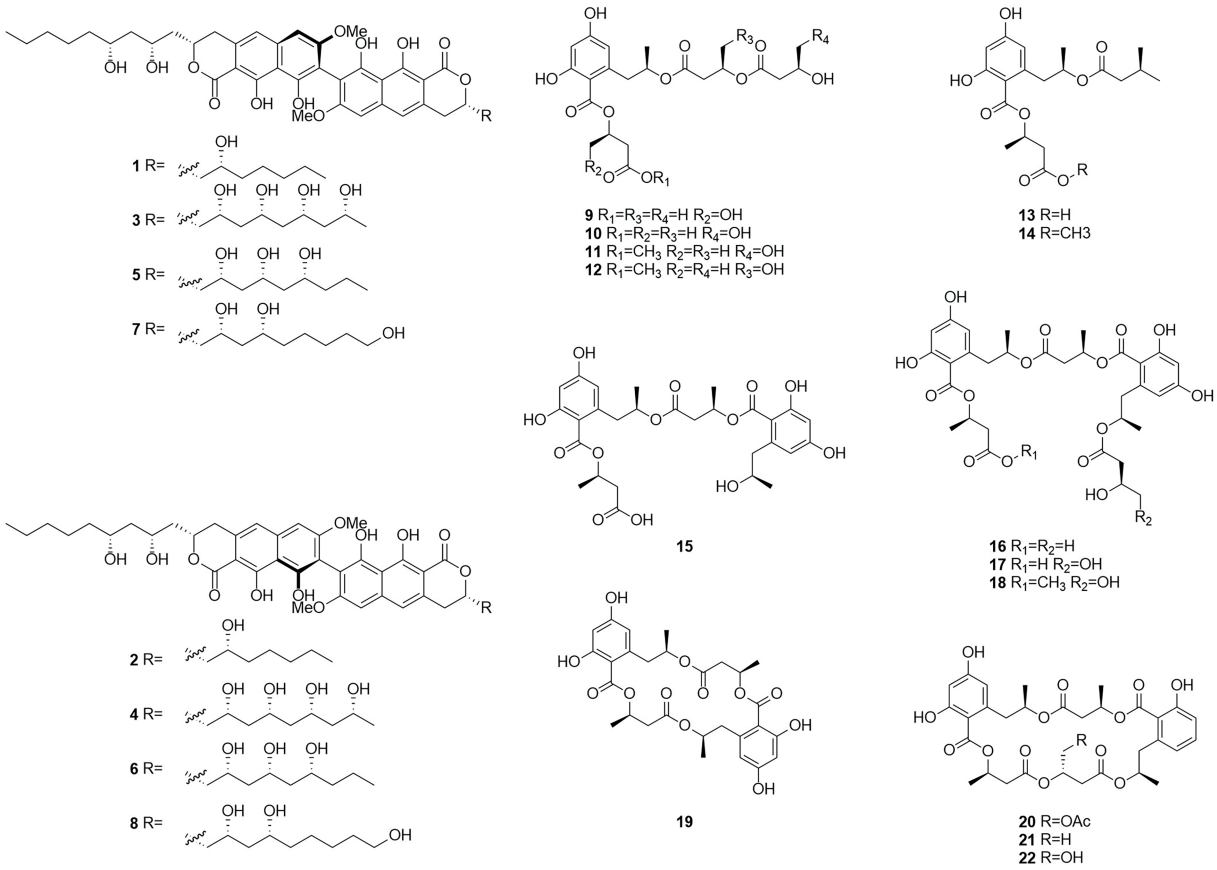

FIGURE 3
Chemical structures of compounds **1–22**.

epiphytic fungal strain *T. pinophilus* AF-02, which was isolated from green Chinese onion, in 2015 (Zhai et al., 2015). Compound **26** [minimum inhibitory concentration (MIC) = 12.5 μg/ml] showed stronger inhibitory activity against *Clostridium perfringens* than erythromycin, streptomycin, acheomycin, and ampicillin. Compound **26** (MIC = 6.25 μg/ml) showed similar inhibitory activity to acheomycin and was superior to levofloxacin, ampicillin, and streptomycin against *Bacillus subtilis*. Compound **27** (MIC = 12.5 μg/ml) showed higher inhibitory activity than erythromycin and ampicillin against *Bacillus megaterium* and higher inhibitory activity than erythromycin, ampicillin, and streptomycin against *Escherichia coli* (MIC = 25 μg/ml). Compound **28** (MIC = 25 μg/ml) was more active against *C. perfringens* than erythromycin, streptomycin, acheomycin and ampicillin.

In 2015, the structures of compounds **33** and **34** were characterized as deacetylisowortmins A and B, which were isolated from *T. wortmannii* LGT-4 derived from the leaves of a mangrove plant *Acanthus ilicifolius* (Fu et al., 2016). Four esters, talaromyones A and B (**35** and **36**), penicillide (**32**), and purpactin A (**37**), were obtained from a fermentation product of the mangrove endophytic fungus *T. stipitatus* SK-4 in 2016 (Cai et al., 2017). Compound **36** exhibited antibacterial activity against *B. subtilis* with an MIC value of 12.5 μg/ml. In the α-glucosidase inhibition assay, compounds **36** and **37** showed some inhibitory activity with an IC_{50} values of 48.4–99.8 μM.

Five butenolides (**38**–**42**), seven (3S)-resorcylide derivatives (**43**–**49**) (Figure 5), two butenolide-resorcylide dimers (**50** and **51**) were yielded by culture on a solid rice medium of *T. rugulosus* isolated from the Mediterranean sponge *Axinella cannabina* (Küppers et al., 2017). The butenolide–resorcylide dimers talarodilactones A and B (**50** and **51**) was highly cytotoxic to the L5178Y mouse lymphoma cell line with IC_{50} of 3.9 μM and 1.3 μM, respectively.

Talaromycin A (**52**) and clearanol A (**53**) were isolated from the endophytic fungus *Talaromyces* sp. MH551540 associated with *Xanthoparmelia angustiphylla* in 2018 (Yuan et al., 2018). Compound **52** and **53** had selective cytotoxicity against MDA-MB-231 cells. Compound **54**, which was identified as wortmannine F, was obtained from cultures of the endophytic fungus *T. wortmannii* LGT-4 isolated from *Tripterygium wilfordii* and has a strong phosphoinositide-3-kinase-α (PI3K-α) inhibitory activity with an IC_{50} value of 25 μM (Zhao et al., 2019b). Pentalsamonin (**55**) was isolated from submerged fermentation on Bengal gram husk (BegH) of *T. purpureogenus* CFRM-02 (Pandit et al., 2018). The MIC and MBC of pentalsamonin (**55**)

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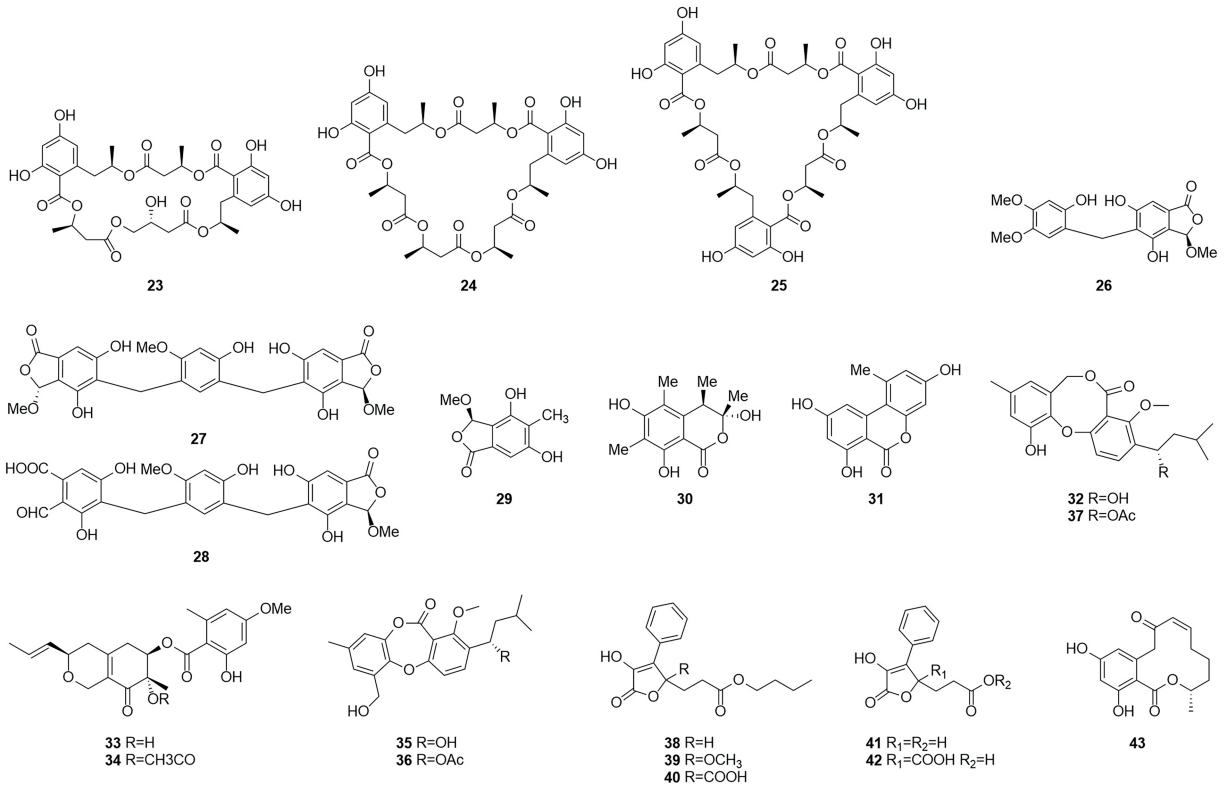

FIGURE 4
Chemical structures of compounds **23–43**.

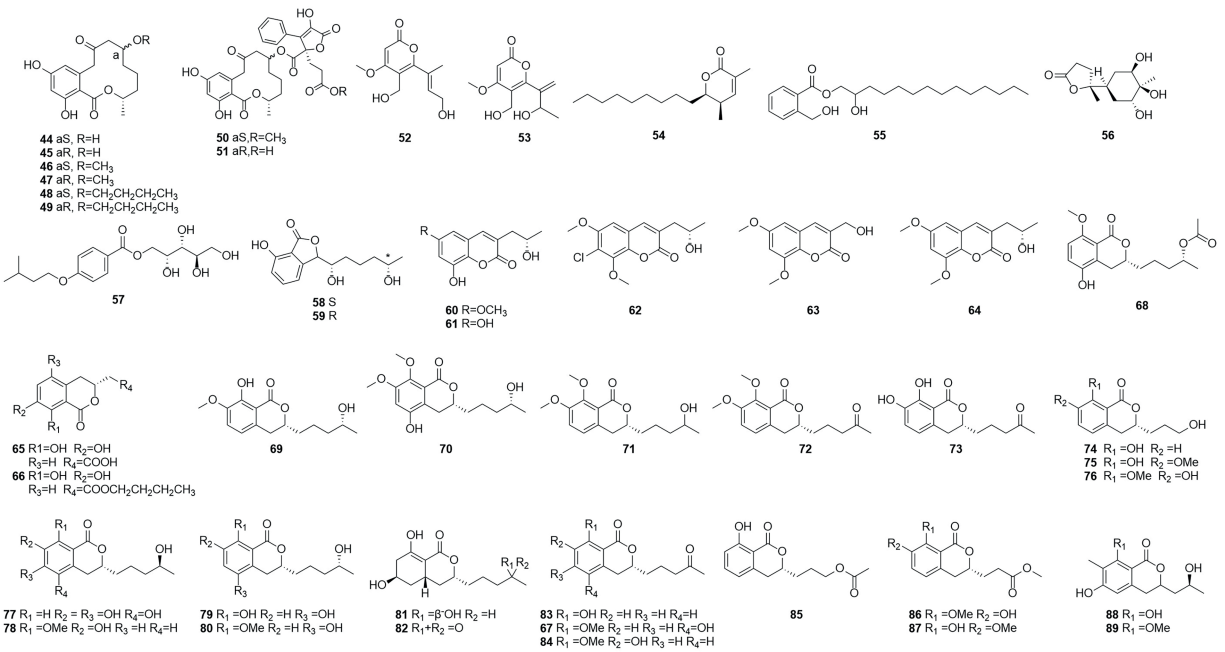

FIGURE 5
Chemical structures of compounds **44–89**.

against *B. subtilis*, *Staphylococcus aureus*, *E. coli*, and *Klebsiella pneumoniae* were 62.5–125 and 125–250 μg/ml, respectively.

