A Review on Bioactive Compounds from Marine-Derived Chaetomium Species

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Filamentous marine fungi have proven to be a plentiful source of new natural products. Chaetomium, a widely distributed fungal genus in the marine environment, has gained much interest within the scientific community. In the last 20 years, many potential secondary metabolites have been detected from marine-derived Chaetomium. In this review, we attempt to provide a comprehensive summary of the natural products produced by marine-derived Chaetomium species. A total of 122 secondary metabolites that were described from 2001 to 2021 are covered. The structural diversity of the compounds, along with details of the sources and relevant biological properties are also provided, while the relationships between structures and their bioactivities are discussed. It is our expectation that this review will be of benefit to drug development and innovation.

Keywords: Chaetomium, secondary metabolite, structural diversity, biological activity

Introduction

Chaetomium is a large genus in the Chaetomiaceae family of Ascomycota, which contains more than 100 species [1]. Chaetomium is widely distributed in soil, air, animals and plants. It is an important resource for its production of active natural products and its main types of metabolites include cytochalasans, indole alkaloids, terpenoids, steroids, flavonoids, and so on, and their biological functions include enzyme inhibitory, antitumor, antimicrobial, antioxidant, antibacterial and other activities [2].

The progress of research into the secondary metabolites originating from the genus Chaetomium has attracted much attention, and a series of excellent reviews on this topic have so far been published [2-5]. In 2012, Zhang et al. reviewed the extraction, elucidation, structural diversity and biological activities of natural products from terrestrial and marine-derived Chaetomium between 1936 and 2010. The secondary products were categorized into 21 structural types and included chaetoglobosins, diketopiperazines, tetramic acids, isouquinolines, azaphilones, terpenoids, etc. Some bioactive compounds as well as their mechanisms of action and structure-activity relationships were highlighted in the literature [2]. In 2016, Nighat et al. reviewed the isolation of Chaetomium endophytes, the extraction and isolation of metabolites, and their biological activities. The bioactive molecules were classified into five types, including anticancer and cytotoxic metabolites, antimicrobial metabolites, enzyme inhibitors, antimalarial and antitrypanosomal metabolites, as well as antioxidant metabolites [3]. Non-endophytic Chaetomium species were not included in the literature. In 2018, two Chinese studies reported the progress of various research projects involving Chaetomium. Xu et al. summarized the information on 208 secondary metabolites from Chaetomium fungi, which had been reported from 2011 to 2016 [4]. Liang reviewed the diversities and bioactivities of the secondary metabolites from Chaetomium globosum between 2015 and 2017 [5]. However, no work has been specifically focused on Chaetomium species from the marine environment. Marine fungi are important sources of secondary metabolites for drug discovery [6], and moreover, reports of new natural products from marine-derived fungi have increased dramatically over the last few decades [7]. It is believed that the exploration of fungi living in the marine environment will advance the isolation of new fungal species and lead to the discovery of novel compounds [8].

Therefore, in this review, we describe the structural diversities and biological activities of 122 compounds isolated from marine-derived Chaetomium species over the past 20 years (2001 to 2021). The review also expounds the relationship between the structures and functions of the natural products, and improve understanding of the fascinating chemistry and bioactivity of the natural products resulting from marine Chaetomium species.