Talaromarnine A (**56**) and talaromarnine B (**57**) were obtained from cultures of *T. marneffei*, an endophytic fungus of *Epilobium angustifolium* (Yang et al., 2021). Two previously undescribed phthalides, amestolkins A (**58**) and B (**59**) were isolated from *T. amestolkiae* derived from *Syngnathus acus* Linnaeus in Lingshui Li Autonomous County, Hainan Province, China, which has the same planar structure of (1,5-dihydroxyhexyl)-7-hydroxyisobenzofuran-1(3H)-one. They were shown to inhibit gene expressions of proinflammatory factors including C-C motif chemokine ligand 2 (CCL-2), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) as well as reducing the secretion of inducible nitric oxide synthase (iNOS) in BV2 microglia at the concentration of 30 μM (Huang et al., 2022).

Coumarins

Coumarinic compounds are lactones resulting from the fusion of a benzene ring and a α-pyrone ring (Batista et al., 2021). Talacoumarins A and B (**60** and **61**), which were characterized as coumarins, were isolated from the fermentation broth of the wetland soil fungus *T. flavus* (He et al., 2014c). Activity tests showed that compounds **60** and **61** exhibited moderate activity against the aggregation of Aβ42. This was the first report to state that a coumarin can inhibit Aβ42 aggregation. A new compound **62**, chloropestalasin A was isolated from *T. amestolkiae* derived from submerged wood collected from fresh water, along with 3-hydroxymethyl-6,8-dimethoxycoumarin (**63**) and pestalasin A (**64**) (El-Elimat et al., 2021).

Isocoumarin

Isocoumarin is the common name for 1H-2-benzopyran-1-one skeleton (Braca et al., 2012). Three dihydroisocoumarins (**65**–**67**) were yielded by culture on a solid rice medium of *T. rugulosus* isolated from the Mediterranean sponge *Axinella cannabina* (Küppers et al., 2017). Six new isocoumarin derivatives, talaromarins A-F (**68**–**73**), and 17 known analogues (**67**, **74**–**89**), were isolated from the mangrove-derived fungus *T. flavus* (Eurotiales: Trichocomaceae) TGGP35 (Cai et al., 2022). Compounds **67**, **73**–**78**, **84**–**85** and **87**–**89** showed similar or better IC_{50} values for antioxidant activity ranged from 0.009 mM to 0.27 mM, compared to the positive control trolox (IC_{50} = 0.29 mM). Compounds **77**, **84**, **87** and **89** showed strong inhibitory activity. IC_{50} values of 0.10 ~ 0.62 mM against α-glucosidase and 0.5 mM for the positive control acarbose activity at 50 μg/ml and 1 mg/ml concentrations. These results suggest that isocoumarins have important applications in the development of antioxidants and in the control of diabetes mellitus. Talaroisocoumarin A (**73**) was obtained from marine-derived *Talaromyces* sp. ZZ1616 in potato dextrose broth medium. The MIC values of talaroisocoumarin A against methicillin-resistant *S. aureus*, *E. coli* and *Candida albicans* were 36.0 μg/ml, 32.0 μg/ml and 26.0 μg/ml, respectively (Ma et al., 2022).

Polyketones

Polyketides were named in the 1890s to refer to a structurally diverse group of natural products that contained many carbonyls and alcohols, generally separated by methylene carbons. They are synthesized by a series of decarboxylative condensation reactions between small carboxylic acids and malonate using polyketide synthases (PKSs; Richardson and Khosla, 1999). Two polyketones, mitorubrin (**90**) and monascorubrin (**91**) (Figure 6), were isolated from *T. atroroseus* (Frisvad et al., 2013). Because no citrinin was found in any *Talaromyces* species, it may be a good alternative for red pigment production. Compound **92**, which was characterized as a polyketone and named talaroxanthone, was obtained from the fermentation products of an endophytic strain of a *Talaromyces* sp. isolated from the Amazonian rainforest plant *Duguetia stelechantha* root (Koolen et al., 2013). Five compounds, 9a-epi-bacillisporin E (**93**), 1-epi-bacillisporin *F* (**94**), and bacillisporins F-H (**95**–**97**) were isolated from the fermentation products of the soil fungus *T. stipitatus* (Zang et al., 2016). Compound **97** exhibited some antibacterial activity and some cytotoxicity against HeLa cells. Compounds **98**–**100**, wortmannilactones I1-I3, which were identified and characterized as three new polyketides, were purified from *T. wortmannii* using the one strain–many compounds strategy. These compounds showed selective inhibitory activity against NADH fumarate reductase (Liu et al., 2016).

The polyketone 3-O-methylfunicone (**101**) was isolated from the culture filtrate of an endophytic strain of *T. pinophilus* obtained from the strawberry tree (*Arbutus unedo*) in 2017 (Vinale et al., 2017). On water agar at a concentration of 0.1 mg/ml, it completely inhibited the growth of phytopathogenic fungi such as *Rhizoctonia solani* (De Stefano et al., 1999). Eleven polyketones, talaraculones A–F (**102**–**107**), pinazaphilone B (**108**), pinophilin B (**109**), Sch 725680 (**110**), (−)-mitorubrin (**111**), and (−)-mitorubrinol (**112**), were obtained from the fungus *T. aculeatus*, which was isolated from saline-alkali soil (Ren et al., 2017). The results of the activity tests showed that compounds **102** and **103** exhibited very high levels of inhibitory activity against α-glucosidase than the positive control acarbose (IC_{50} = 101.5 μM), with IC_{50} values of 78.6 and 22.9 μM, respectively. Compounds that were defined and characterized as six polyketones, paecillin D (**113**), secalonic acid A (**114**), blennolide G (**115**), versixanthone A (**116**) (Figure 7), penicillixanthone A (**117**), and paecillin B (**118**), were isolated from the fermentation products of three Amazonian plants endophytic strains of *T. stipitatus* in 2018 (da Silva et al., 2017). Activity tests showed that compounds **113** and **116** were active against yeasts (MICs of 15.6 μg/ml and 31.3 μg/ml, respectively).

Six new nonadride derivatives, named talarodrides A–F (**119**–**124**), were isolated from the antarctic sponge-derived fungus *Talaromyces* sp. HDN1820200. Talarodride A (**119**) and talarodride B (**120**) showed selective inhibitory effects against *Proteus mirabilis* and *Vibrio parahemolyticus* with MICs of 3.13–12.5 μM (Zhao et al., 2021b).

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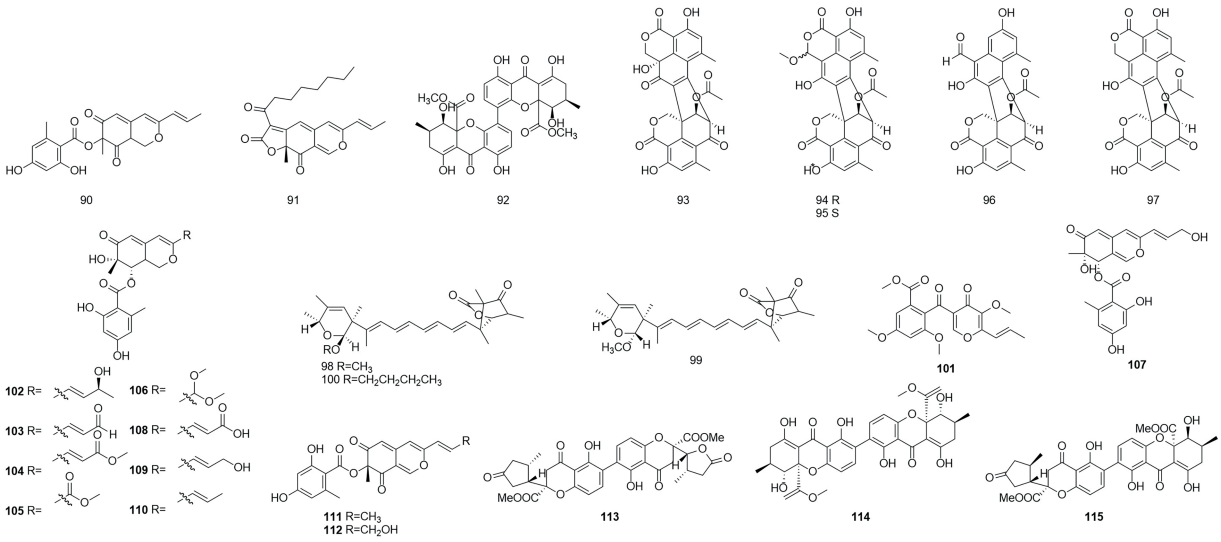

FIGURE 6
Chemical structures of compounds **90–115**.

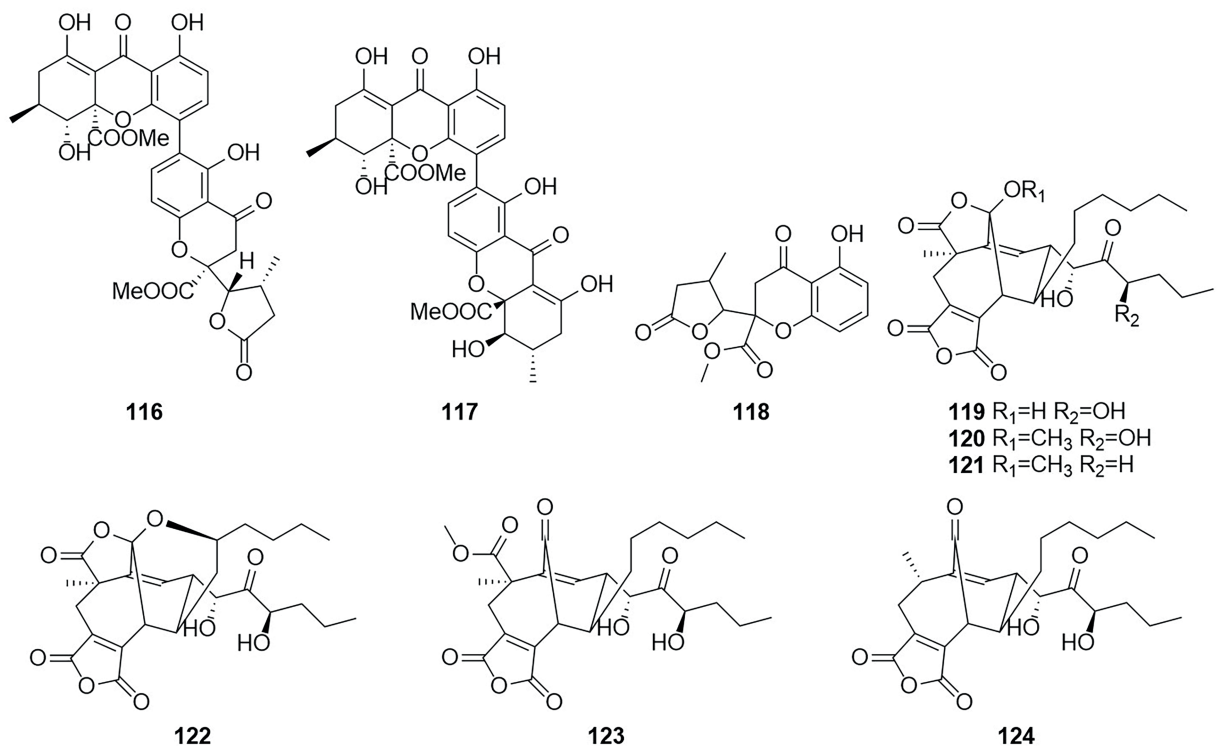

FIGURE 7
Chemical structures of compounds **116–124**.

Anthraquinone

Anthraquinones (AQs) are derived from anthracenes and have two keto groups, mostly in positions 9 and 10. The basal compound, anthraquinone (9,10-dioxoanthracene), can be substituted in various ways, resulting in a great diversity of structures (Vasil et al., 1984). Two anthraquinone compounds skyrin (**125**) and emodin (**126**) (Figure 8) were obtained from an extract of the mangrove

endophytic fungus *Talaromyces* sp. ZH-154, which was isolated from the stem bark of *Kandelia candel* (Liu et al., 2010). Both compounds exhibited moderate cytotoxic activity against KB and KBv200 cells. The anthraquinone monomer (**126**) showed higher bioactivity than the dimer dianthraquinone (**125**). A new anthraquinones biemodin (**127**) and five known anthraquinones emodic acid (**128**), skyrin (**125**), oxyskyrin (**129**), and rugulosins A and B (**130** and **131**) were isolated from cultures of the endophytic fungus *T. wortmannii* obtained from healthy inner tissues of *Aloe vera* (Bara et al., 2013a). In the same year, two anthraquinone compounds, talaromannins A and B (**132** and **133**), were obtained from *T. wortmannii* in *A. vera* (Bara et al., 2013b). Both compounds displayed moderate MICs in a comparable concentration range for *S. aureus* and **132** represented the most active congeners.

Five anthraquinones were isolated from the solid fermentation products of the endophytic fungus *Talaromyces* sp. YE3016 (Xie et al., 2016). These compounds were 3-demethyl-3-(2-hydroxypropyl)-skyrin (**134**), skyrin (**125**), oxyskyrin (**129**), emodin (**126**), and 1,3,6-trihydroxy-8-methylanthraquinone (**135**). Activity tests showed that compounds **134**, **125**, and **129** displayed moderate cytotoxic activity against the MCF-7 cell line. Six anthraquinone compounds, 2,2′-bis-(7-methyl-1,4,5-trihydroxy-anthracene-9,10-dione) (**136**), emodin (**126**), questinol (**137**), citreorosein (**138**), fallacinol (**139**), and rheoemodin (**140**), were obtained from an ethyl acetate extract of a culture of the fungus *T. stipitatus* KUFA 0207, which is derived with a marine sponge (Noinart et al., 2017). Emodin (**126**), questinol (**137**), citreorosein (**138**), fallacinol (**139**), and rheoemodin (**140**) were tested for their anti-obesity activity using the zebrafish Nile red assay. The results showed that only the anthraquinones questinol (**137**) and citreorosein (**138**) had significant anti-obesity activity. Questinol (**137**) and citreorosein (**138**) reduced >60% and > 90% of the stained lipids with the IC_{50} values of 0.95 and 0.17 μM, respectively. The positive control resveratrol (REV) had an IC_{50} value of 0.6 μM. Emodin (**140**) caused toxicity (death) for all exposed zebrafish larvae after 24 h, while fallacinol (**139**) and rheoemodin (**140**) did not have any significant effects. It is interesting to observe that questinol (**137**), citreorosein (**138**) and fallacinol (**139**) are structurally similar, all having a hydroxymethyl group on C-6 and a hydroxyl group on C-8. Replacing the hydroxyl group on C-1 by a methoxyl group, as in questinol (**137**), diminishes the activity whereas replacing the hydroxyl group on C-3 with a methoxyl group, as in fallacinol (**139**), completely removes the anti-obesity activity. Therefore, it seems that the hydroxymethyl group on C-6 and the hydroxyl groups on C-3 and C-8 are necessary for the anti-obesity activity of the polyhydroxy anthraquinones.

Terpenoids

Terpenoids otherwise known as isoprenoids are a large and diverse class of naturally occurring compounds derived from five carbon isoprene units (Reyes et al., 2018). Terpenoids are classified as hemiterpenes (C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), sesterterpenes (C25), triterpenes (C30), and tetraterpenes/carotenoids (C40) (Adefegha et al., 2022).

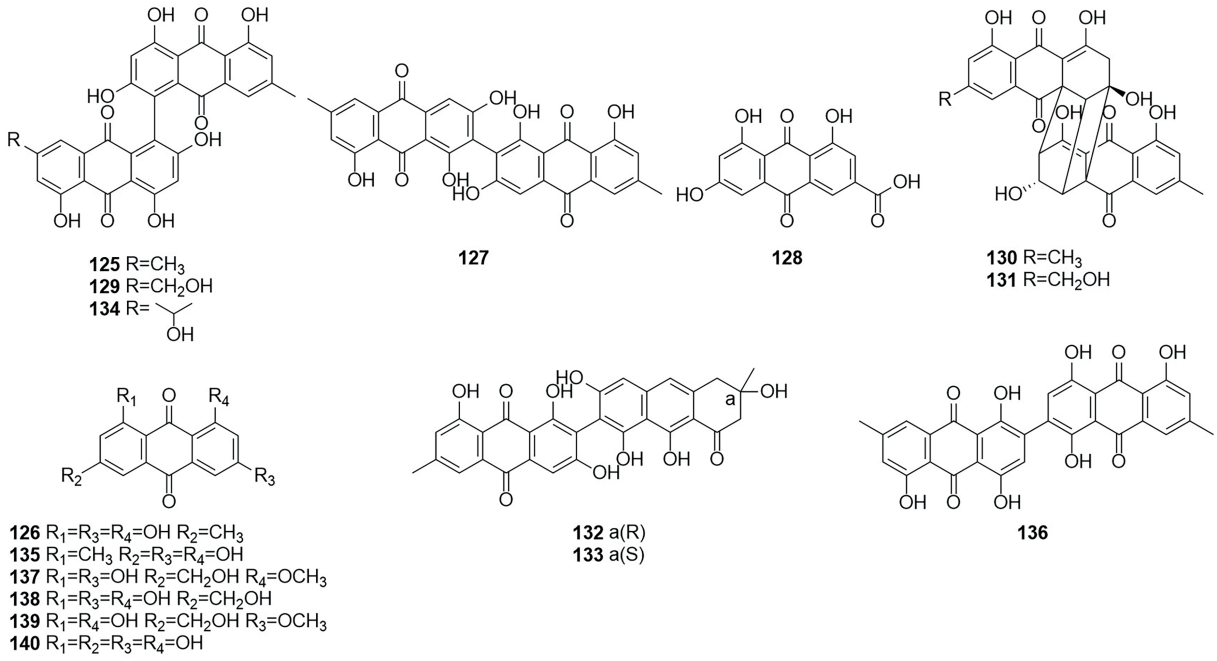

FIGURE 8
Chemical structures of compounds **125–140**.

Compound **141** (Figure 9), which was characterized as a new fusicoccane diterpene and named pinophicin A, was obtained from the endophytic fungus *T. pinophilus* collected from the aerial parts of *Salvia miltiorrhiza* in 2019 (Zhao et al., 2021a). Four new sesquiterpene peroxides, talaperoxides A–D (**142**–**145**), were isolated from the fermentation products of the mangrove endophytic fungus *T. flavus* (Li et al., 2011). Of these compounds, compounds **143** and **145** showed cytotoxicity against human cancer cell lines MCF-7 and MDA-MB-435, HepG2, HeLa and PC-3 with IC_{50} values between 0.70 and 2.78 μg/ml. Compound **146**, which was characterized as a new nardosinane-type sesquiterpene and named talaflavuterpenoid A, was isolated from the fermentation products of *T. flavus* (He et al., 2014a).

The new diterpenoid roussoellol C (**147**) was isolated from the fermentation products of *T. purpureogenus* (Wang et al., 2018). Compound **147** had an inhibitory effect on the MCF-7 cancer cell line, with an IC_{50} value of 6.5 μM. A new spiroaxane sesquiterpenoid talaminoid A (**148**) and two drimane sesquiterpenoid talaminoids B and C (**149** and **150**), together with four known compounds (**151**–**154**) were obtained from the fermentation broth of *T. minioluteus* (Nie et al., 2019). Compounds **148**, **151**, and **152** showed significant suppressive effect on the production of NO on LPS-induced BV-2 cells, with IC_{50} values ranging from 4.97 to 7.81 μM. In addition, **148**, **151**, and **152** exhibited significant anti-inflammatory activities against the production of TNF-α and IL-6. Further immunofluorescence experiments revealed the mechanism of action to be inhibitory the NF-kB-activated pathway. The structure of compound **155** was defined and characterized as sordarin, which was isolated from the Australian fungus *Talaromyces* sp. CMB-TU011, which is associated with a marine tunicate (Dewapriya et al., 2017). According to a related study, this compound exhibited antifungal activity (Domínguez et al., 1998). Four new sesquiterpene lactones (**156**–**159**) and three known compounds, purpuride (**151**), berkedrimane B (**152**) and purpuride B (**160**), were isolated from cultures of the marine fungus *T. minioluteus* (Ngokpol et al., 2015). Compounds **152, 156, 159** exhibited weak cytotoxic activity against the HepG2 cancer cell line.

Meroterpenoids

Meroterpenoids are natural products that are partially derived from terpenoid biosynthetic pathways, since the prefix "mero-" has the meanings of "part," "partial," and "fragment" (Matsuda and Abe, 2020). Four meroterpenoids talaromyolides A–D (**161**–**164**) and Talaromytin (**165**) (Figure 10) were isolated from the marine fungus *Talaromyces* sp. CX11 (Nie et al., 2019). Compound **164** exhibited potent antiviral activity against pseudorabies virus (PRV) with a IC_{50} value of 3.35 μM. Activity tests showed that this compound did not exhibit *in vitro* growth-inhibiting activity against MCF-7 breast adenocarcinoma, NCI-H460 non-small-cell lung cancer, or A375-C5 melanoma cell lines by a method based on the protein-binding dye sulforhodamine B.

A new meroterpenoid, taladrimanin A (**166**), was isolated from the marine-derived fungus *Talaromyces* sp. HM6-1-1. Compound **166** exhibited antitumor activity against MGC803 and MKN28 gastric cancer cells; it also inhibited colony formation and induced apoptosis in MGC803 cells both in a concentration-dependent manner. Additionally, **166** displayed selective antibacterial activity against *S. aureus* 6538P, and low activities toward strains of *V. parahaemolyticus* and *E. coli* (Hong et al., 2022). The structures of compounds **167**–**173**, which were obtained from the fermentation products of the soil fungus *Talaromyces* sp. YO-2 in Osaka, Japan, were defined and characterized as the seven meroterpenoids chrodrimanin A–H (Hayashi et al., 2012a,b). Chrodrimanin B (**168**) exhibited insecticidal activity with an LD_{50} value of 10 ug/g of diet. Chrodrimanins D–F (**170**–**172**) showed insecticidal activity against silkworms with respective LD_{50} values of 20, 10, and 50 ug/g of diet. Compounds 145–148, which were identified as the four meroterpenoid compounds talarolutin A–D, were isolated from the fermentation broth of a strain of the fungus *T. minioluteus* obtained from healthy surface sterilized leaves of milk thistle (Kaur et al., 2016).