Bioactive Compounds from Marine-Derived Chaetomium Species

Marine Chaetomium-derived compounds with various structures offer abundant bioactive core skeletons for new medicinal lead molecules. The different structural types of these compounds, including cytochalasans,
| Structure            | Natural product | Species             | Bioactivity                      | Source                      | Ref.  |
|----------------------|-----------------|---------------------|-----------------------------------|-----------------------------|-------|
| Cytochalasan         | Cytochalasins   | C. globosum         | Cytotoxicity                      | Marine green alga           | [13]  |
|                      | A–G (1–7)       |         QEN-14        |                                   | Ulva pertusa                |       |
|                      | Isocytotoxiclasins D (8) |             |                                   |                              |       |
|                      | Chaetoglogbasin F (9) |         |                                   |                              |       |
| Cytochalasan         | Chaetoglogbasins A, B, I (10–12) | C. globosum | Immunosuppressive activity        | Ocean fish                  | [14]  |
|                      | Halogenated derivatives (13–21) | 1C51        |                                   | Epinephalus drummondhuiyi   |       |
| Cytochalasan         | Chaetoglogbasins B (2), C (3), H (22), I (23), Chaetoglogbasins F (9), F (24), E (25), B (11), Isocytotoxiclasins D (8) | C. globosum | Antiprofliorative activity        | Deep-sea sediments           | [15]  |
| Cytochalasan         | Chaetoglogbasins A (10), B (11), D–F (26, 25, 24) | C. globosum | Antibacterial activity            | Gorgonian                   | [16]  |
|                      | Cytochalasin C (3) |             |                                   | Anthogorgia ochracea        |       |
| Cytochalasan         | Chaetoglogbasin X (27), Chaetoglogbasin F (9), G (28), B (11) | C. globosum | Antibacterial activity            | Sea cucumber                 | [17]  |
| Cytochalasan         | 6-O-methyl-cytotoxiclasin Q (29) | C. globosum | Cytotoxicity                      | Coral Poliplora damicornis  | [18]  |
|                      | Chaetoglogbasins A (11), B (12), C (30), D (26), E (25), F (24), G (26), F (9), V (35), Y (36) |             |                                   |                              |       |
|                      | Aurochetoxytoclasin (31) |             |                                   |                              |       |
|                      | Isocytotoxiclasin D (8) |             |                                   |                              |       |
|                      | Penochalasin G (32) |             |                                   |                              |       |
|                      | Armochaetoglogbin G (33) |             |                                   |                              |       |
|                      | Prochaetoglogbin I (34) |             |                                   |                              |       |
| Dioxopiperazine      | Cristamine (37) | C. cristatum       | Radical-scavenging activity       | Mudflat sediment             | [26]  |
|                      | Chetomin (38)   |             | Cytotoxicity                      |                              |       |
|                      | Neochinulin A (39) |             | Antimicrobial activity            |                              |       |
|                      | Golmaenone (40) |             | Anti-inflammatory effect SARS-CoV-2 Mpro Inhibitor |                              |       |
|                      |                 |             | Cytoprotection                    |                              |       |
|                      |                 |             | Memory improvement                |                              |       |
|                      |                 |             | Antidepressant-like effects       |                              |       |
| Indole alkaloid       | Cycholodin (41) | C. globosum         | None                              | Sea cucumber                 | [17]  |
|                      | E-C-2           |         |                                   | Apostichopus japonicus      |       |
| Indole alkaloid       | Chaetogline A–H (42–49) | C. globosum | Antibacterial and antifungal activity | Marine fish                  | [42, 43] |
|                      | Chaetindolone A–D (50–53) | 1C51        |                                   | Epinephalus drummondhuiyi   |       |
|                      | 19-O-Demethylchaetogline A (54) |             |                                   |                              |       |
|                      | 20-O-Demethylchaetogline F (55) |             |                                   |                              |       |
| Azaphilone            | Chaetomulgins A–O (56–70) | C. globosum | Cytotoxicity                      | Marine fish                  | [47-54] |
|                      | Seco-chaetomulgins A, D (71, 72) | OUPS-T106B-6 |                                   | Magil cephalis               |       |
|                      | 11-Epichetoxytoclasin A (73) |             |                                   |                              |       |
|                      | 4′-Epichetoxytoclasin A (74) |             |                                   |                              |       |
|                      | Chaetomulgins P–R (75–77) |             |                                   |                              |       |
|                      | 11-epi-Chetoxytoclasin I (78) |             |                                   |                              |       |
|                      | Chaetomulgins S–U (79–81) |             |                                   |                              |       |
| Azaphilone            | Chaetophucine C (82) | Chaetomium sp. NA-S01-R1 | Antibacterial activity and cytotoxicity | Deep sea water               | [56]  |
|                      | Chaetoxytocridides A–C (83–85) |             |                                   |                              |       |
|                      | Chaetoxytocridins A, E (86, 87) |             |                                   |                              |       |
|                      | Chaetoxytocridin D (59) |             |                                   |                              |       |
|                      | Cochloiodone A (88) |             |                                   |                              |       |
| Azaphilone            | N-glutarocetoxytocridins A–C (89–91) | C. globosum | Cytotoxicity                      | Deep sea sediment            | [57]  |
|                      | Chaetoxytocridins A, C (56,58) | HDN151398 |                                   |                              |       |
| Azaphilone            | Nitrogenated azaphilones (92–99) |             | Cytotoxicity                      | Deep sea water               | [58]  |
| Azaphilone            | Chaetoxytocridins A (86), E (87), B (100) | C. globosum | None                              | Sea cucumber                 | [17]  |
|                      | Chaetoxytocridin A (56) | E-C-2        |                                   |                              |       |
| Xanthone derivative   | Chaetoxytoclines A–C (101–103) | Chaetomium sp. G0 100/2 | Antifungal activity              | Marine algae                 | [70]  |
| Xanthone derivative   | Chaetoxytoxanes A–C (104–106) | Chaetomium sp. 620/GrK 1a | Anti-parasitic activity          | Marine algae                 | [71]  |
| Tetralone derivative  | Xylariol A (107) | C. globosum         | None                              | Gorgonian                    | [16]  |
|                      | RA07-3          |             |                                   | Anthogorgia ochracea         |       |
| Isocoumarin derivative| (3R,4S)-6,8-Dihydroxy-3,4,5-trimethylisochroman 1-one (108) | C. globosum | None                              | Gorgonian                    | [16]  |
| O-phthalate derivative| 2,5,8-Benzotrioxacycloundecin 1,9-dione (109) | C. globosum | None                              | Gorgonian                    | [16]  |
Cytochalasans