Steroids

Steroids are extremely important medicinally active organic compounds with four rings constructed in a highly specific perhydrocyclopentano[α]phenanthrene orientation. In general, the steroid core structure has 17 carbon atoms connected with 4 fused rings in a specific way. Three of these are cyclohexanes (A, B, and C) and one is cyclopentane system (D ring) (Borah and Banik, 2020). Talasterone A (**174**) (Figure 11), an unprecedented 6/6/5 tricyclic 13 (14 → 8) abeo-8,14-seco-ergostane steroid, was characterized from *T. adpressus* isolated from soil collected from Yalong Bay in Sanya, Hainan (Zhang et al., 2022a). A new compound 3-acetylergosterol-5,8-endoperoxide (**175**) was obtained from the fermentation products of the sponge endophytic fungus *T. trachyspermus* KUFA 0021 (Kuml et al., 2014). In 2017, the new compound talarosterone (**176**) and cyathisterone (**177**) were obtained from the fermentation products of the sponge fungus *T. stipitatus* KUFA 0207 (Noinart et al., 2017). A new withanolide, talasteroid (**178**) was obtained from rice culture of the marine-derived fungus *T. stollii* HBU-115 (Zhang et al., 2022c). Five undescribed sterol derivatives (**179–183**), (22E,24R)-7α-methoxy-5α,6α-epoxyergosta-8(14),22-diene-3β,15β-diol, (22E,24R)-5α,6α-epoxyergosta-8(14),22-diene-3β,7β,15α-triol, (22E,24R)-3β,5α-dihydroxy-14β,15β-epoxyergosta-7,22-diene-6-one, (22E,24R)-6α-methoxy-7α,15β-dihydroxyergosta-4,8(14),22-triene-3-one, and (25S)-ergosta-7,24(28)-diene-3β,4α,6α,26-tetraol were isolated from the extract of *T. stipitatus* (Zhang et al., 2021). The antiproliferative activities of compound **179**–**183** were mainly mediated by inducing cell apoptosis.

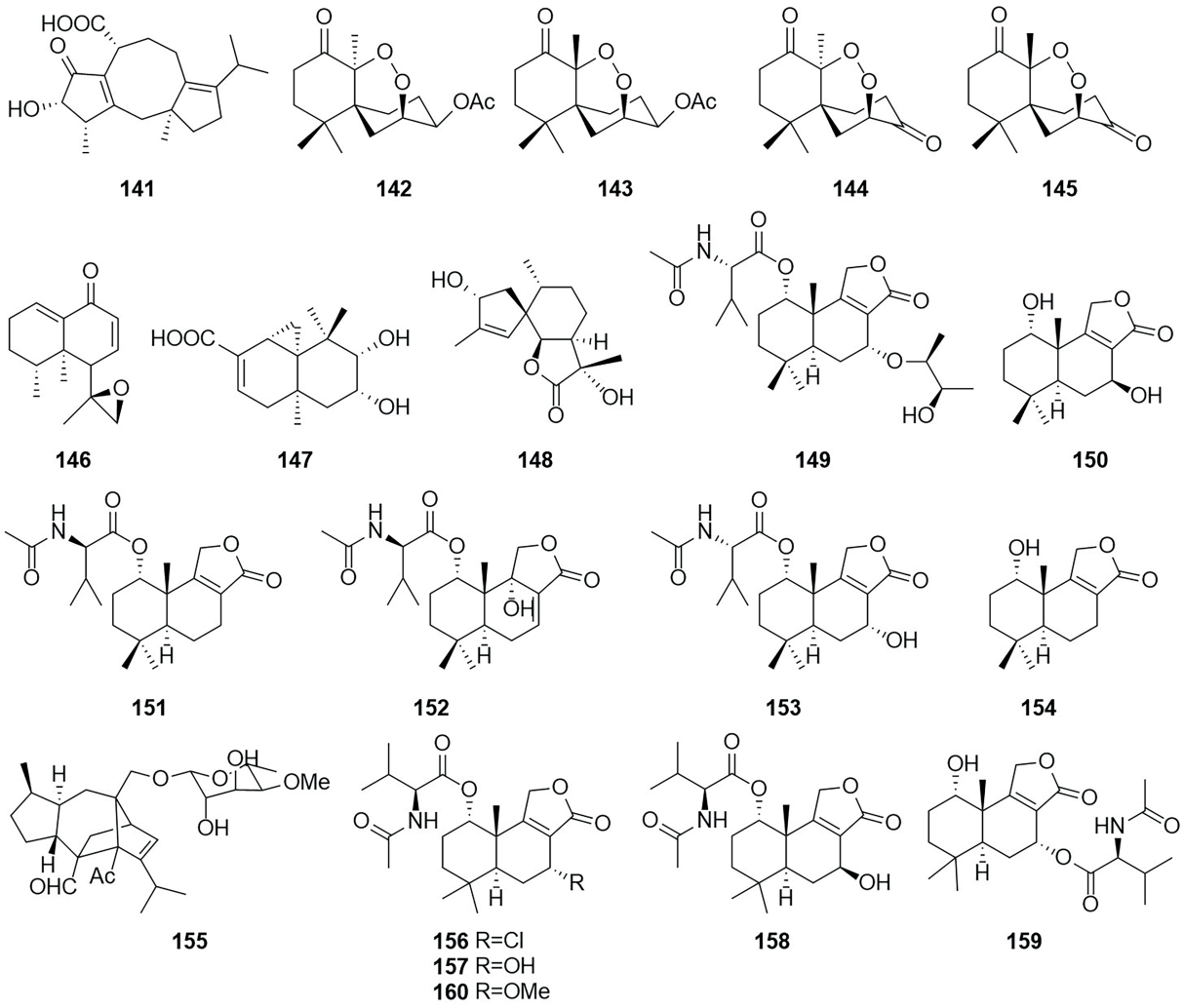

FIGURE 9
Chemical structures of compounds **141–160**.

Nitrogen-containing compound

Alkaloids

Alkaloids are structurally diverse compounds generally classified as such due to the basic character of the molecule (from Latin alkali) and a presence of at least one nitrogen atom, preferably in a heterocycle (Zotchev, 2013). The compound PP-R (**184**) (Figure 12) was isolated from *T. atroroseus* (Frisvad et al., 2013). The red pigments is of interest for the industry as they are stable and non-toxic and can be used as food colorants. Herquline B (**185**) was isolated from the culture filtrate of an endophytic strain of *T. pinophilus* obtained from the strawberry tree (*A. unedo*) (Vinale et al., 2017). In 2011, six indole alkaloids, talathermophilins A–E (**186–188**,**190–191**) and cyclo(glycyltryptophyl) (**189**), were obtained from the thermophilic fungal strain *T. thermophilus* YM3-4 (Guo et al., 2011, 3–4). ZG-1494α (**192**) was isolated from an ethyl acetate extract of a culture broth of *T. atroroseus* (Frisvad et al., 2013). According to a related study, compound **192** can be used as a novel inhibitor of platelet-activating factor acetyl-transferase (West et al., 1996). Nine alkaloids, 2-[(S)-hydroxy(phenyl) methyl]-3-methylquinazolin-4(3H)-one (**193**), 2-[(R)-hydroxy(phenyl)methyl]-3-methylquinazolin-4(3H)-one (**194**), roquefortine C (**195**), Z-roquefortine C (**196**), viridicatol (**197**), penitrem A (**198**), penijanthine A (**199**), paspaline (**200**), and 3-deoxo-4b-deoxypaxilline (**201**), were isolated from the fermentation broth of the algal endophytic fungus *Talaromyces* sp. *cf*-16 in 2014, of which compounds **196–199** could inhibit *S. aureus* (Yang et al., 2016).

Five new compounds, namely talaromanloid A (**202**), 10-hydroxy-8-demethyltalaromydine and 11-hydroxy-8-demethyltalaromydine (**203** and **204**) and ditalaromylectones A and B (**205** and **206**) were identified from the marine-derived fungus *T.* mangshanicus BTBU20211089, which was isolated

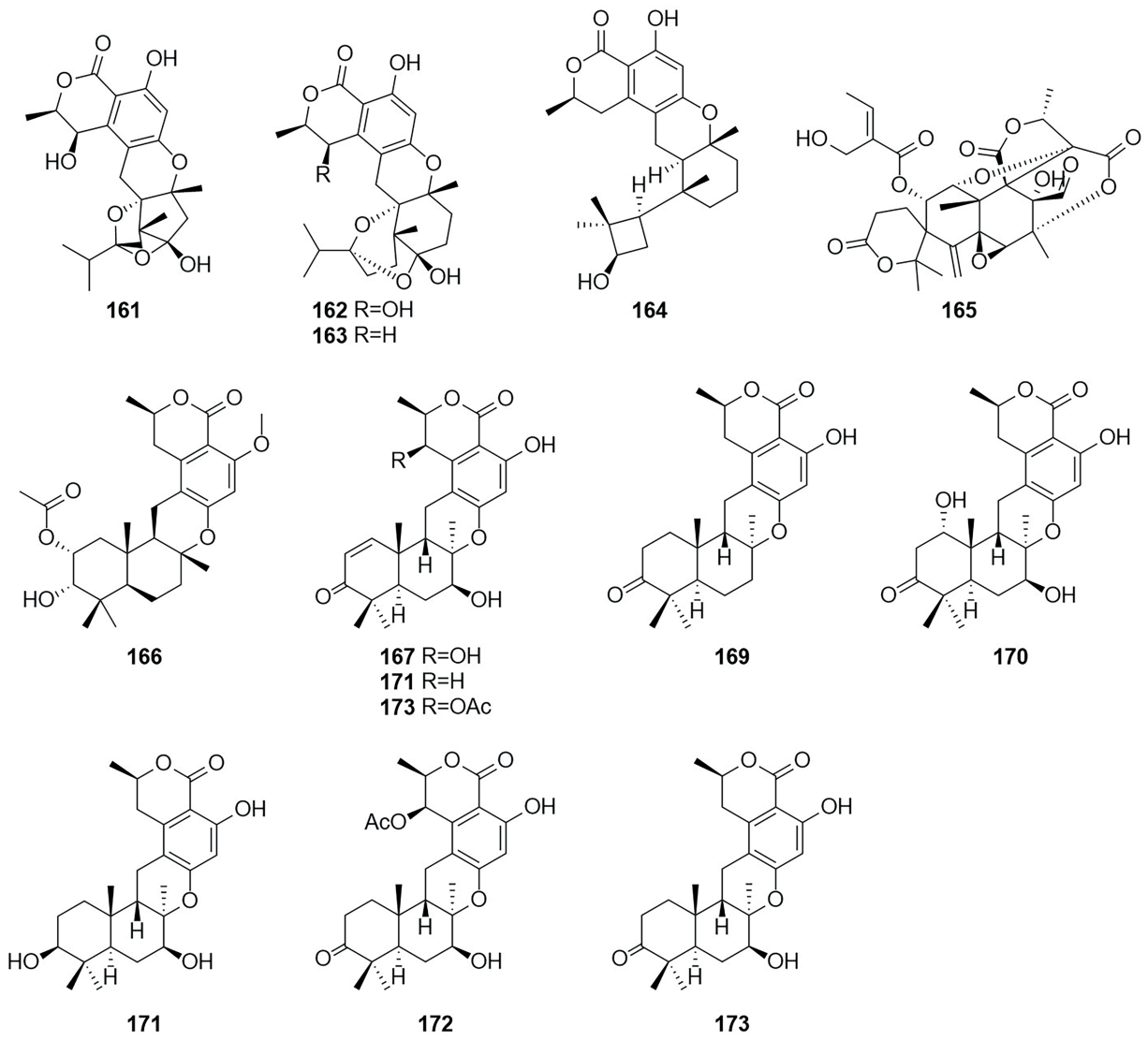

FIGURE 10
Chemical structures of compounds **161–173**.

from a sediment sample collected from the South China Sea. Compound **205** showed an inhibitory effect against *C. albicans* with an MIC value of 200 μg/ml (Zhang et al., 2022b). The endophytic fungus *T. radicus* isolated from Catharanthus roseus was cultured in M2 liquid fermentation medium and PDA fermentation medium. Vincristine (**207**) and vinblastine (**208**) were obtained from this fungus, of which HeLa cells exhibited the highest susceptibility to vincristine. In addition, the apoptosis-inducing activity of vincristine obtained from this fungus was established *via* cell cycle analysis, loss of mitochondrial membrane potential, and DNA fragmentation patterns (Palem et al., 2015). In 2017, the alkaloid talaramide A (**209**) was obtained by culturing of the mangrove endophytic fungus *Talaromyces* sp. HZ-YX1 on a solid rice medium with sea water displayed promising inhibition of the activity of mycobacterial protein kinase G, with an IC_{50} value of 55 μM. A possible biosynthetic pathway was proposed in the paper (Chen et al., 2017).