Cytochalasans are a large group of fungal alkaloids with a wide range of biological activities. They have been an important chemical tool in cell and molecular biology. Some of them also possess phytotoxic, cytotoxic, and antibiotic activities [9, 10]. Cytochalasans are characterized by a highly substituted perhydro-isoindolone moiety incorporating a macrocyclic ring [11]. The fungal polyketide synthase nonribosomal peptide synthetase (PKS-NRPS) plays an important role in forming cytochalasans [12].

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Cytochalasans, chaetoglobosins and penochalasins are common classes of cytochalasan alkaloids in Chaetomium. Seven new cytochalasan derivatives cytochalosins A–G (1–7), together with two known, structurally related compounds, isochaetoglobosin D (8) and chaetoglobosin Fex (9) (Fig. 1), were isolated from C. Globosum QEN-14, an endophytic fungus derived from the marine green alga Ulva pertusa. Cytochalosins C (3) and D (4) showed moderate activity against A-549 cell line with IC\textsubscript{50} values of 2.26 and 2.55 μM, respectively [13]. From C. globosum LC51, a fungus residing inside the gut of an ocean fish, Epinephelus drummondhayi, three metabolite chaetoglobosins, A, B and J (10–12) (Fig. 1), were obtained with high yields. Using precursor-directed biosynthesis, nine halogenated derivatives were produced (13–21) (Fig. 1). All isolated compounds were tested and found to be immunosuppressive, and compound 18 had the most potential with a high selectivity index (SI = 26.6) [14].

Chemical investigation of deep-sea-derived fungus C. globosum MCCC 3000607 resulted in obtaining two new compounds, cytochalosins H (22) and I (23), together with seven known ones: cytochalosins B (2) and C (3), chaetoglobosins F\textsubscript{ex} (9), F (24), E (25), and B (11), and isochaetoglobosin D (8) (Fig. 1). Compound 25 exhibited significant antiproliferative activity on LNCaP human prostate cancer cells and B16F10 mouse melanoma cells with IC\textsubscript{50} values of 0.62 and 2.78 μM, respectively [15]. Chemical investigation of the EtOAc extract of the gorgonian-derived fungus C. globosum RA07-3 resulted in the isolation of six chaetoglobosans, chaetoglobosins A and B (10 and 11), cytochalosins C (3), chaetoglobosins D–F (26, 25, 24) (Fig. 1), together with three other compounds, xylariol A (107), (3R,4S)-6,8-dihydroxy-3,4,5-trimethylisochroman-1-one (108), and 2,5,8-benzotiazacycloundecin-1,9-dione (109) (Fig. 7). Compounds 10 and 11 exhibited moderate brine shrimp lethality with LC\textsubscript{50} values of 9.72 and 12.41 μg/mL, respectively. Compounds 10, 11 and 3 also exhibited strong antibacterial activities against Tetragnococcus halophilius with MIC values of 0.7, 0.4, and 0.7 μM, respectively [16].

Gene mining of the sea cucumber–associated fungus C. globosum led to the new cytochalosin X (27) and the known cytochalasans chaetoglobosin F\textsubscript{ex} (9), G (28), and B (11) (Fig. 1), together with a known indole alkaloid cochlodinol (41) (Fig. 3) and four known azaphilones, chaetomugilin A (56) (Fig. 4), and chaetovirdins A (86), E (87), and B (100) (Fig. 5). Compound 11 showed moderate activity against Staphylococcus aureus and methicillin-resistant S. aureus (MRSA) with MIC values of 47.3 and 94.6 μM, respectively [17]. Recently, sixteen structurally diverse chaetoglobosins were isolated from the coral-associated fungus C. globosum C2F17, including a new one, 6-O-methyl-chaetoglobin Q (29), along with the previously isolated chaetoglobosins A (11), B (12), C (30), D (26), E (25), F (24), G (28), and aurechothraebosin (31), isochataebosin D (8), chaetoglobin F\textsubscript{ex} (9), penochalasin G (32), armochaetoglobin G (33), prochaetoglobin I (34), chaetoglobosin V (35), and chaetoglobosin Y (36) (Fig. 1). Among them, compound 25 showed significant cytotoxicity against K562, A549, Huh7, H1975, MCF-7, U937, BGC823, HL60, HeLa, and MOLT-4 cell lines, with IC\textsubscript{50} values ranging from 1.4 to 9.2 μM. Additionally, compound 9 displayed selective cytotoxic activity against Huh7, MCF-7, U937 and MOLT-4 cell lines, with IC\textsubscript{50} values of 3.0, 7.5, 4.9, and 2.9 μM, respectively [18].

| Table 1. Continued. |
|---------------------|
| Structure | Natural product | Species | Bioactivity | Source | Ref. |
| Benzaldehyde derivative | 2-(2,3-Epoxy-1,3-heptadienyl)-6-hydroxy-5-(3-methyl-2-butenyl)benzaldehyde | C. Globosum C2TCC AF 206003 | Radical-scavenging activity | Marine red alga Polysiphonia urceolata | [72] |
| Anthraquinone derivative | Erythroglaucin | C. Globosum C2TCC AF 206003 | Radical-scavenging activity | Marine red alga Polysiphonia urceolata | [72] |
| Asperentin derivative | 5'-Hydroxyasperentin | C. Globosum C2TCC AF 206003 | None | Marine red alga Polysiphonia urceolata | [72] |
| Benzozaphthyridine derivative | Chaetomimidione | Chaetomium sp. | Enzyme inhibitory activity | Marine alga Valonia utricularis | [73] |
| Furan derivatives | 2-Furancarboxylic acid | Chaetomium sp. | Enzyme inhibitory activity | Marine alga Valonia utricularis | [73] |
A total of 36 cytochalasans were obtained from marine-derived *Chaetomium* species, among which, compounds 3, 4, 9, and 25 showed cytotoxic activity. Several researchers have investigated the structure-activity relationships of cytochalasans and concluded that besides the intact macrocycle, the hydroxyl function at C-7 was an important pharmacophore concerning cytotoxic activity [19-21]. In this review, except compound 4, all of the compounds with cytotoxicity have hydroxyl function at C-7. All of the halogenated cytochalasans (13–21) were found to be immunosuppressive, indicating that halogen atoms may be important functional groups that confer immunosuppressive activity. It has been reported that the presence of an α,β-unsaturated carbonyl group in the macrolide moiety was a prerequisite for activity against gram-positive bacteria [22]. Furthermore, the three bacteriostatic compounds, 3, 10, and 11 all have the C-7 α,β-unsaturated carbonyl group in their structures. As more cytochalasans are increasingly being discovered, researchers are continually gaining new insights into the structure-activity relationship.

**Dioxopiperazines**

Dioxopiperazines are common metabolites of microorganisms that are distributed in a diverse range of filamentous fungi [23, 24]. Many dioxopiperazines reported from marine-derived fungi display a variety of pharmacological properties, particularly in the field of antitumor and antimicrobial therapy [25].

A new dioxopiperazine alkaloid crystalline (37), together with three known ones, chetomin (38), neoecchinulin A (39), and golmaenone (40) (Fig. 2), were isolated from the mudflat-sediment-derived fungus *C. cristatum*. Compounds 37–40 showed potent radical-scavenging activity against DPPH, with similar IC₅₀ values to that of the positive control (ascorbic acid). Compound 37 also displayed cytotoxic activity against human cervical carcinoma (HeLa) cells, with an IC₅₀ value of 0.5 μM [26].

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**Fig. 1. Cytochalasans produced by marine-derived *Chaetomium* species.**

![Diagram of cytochalasans](image-url)
Recently, cristazine (37) was evidenced to have great potential for inducing apoptosis via the death receptor pathway in human epidermoid carcinoma (A431) cells [27]. Chetomin (38) is an antibiotic discovered more than 70 years ago [28]. Recently, it was found to be a potent HIF-1 inhibitor [29] and exhibited antitumor activity in lung cancer, multiple myeloma, and breast cancer [30-32]. Neoechinulin A (39) was shown to possess a variety of activities, including anti-inflammatory [33], SARS-CoV-2 M<sub>pro</sub> inhibiting [34], cytoprotective [35], memory improvement and antidepressant-like effects [36]. In addition, the structure-activity relationship of neoechinulin A revealed that the presence of a diketopiperazine ring was essential for its antioxidant and anti-nitration activities [37].