Amides

Amides are amines with a carbonyl group associated with the ammonia-associated carbon (Jackson, 2008). Six macrolides, thermolides A–F (**210**–**215**) (Figure 13), were isolated from the fermentation products of the thermophilic fungus *T. thermophilus* in 2012 (Guo et al., 2012). Of these compounds, compounds **210** and **211** exhibited strong inhibitory activity against nematodes, with LC_{50} values of 0.5–1.0 μg/ml. Two new compounds, namely talaromydene (**216**) and talaromylectone (**217**) were identified from the marine-derived fungus *T. mangshanicus* BTBU20211089, which was isolated from a

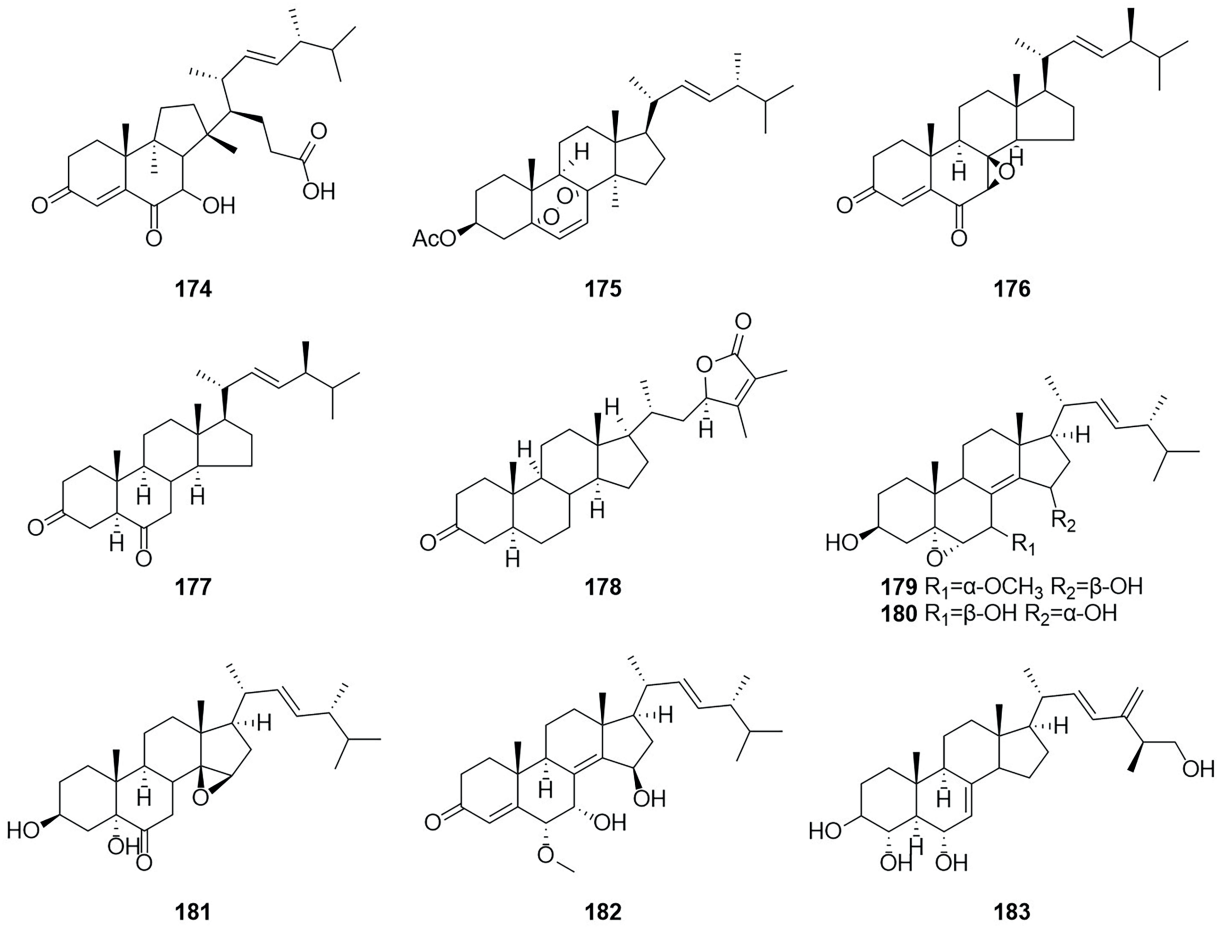

FIGURE 11
Chemical structures of compounds **174–183**.

sediment sample collected from the South China Sea (Zhang et al., 2022b). Cerebroside C (**218**) was obtained from the endophytic fungus *T. purpureogenus* hosted in *Tylophora ovate* (Zhao et al., 2020).

Acid

A compound, namely, (R)-2-[5-methoxycarbonyl-4-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl] acetic acid (61), which was obtained from cultures of the endophytic fungus *T. purpureogenus* hosted in *T. ovate*, showed some inhibitory activity against XOD at a concentration of 10 μM with the inhibition rate of 69.9% (Zhao et al., 2020). A new octadienoic acid derivative, oxoberkedienoic acid (**219**) (Figure 14), was isolated from a culture of *T. verruculosus* FKI-5393. The IC_{50} value against Jurkat cells of **219** was 6.1 μg/ml (Sakai et al., 2018). The IC_{50} value against Jurkat cells of **219** was 6.1 mg/ml. (R)-(−)-Hydroxysydonic acid (**220**) was isolated from the strain *Talaromyces* sp. C21-1 obtained from the coral Porites pukoensis collected in Xuwen, Guangdong Province (Nie et al., 2019). The compound **220** showed moderate inhibitory activities to *C. albicans* and methicillin-resistant *S. aureus* (MRSA) with the MICs at 0.075 mM and 0.2 mM, respectively. Rubratoxin acid A-E (**221**–**225**) were isolated from the endophytic fungus *T. purpureogenus* obtained from fresh leaves of the toxic medicinal plant *T. ovate* (Zhao et al., 2019a). Compound **221** showed significant inhibitory activity against NO production in LPS-induced RAW264.7 cells with an IC_{50} value of 1.9 μM. Compounds **222** showed moderate inhibitory activities toward XOD and PTP1b at 10 μM with inhibition rates of 67%. Compound **226**, which was identified as a new spiculisporic acid derivative, spic ulisporic acid E, was isolated from a culture of the fungus *T. trachyspermus* KUFA 0021, which is associated with a marine sponge (Kuml et al., 2014).

Others

The compounds 2,2',3,5'-tetrahydroxy-3'-methylbenzophenone (**227**) and 2,2',5'-trihydroxy-3-methoxy-3'-methylbenzophenone (**228**) (Figure 15), were obtained from *T. islandicus* EN-501, which is an endophytic fungus obtained from the freshly collected marine

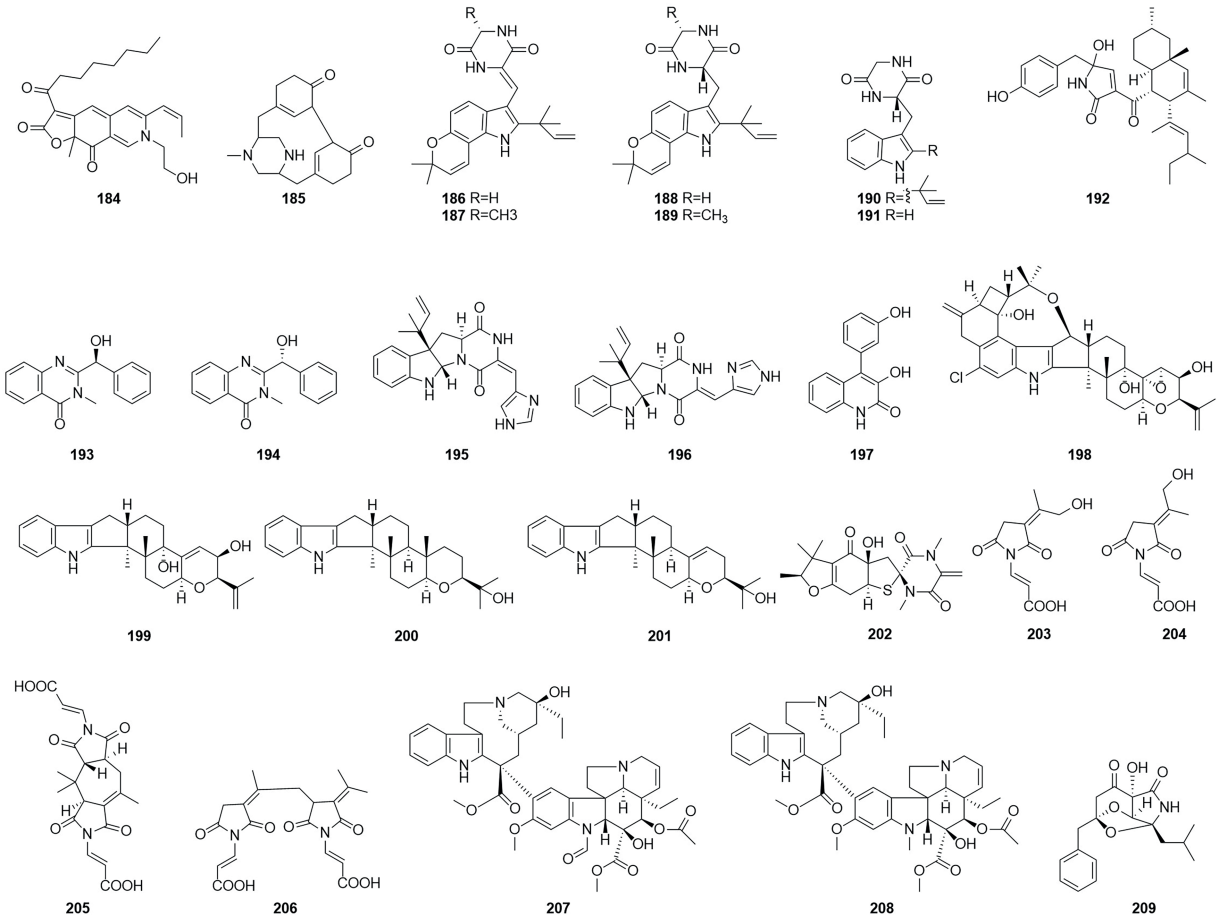

FIGURE 12
Chemical structures of compounds **184–209**.

red alga *Laurencia okamurai* (Li et al., 2016). Compounds **227–228** showed strong antioxidant activity against DPPH and ABTS radicals with IC_{50} values of 0.58 ~ 6.92 μg/ml, which were stronger than the positive controls BHT and ascorbic acid. Compounds **227** displayed potent activities against three human pathogens (*E. coli*, *Pseudomonas aeruginosa*, and *S. aureus*) and three aquatic bacteria (*V. alginolyticus*, *V. harveyi*, and *V. parahaemolyticus*) with MIC values ranging from 4 to 32 μg/ml. compound **228** showed weak activity against the tested bacteria (IC_{50} > 64 μg/ml), suggesting that methoxylation at C-3 weakened the antibacterial activities. A new phenylpentenol, wortmannine H (**229**), was isolated from *T. wortmannii* LGT-4, which is an endophytic fungus obtained from *T. wilfordii* (Li et al., 2021).

Talarodride (**230**) were isolated from the endophytic fungus *T. purpureogenus* obtained from fresh leaves of the toxic medicinal plant *T. ovate* (Zhao et al., 2019a). Compounds **230** showed moderate inhibitory activities toward XOD and PTP1b, respectively at 10 μM with inhibition rates of 76%. Four wortmannin derivative compounds, wortmannin B (**231**), wortmannin (**232**), amino adduct 3a (**233**), and wortmannin-diol (VIII) (**234**), were obtained from cultures of the aloe endophytic fungus *T. wortmannii* in 2013 (Bara et al., 2013a) Three new diphenyl ether derivatives, talaromycins A–C (**235–237**), together with a known analog (**238**), were obtained from a gorgonian-derived *Talaromyces* sp. (Chen et al., 2015). Compounds **237** showed potent antifouling activities against the larval settlement of the barnacle *Balanus amphitrite* with the EC_{50} values ranging from 2.2 to 4.8 mg/ml. Compounds **238** showed strong cytotoxicity against the human hepatoma HepG2 and Hep3B, human breast cancer MCF-7/ADR, human prostatic cancer PC-3, and human colon carcinoma HCT-116 cell lines with the IC_{50} values ranging from 4.3 to 9.8 mM.

Summary

Owing to their wide variety of species and abundance in secondary metabolites, *Talaromyces* fungi have great potential in medicine, food, cosmetics, agriculture, and environmental protection. In this paper, the secondary metabolites produced by *Talaromyces* species that have been studied over the past

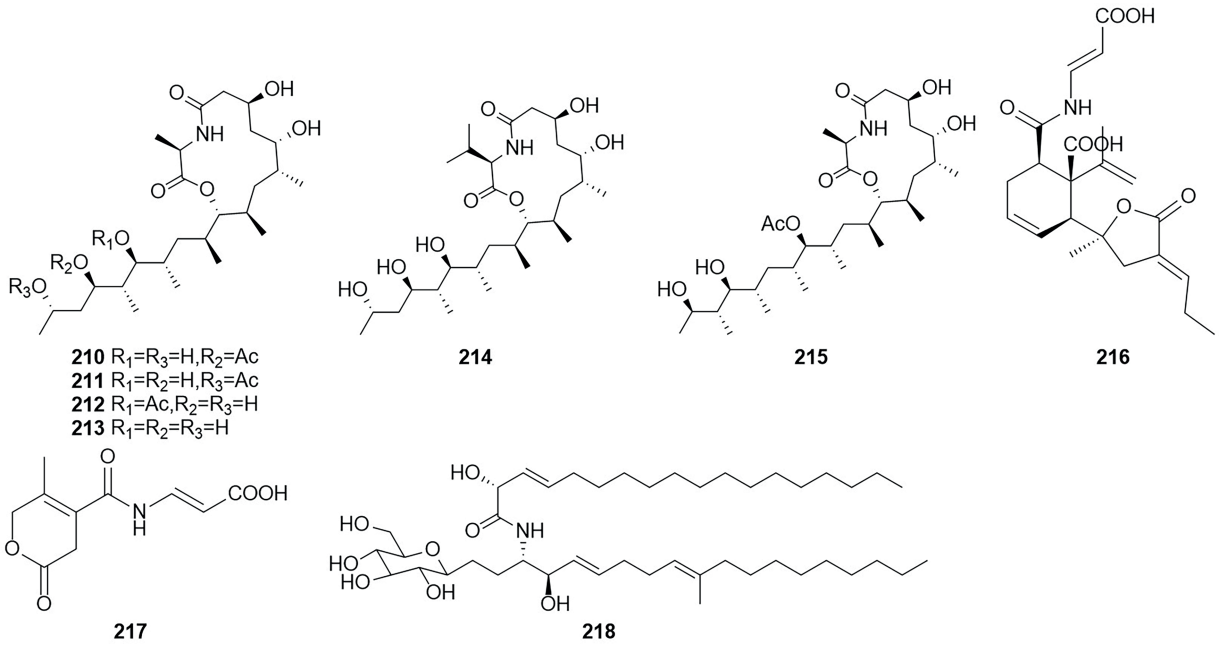

FIGURE 13
Chemical structures of compounds **210–218**.

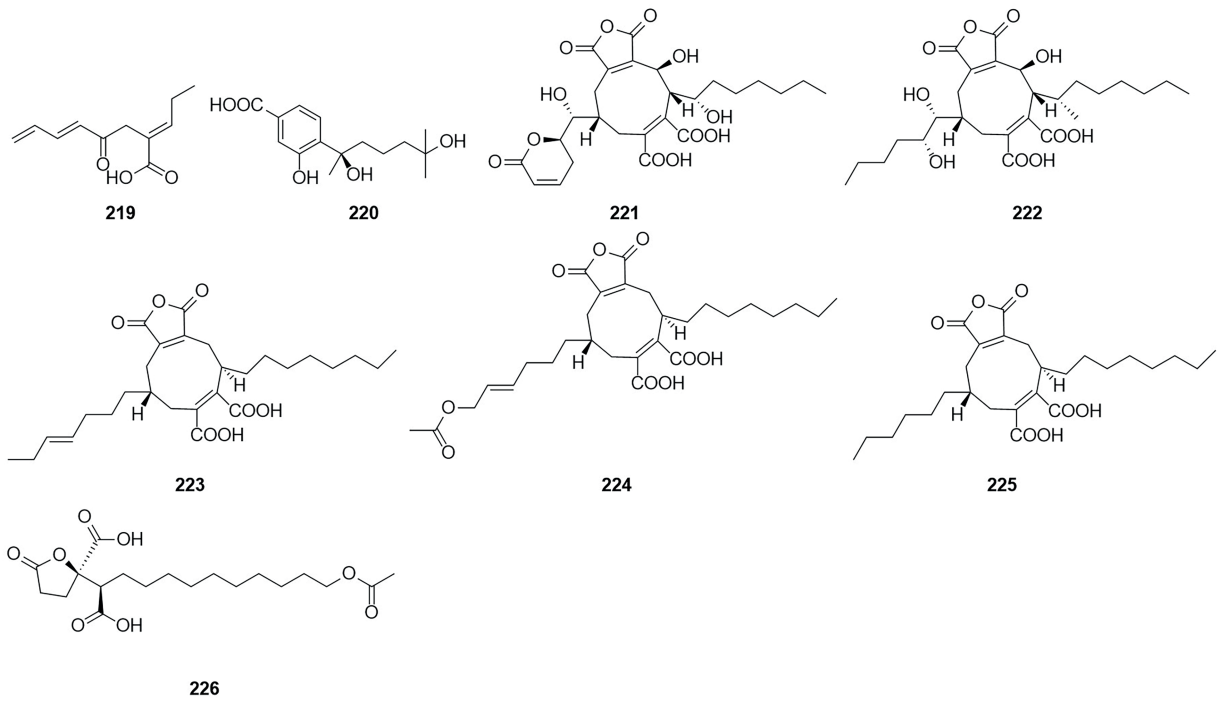

FIGURE 14
Chemical structures of compounds **219–226**.

several years are classified and summarized according to the types of compounds (Table 1). Secondary metabolites from more than ten *Talaromyces* species, including *T. wortmannii*, *T. pinophilus*, *T. flavus*, *T. stipitatus*, *T. purpureogenus*, and *T. minioluteus*, have been covered in this paper. These metabolites included 89 esters, 35 polyketones, 16

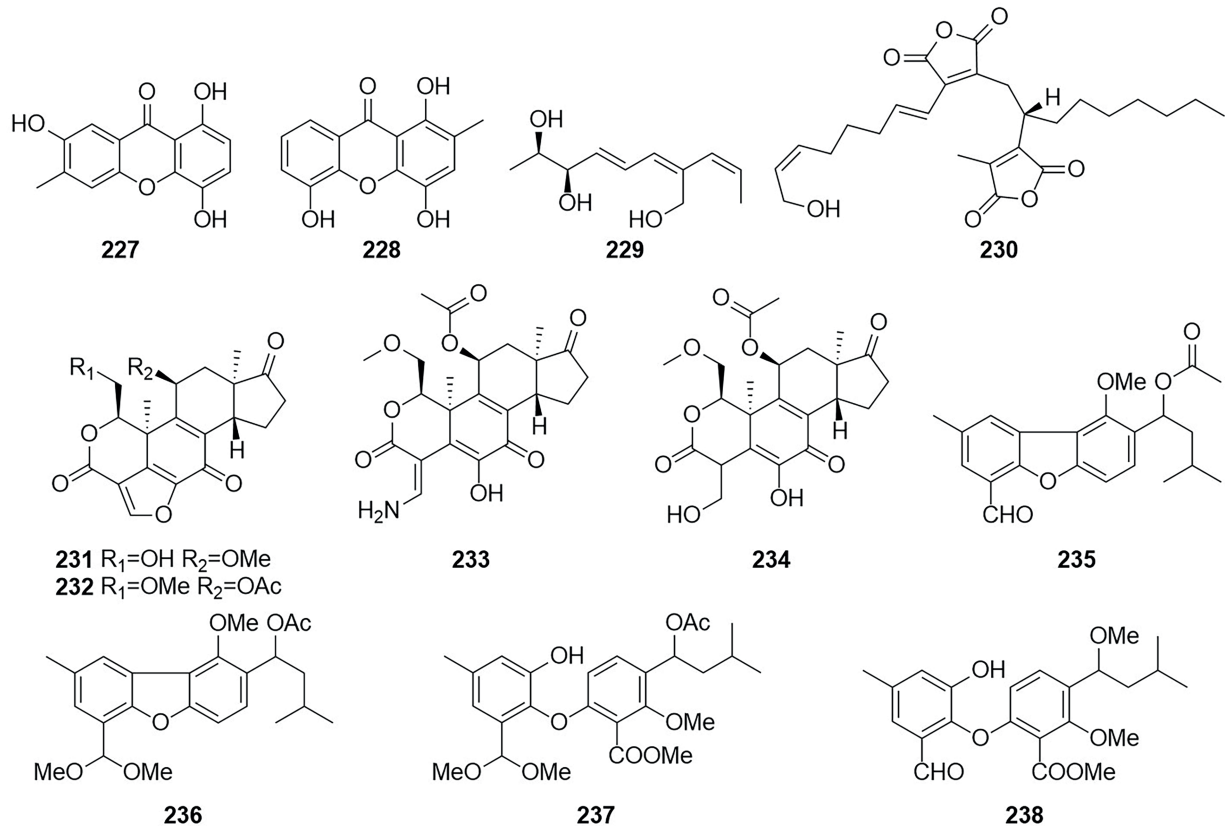

FIGURE 15
Chemical structures of compounds **227–238**.

anthraquinone, 20 terpenoids, 13 meroterpenoids, 10 steroids, 35 nitrogen compounds, 8 acids, and 12 other compounds. Most of these compounds have useful biological activities, such as anti-inflammatory, antibacterial, antitumor, hypolipidemic, or nematocidal activities or inhibition of α-glucosidase, xanthine oxidase, acetyltransferase, NADH fumarate reductase, PI3K-α, Aβ42 aggregation, or the production of NO induced by lipopolysaccharide.

Prospects

Talaromyces fungi include some of the most important species of microorganisms. The secondary metabolites from *Talaromyces* species that have unique structures and useful activities are of great value in research and development. However, there are still some problems to be solved in the study of fungal secondary metabolites. Firstly, owing to the limitations of strain isolation techniques and fungal culture conditions, some fungi cannot be isolated or do not grow well. Now often use fungal culture mediums are: PDA medium, PDB medium, BegH medium, rice solid medium and so on. Among them, rice medium is the most used (Table 1), which may be due to more fungal metabolites cultured in solid medium than liquid medium. It also reflected the problems of single nutrition and limited culture in the application of fungus synthesis medium. It is hoped that unconventional media can be used and new media can be developed. Secondly, it had been reported in available reports that the addition of epigenetic modifications to the culture medium can stimulate the expression of silenced genes thereby enabling the production of novel secondary metabolites. However, none of the literature in the study of secondary metabolites of the *Talaromyces* has investigated the effect of epigenetic modifiers. Therefore, epigenetic modifiers can be added to stimulate the expression of their silent genes. Finally, many existing studies have been done on the ethyl acetate part of the ferment, which is moderately polar and easy to separate. The aqueous part, on the other hand, has been ignored or even discarded due to its high polarity and difficulty of separation. Therefore, it is hoped that methods for the separation of compounds with high polarity will be developed as well as the development of related fillers. In a word, we should make full use of modern scientific and technological methods to carry out an in-depth study of the secondary metabolites produced by *Talaromyces* fungi and identify new active components to provide lead compounds for the research and development of innovative drugs.

TABLE 1 Name of *Talaromyces'* secondary metabolites, source strains, activity and their culture media.

Category	Compound name	Fungus	Pharmacological activity or application	Medium	References
Esters	Dinapinones AB1 (**1**)	*T. pinophilus* FKI-3864	/	Miura's medium	Kawaguchi et al., 2013
	Dinapinones AB2 (**2**)	*T. pinophilus* FKI-3864	Inhabit triacylglycerol synthesis in intact mammalian cells, with an IC_{50} value of 1.17 μM	Miura's medium	Kawaguchi et al., 2013
	Dinapinones AC1 (**3**)	*T. pinophilus* FKI-3864	/	Miura's medium	Kawaguchi et al., 2013
	Dinapinones AC2 (**4**)	*T. pinophilus* FKI-3864	/	Miura's medium	Kawaguchi et al., 2013
	Dinapinones AD1 (**5**)	*T. pinophilus* FKI-3864	/	Miura's medium	Kawaguchi et al., 2013
	Dinapinones AD2 (**6**)	*T. pinophilus* FKI-3864	/	Miura's medium	Kawaguchi et al., 2013
	Dinapinones AE1 (**7**)	*T. pinophilus* FKI-3864	/	Miura's medium	Kawaguchi et al., 2013
	Dinapinones AE2 (**8**)	*T. pinophilus* FKI-3864	/	Miura's medium	Kawaguchi et al., 2013
	Talapolyesters A (**9**)	*T. flavus*	/	potato dextrose agar (PDA); potato dextrose broth (PDB); rice solid medium	He et al., 2014b
	Talapolyesters B (**10**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	Talapolyesters C (**11**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	Talapolyesters D (**12**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	15G256ν (**13**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	15G256ν-me (**14**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	15G256π (**15**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	15G256β-2 (**16**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	15G256α-2 (**17**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	15G256α-2-me (**18**)	*T. flavus*	/	PDA; PDB; rice solid medium	He et al., 2014b
	15G256ι (**19**)	*T. flavus*	Antitumor	PDA; PDB; rice solid medium	He et al., 2014b
	15G256β (**20**)	*T. flavus*	Antitumor	PDA; PDB; rice solid medium	He et al., 2014b
	15G256α (**21**)	*T. flavus*	Antitumor	PDA; PDB; rice solid medium	He et al., 2014b
	Talapolyesters E (**22**)	*T. flavus*	Antitumor	PDA; PDB; rice solid medium	He et al., 2014b
	15G256α-1 (**23**)	*T. flavus*	Antitumor	PDA; PDB; rice solid medium	He et al., 2014b
	Talapolyesters E (**24**)	*T. flavus*	Antitumor	PDA; PDB; rice solid medium	He et al., 2014b
	15G256ω (**25**)	*T. flavus*	Antitumor	PDA; PDB; rice solid medium	He et al., 2014b
	Talaromycolides A (**26**)	*T. pinophilus* AF-02	Antibacterial	YES liquid medium	Zhai et al., 2015
	Talaromycolides B (**27**)	*T. pinophilus* AF-02	Antibacterial	YES liquid medium	Zhai et al., 2015
	Talaromycolides C (**28**)	*T. pinophilus* AF-02	Antibacterial	YES liquid medium	Zhai et al., 2015
	Rubralide C (**29**)	*T. pinophilus* AF-02	/	YES liquid medium	Zhai et al., 2015
	Sclerotinin A (**30**)	*T. pinophilus* AF-02	/	YES liquid medium	Zhai et al., 2015
	Alternariol (**31**)	*T. pinophilus* AF-02	/	YES liquid medium	Zhai et al., 2015
	Penicillide (**32**)	*T. pinophilus* AF-02	/	YES liquid medium	Zhai et al., 2015
	Deacetylisowortmins A (**33**)	*T. wortmannii* LGT-4	/	PDA	Fu et al., 2016
	Deacetylisowortmins B (**34**)	*T. wortmannii* LGT-4	/	PDA	Fu et al., 2016
	Talaromyones A (**35**)	*T. stipitatus* SK-4	/	Autoclaved wheat solid-substrate medium	Cai et al., 2017
	Talaromyones B (**36**)	*T. stipitatus* SK-4	Antibacterial; inhibitα-glucosidase	Autoclaved wheat solid-substrate medium	Cai et al., 2017
	Purpactin A (**37**)	*T. stipitatus* SK-4	Inhibit α-glucosidase	Autoclaved wheat solid-substrate medium	Cai et al., 2017

(Continued)

TABLE 1 Continued

Category	Compound name	Fungus	Pharmacological activity or application	Medium	References
	Butenolides (**38**–**42**)	*T. rugulosus*	/	Solid rice medium	Küppers et al., 2017
	(3S)-resorcylide derivatives (**43**–**49**)		/		
	Talarodilactones A and B (**50** and **51**)		Antitumor		
	Talaromycin A (**52**)	*Talaromyces* sp.	Antitumor	Co-culture with *X. angustiphylla*	Yuan et al., 2018
	Clearanol A (**53**)	MH551540	Antitumor		
	Wortmannine *F* (**54**)	*T. wortmannii* LGT-4	Antitumor	King's B Medium	Zhao et al., 2019b
	Pentalsamonin (**55**)	*T. purpureogenus* CFRM02	Antibacterial	Bengal gram husk (BegH)	Pandit et al., 2018
	Talaromarnine A (**56**)	*T. marneffei*	/	Corn medium	Yang et al., 2021
	Talaromarnine B (**57**)	*T. marneffei*	/	Corn medium	Yang et al., 2021
	Amestolkins A (**58**)	*T. amestolkiae*	Anti-inflammatory	M1 liquid medium	Huang et al., 2022
	Amestolkins B (**59**)		/		
	Talacoumarins A (**60**)	*T. flavus*	Anti-Aβ42 aggregation activity	PDA; PDB; rice	He et al., 2014c
	Talacoumarins B (**61**)	*T. flavus*	Anti-Aβ42 aggregation activity	PDA; PDB; rice	He et al., 2014c
	Chloropestalasin A (**62**)	*T. amestolkiae*	/	Solid cultures	El-Elimat et al., 2021
	3-Hydroxymethyl-6,8-dimethoxycoumarin (**63**)	*T. amestolkiae*	/	Solid cultures	El-Elimat et al., 2021
	Pestalasin A (**64**)	*T. amestolkiae*	/	Solid cultures	El-Elimat et al., 2021
	Dihydroisocoumarins (**65**–**67**)	*T. rugulosus*		Solid rice medium	Küppers et al., 2017
	Talaromarins A-F (**68**–**73**)	*T. flavus* TGGP35; *Talaromyces* sp. ZZ1616	Antioxidant; antimicrobial	PDB; rice solid medium	Cai et al., 2022; Ma et al., 2022
	Analogues (**67**,**74**–**89**)	*T. flavus* TGGP35	Antioxidant	Rice solid medium	Cai et al., 2022
Polyketons	Mitorubrin (**90**)	*T. atroroseus*	Red pigment production	Solid medium	Frisvad et al., 2013
	Monascorubrin (**91**)	*T. atroroseus*	Red pigment production	Solid medium	Frisvad et al., 2013
	Talaroxanthone (**92**)	*Talaromyces* sp.	/	ISP2-agar medium	Koolen et al., 2013
	9a-Epi-bacillisporin E (**93**)	*T. stipitatus*	/	PDA	Zang et al., 2016
	1-Epi-bacillisporin *F* (**94**)	*T. stipitatus*	/	PDA	Zang et al., 2016
	Bacillisporins F-H (**95**–**97**)	*T. stipitatus*	Antibacterial	PDA	Zang et al., 2016
	Wortmannilactones I1-I3(98–100)	*T. wortmannii*	Antioxidant	Corn plate medium	Liu et al., 2016
	Talaraculones A–F (**102**–**107**)	*T. aculeatus*	Inhibit α-glucosidase	PDA	Ren et al., 2017
	Pinazaphilone B (**108**)	*T. aculeatus*	Inhibit α-glucosidase	PDA	Ren et al., 2017
	Pinophilin B (**109**)	*T. aculeatus*	/	PDA	Ren et al., 2017
	Sch 725680 (**110**)	*T. aculeatus*	/	PDA	Ren et al., 2017
	(−)-Mitorubrin (**111**)	*T. aculeatus*	/	PDA	Ren et al., 2017
	(−)-Mitorubrinol (**112**)	*T. aculeatus*	/	PDA	Ren et al., 2017
	Paecillin D (**113**)	*T. stipitatus*	Antifungal	International streptomyces project 2 liquid medium (ISP2)	da Silva et al., 2017
	Secalonic acid A (**114**)	*T. stipitatus*	Antifungal	ISP2	da Silva et al., 2017
	Blennolide G (**115**)	*T. stipitatus*	Antifungal	ISP2	da Silva et al., 2017
	Versixanthone A (**116**)	*T. stipitatus*	Antifungal	ISP2	da Silva et al., 2017
	Penicillixanthone A (**117**)	*T. stipitatus*	/	ISP2	da Silva et al., 2017
	Paecillin B (**118**)	*T. stipitatus*	/	ISP2	da Silva et al., 2017

(Continued)

TABLE 1 Continued

Category	Compound name	Fungus	Pharmacological activity or application	Medium	References
	Talarodrides A – F (**119–124**)	*Talaromyces* sp. HDN1820200	Antimicrobial	PDB	Zhao et al., 2021b
Anthraquinone	Skyrin (**125**)	*Talaromyces* sp. ZH-154	Antitumor	PDA, PDB	Liu et al., 2010; Xie et al., 2016
	Emodin (**126**)	*Talaromyces* sp. ZH-154	Antitumor	PDA, PDB	Liu et al., 2010
	Biemodin (**127**)	*T. wortmannii*	/	Rice solid medium	Bara et al., 2013a
	Emodic acid (**128**)	*T. wortmannii*	/	Rice solid medium	Bara et al., 2013a
	Oxyskyrin (**129**)	*T. wortmannii*	Antitumor	Rice solid medium	Bara et al., 2013a; Xie et al., 2016
	Rugulosins A - B (**130–131**)	*T. wortmannii*	/	Rice solid medium	Bara et al., 2013a
	Talaromannins A-B (**132–133**)	*T. wortmannii*	Antibacterial	Rice solid medium	Bara et al., 2013b
	3-Demethyl-3-(2-hydroxypropyl)-skyrin (**134**)	*Talaromyces* sp. YE 3016	Antitumor	Rice solid medium	Xie et al., 2016
	1,3,6-Trihydroxy-8-methylanthraquinone (**135**)	*Talaromyces* sp. YE 3016	/	Rice solid medium	Xie et al., 2016
	2,2'-bis-(7-methyl-1,4,5-trihydroxy-anthracene-9,10-dione) (**136**)	*T. stipitatus* KUFA 0207	/	Rice solid medium	Noinart et al., 2017
	Questinol (**137**)	*T. stipitatus* KUFA 0207	Anti-obesity activity	Rice solid medium	Noinart et al., 2017
	Citreorosein (**138**)	*T. stipitatus* KUFA 0207	Anti-obesity activity	Rice solid medium	Noinart et al., 2017
	Fallacinol (**139**)	*T. stipitatus* KUFA 0207	/	Rice solid medium	Noinart et al., 2017
	Rheoemodin (**140**)	*T. stipitatus* KUFA 0207	/	Rice solid medium	Noinart et al., 2017
Terpenoids	Pinophicin A (**141**)	*T. pinophilus*	/	MEB medium	Zhao et al., 2021a
	Talaperoxides A–D (**142–145**)	*T. flavus*	Antitumor	Autoclaved rice solid-substrate medium	Li et al., 2011
	Talaflavuterpenoid A (**146**)	*T. flavus*	/	Rice solid medium	He et al., 2014a
	Roussoellol C (**147**)	*T. purpureogenus*	Antitumor	Rice solid medium	Wang et al., 2018
	Talaminoid A (**148**)	*T. minioluteus*	Anti-inflammatory	Rice solid medium	Chen et al., 2019
	Talaminoids B - C (**149–150**)	*T. minioluteus*	/	Rice solid medium	Chen et al., 2019
	Purpuride (**151**)	*T. minioluteus*	Anti-inflammatory	Rice solid medium	Chen et al., 2019
	Berkedrimanes B (**152**)	*T. minioluteus*	Anti-inflammatory	Rice solid medium	Chen et al., 2019
	Minioluteumide B (**153**)	*T. minioluteus*	/	Rice solid medium	Chen et al., 2019
	1αHydroxyconfertifolin (**154**)	*T. minioluteus*	/	Rice solid medium	Chen et al., 2019
	Sordarin (**155**)	*Talaromyces* sp. (CMB-TU011)	Antifungal	M1 agar plate	Domínguez et al., 1998; Dewapriya et al., 2017
	Four new sesquiterpene lactones (**156–159**)	*T. minioluteus*	Antitumor	PDB	Ngokpol et al., 2015
	Purpuride B (**160**)	*T. minioluteus*	/	PDB	Ngokpol et al., 2015
Meroterpenoid	Talaromyolides A–D (**161–164**)	*Talaromyces* sp. CX11	Antiviral	Liquid Medium	Cao et al., 2019
	Talaromytin (**165**)	*Talaromyces* sp. CX11	/	Liquid Medium	Cao et al., 2019
	Taladrimanin A (**166**)	*Talaromyces* sp. HM6-1–1	Antitumor activity; antibacterial activity	Rice solid medium	Hong et al., 2022
	Chrodrimanins A-H (**167–173**)	*Talaromyces* sp. YO-2	Antimalarial	Okara	Hayashi et al., 2012a,b
Steroids	Talasterone A (**174**)	*T. adpressus*	Anti-inflammatory	Rice solid medium	Zhang et al., 2022a

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TABLE 1 Continued

Category	Compound name	Fungus	Pharmacological activity or application	Medium	References
	3-Acetylergosterol-5,8-endoperoxide (**175**)	*Talaromyces trachyspermus* KUFA 0021	/	GPMY	Kuml et al., 2014
	Talarosterone (**176**)	*T. stipitatus* KUFA 0207	/	Rice solid medium	Noinart et al., 2017
	Cyathisterone (**177**)		/		
	Talasteroid (**178**)	*T. stollii*	/	PDA	Zhang et al., 2022c
	(22E,24R)-7α-Methoxy-5α,6α-epoxyergosta-8(14),22-diene-3β,15β-diol (**179**)	*T. stipitatus*	Antiproliferative	Rice solid medium	Zhang et al., 2021
	(22E,24R)-5α,6α-Epoxyergosta-8(14),22-diene-3β,7β,15α-triol (**180**)	*T. stipitatus*	/	Rice solid medium	Zhang et al., 2021
	(22E,24R)-3β,5α-Dihydroxy-14β,15β-epoxyergosta-7,22-diene-6-one (**181**)	*T. stipitatus*	/	Rice solid medium	Zhang et al., 2021
	(22E,24R)-6α-Methoxy-7α,15β-dihydroxyergosta-4,8(14),22-triene-3-one (**182**)	*T. stipitatus*	/	Rice solid medium	Zhang et al., 2021
	(25S)- Ergosta-7,24(28)-diene-3β,4α,6α,26-tetraol (**183**)	*T. stipitatus*	Antiproliferative	Rice solid medium	Zhang et al., 2021
Alkaloids	PP-R (**184**)	*T. atroroseus*	Food colorants	Solid medium	Frisvad et al., 2013
	Herquline B (**185**)	*T. pinophilus*	/	Solid medium	Vinale et al., 2017
	Talathermophilins A–E (**186–188**,**190–191**)	*T. thermophilus* YM3-4	/	PDB	Guo et al., 2011
	Cyclo(glycyltryptophyl) (**189**)	*T. thermophilus* YM3-4	/	PDB	Guo et al., 2011
	ZG-1494α (**192**)	*T. atroroseus*	A novel inhibitor of platelet-activating factor acetyl-transferase	PDB	Frisvad et al., 2013
	2-[(S)-Hydroxy(phenyl) methyl]-3-methylquinazolin-4(3H)-one (**193**)	*Talaromyces* sp. *cf*-16	/	PDA	Yang et al., 2016
	2-[(R)-Hydroxy(phenyl) methyl]-3-methylquinazolin-4(3H)-one (**194**)	*Talaromyces* sp. *cf*-16	/	PDA	Yang et al., 2016
	Roquefortine C (**195**)	*Talaromyces* sp. *cf*-16	/	PDA	Yang et al., 2016
	Z-Roquefortine C (**196**)	*Talaromyces* sp. *cf*-16	Antibacterial	PDA	Yang et al., 2016
	Viridicatol (**197**)	*Talaromyces* sp. *cf*-16	Antibacterial	PDA	Yang et al., 2016
	Penitrem A (**198**)	*Talaromyces* sp. *cf*-16	Antibacterial	PDA	Yang et al., 2016
	Penijanthine A (**199**)	*Talaromyces* sp. *cf*-16	Antibacterial	PDA	Yang et al., 2016
	Paspaline (**200**)	*Talaromyces* sp. *cf*-16	/	PDA	Yang et al., 2016
	3-Deoxo-4b-deoxypaxilline (**201**)	*Talaromyces* sp. *cf*-16	/	PDA	Yang et al., 2016
	Talaromanloid A (**202**)	*T. mangshanicus* BTBU20211089	/	Rice solid medium	Zhang et al., 2022b
	10-Hydroxy-8-demethyltalaromydine (**203**)	*T. mangshanicus* BTBU20211089	/	Rice solid medium	Zhang et al., 2022b
	11-Hydroxy-8-demethyltalaromydine (**204**)	*T. mangshanicus* BTBU20211089	/	Rice solid medium	Zhang et al., 2022b

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TABLE 1 Continued

Category	Compound name	Fungus	Pharmacological activity or application	Medium	References
	Ditalaromylectones A (**205**)	*T. mangshanicus* BTBU20211089	Antibacterial	Rice solid medium	Zhang et al., 2022b
	Ditalaromylectones A (**206**)	*T. mangshanicus* BTBU20211089	/	Rice solid medium	Zhang et al., 2022b
	Vincristine (**207**) Vinblastine (**208**)	*T. radicus*	Antitumor /	M2 liquid medium; PDA	Palem et al., 2015
	Talaramide A (**209**)	*Talaromyces* sp. HZ-YX1	Antibacterial	Solid rice medium	Chen et al., 2017
Amides	Thermolides A–F (**210–215**)	*T. thermophilus*	**210–211**: Insect resistance	PDA	Guo et al., 2012
	Talaromydene (**216**)	*T. mangshanicus* BTBU20211089	/	Rice solid medium	Zhang et al., 2022b
	Talaromylectone (**217**)	*T. mangshanicus* BTBU20211089	/	Rice solid medium	Zhang et al., 2022b
	Cerebroside C (**218**)	*T. purpurogenus*	/		Zhao et al., 2020
Acid	Oxoberkedienoic acid (**219**)	*T. verruculosus* FKI-5393	Antitumor	Rice solid medium	Sakai et al., 2018
	(R)-(−)-Hydroxysydonic acid (**220**)	*Talaromyces* sp. C21-1	Antimicrobial	Liquid medium	Nie et al., 2019
	Rubratoxin acid A-E (**221–225**)	*T. purpureogenus*	**221**: Anti-inflammatory **222**: Antioxidant	PDA	Zhao et al., 2019b
	Spic ulisporic acid E (**226**)	*T. trachyspermus* KUFA 0021	/	GPMY	Kuml et al., 2014
Others	2,2',3,5'-tetrahydroxy-3'-methylbenzophenone (**227**)	*T. islandicus* EN-501	Antioxidant; antibacterial activity	Rice solid medium	Li et al., 2016
	2,2',5'-trihydroxy-3-methoxy-3'-methylbenzophenone (**228**)	*T. islandicus* EN-501	Antioxidant; antibacterial Activity	Rice solid medium	Li et al., 2016
	Wortmannine H (**229**)	*T. wortmannii* LGT-4	/	Martin medium	Li et al., 2021
	Talarodride (**230**)	*T. purpurogenus*	Antitumor	Rice solid medium	Zhao et al., 2019b
	Wortmannin B (**231**)	*T. wortmannii*	/	Rice solid medium	Bara et al., 2013a
	Wortmannin (**232**)	*T. wortmannii*	/	Rice solid medium	Bara et al., 2013a
	Amino adduct 3a (**233**)	*T. wortmannii*	/	Rice solid medium	Bara et al., 2013a
	Wortmannin-diol (VIII) (**234**)	*T. wortmannii*	/	Rice solid medium	Bara et al., 2013a
	Talaromycins A–C (**235–237**)	*Talaromyces* sp. SBE-14 (EU236708)	Antifouling	PDA	Chen et al., 2015
	Tienilic acid A methyl ester (**238**)	Talaromyces sp. SBE-14 (EU236708)	/	PDA	Chen et al., 2015

Author contributions

L-RL, L-QG, and M-YJ wrote the paper. JG, RW, and RL cultured and identified the fungus. L-RL, M-DL, and LH collected the STM data. YD checked the paper. G-ZW and DW verified the content. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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