**Indole Alkaloids**

Indole alkaloids are the active moiety of several clinical drugs, such as reserpine, tadalafil and fluvastatin, which are all designed based on an indole skeleton [38, 39]. The indole framework is widely distributed in many fungal natural products [40, 41]. Fig. 3 presents the structures of indole alkaloids produced by marine Chaetomium.

Silent fungal Pictet–Spenglerase (FPS) gene activation by 1-methyl-L-tryptophan (1-MT), eight “unnatural” natural indole alkaloids, chaetoglines A–H (42–49), were produced by fish-derived C. globosum 1C51. Compounds 43 and 47 showed potent antibacterial activity against clinic, pathogenic anaerobes with MIC values ranging from 0.24 to 0.66 μM, which were quite comparable to that of the prescribed antibacterial drug tinidazole. Moreover, compound 47 exhibited moderate AChE inhibitory activity with an IC<sub>50</sub> value of 4.13 μM [42]. Subsequently, biotransformation by C. globosum 1C51, six new indole alkaloids, chaetoindolone A–D (50–53),...
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Fig. 4. Azaphilones produced by marine-derived C. globosum OUPS-T106B-6.

19-O-demethylchaetogline A (54) and 20-O-demethylchaetogline F (55), together with two known ones, 42 and 47, were produced. Compound 50 was found to be antibacterial against Xanthomonas oryzae pv. oryzae (xoo), a pathogen causing rice bacterial leaf blight. Compound 42 was shown to be inhibitory against rape pathogenic fungus Sclerotinia sclerotiorum [43].

Azaphilones

Azaphilones are natural products characterized by an oxygenated bicyclic core that bears an oxygenated nonprotonated carbon in position 7, and are widely distributed in fungi [44, 45]. Azaphilones exhibit broad-spectrum biological activities, including anticancer, antioxidant, anti-inflammatory, antibacterial, antifungal and other activities [46]. Chemical investigation of C. globosum OUPS-T106B-6, which was originally isolated from the marine fish Mugil cephalus, resulted in a series of azaphilones being obtained. The compounds included chaetomugilins A–C (56–58) [47], D–F (59–61) [48], G, H (62, 63) [49], I–O (64–70) [50], seco-chaetomugilins A, D (71, 72) [51], 11-epichaetomugilin A (73) and 4’-epichaetomugilin A (74) [52], chaetomugilins P–R (75–77), 11-epi-chaetomugilin I (78) [53], and chaetomugilins S–U (79–81) [54] (Fig. 4). All of these were tested for cytotoxicity against human cancer cell lines, and chaetomugilins A, C, F, and I showed significant cytotoxic activity against 39 cell lines, while other chaetomugilins exhibited selective growth inhibition of some cultured cancer cell lines. Particularly, chaetomugilin I inhibited PINK1/Parkin-mediated mitophagy to enhance apoptosis in A2780 cells induced by cisplatin [55].

From the deep-sea-derived fungus Chaetomium sp. NA-S01-R1, four novel compounds, chaephilone C (82) and chaetoviridides A–C (83–85), together with four known compounds, chaetoviridin A (86), chaetoviridin E (87), chaetomugilin D (59) and cochliodone A (88), were obtained (Fig. 5). Compounds 82–85 exhibited antibacterial activities against Vibrio rotiferianus, V. vulnificus or MRSA. Compounds 82–84 also showed strong cytotoxic activities towards the Hep G2 cell or the HeLa cell lines [56]. Three new azaphilones containing glutamine residues, namely N-glutarylchaetoviridins A–C (89–91), together with two related compounds, chaetomugilins A and C (56 and 58), were isolated from the extract of deep-sea-derived C. globosum HDN151398 (Fig. 5). Compounds 91, 56, and 58 displayed significant cytotoxic activity against a broad spectrum of cancer cell lines [57]. Chemical investigation of the deep-sea-derived fungus C. globosum MP4-S01-7 led to the discovery of eight new nitrogenated azaphilones (92–99) and two known compounds, 86 and 87 (Fig. 5). Most of the compounds exhibited cytotoxicity against the gastric cancer cell lines MGC803 and AGS. Among them, compounds 92, 93, and 96 exerted the most potent activities, with IC50 values less than 1 μM [58].
Except for the antimicrobial and cytotoxic activities mentioned above, chaetomugilins and the closely related chaetoviridins also displayed many other bioactivities. Chaetomugilins A (56), D (59), I (64), J (65), O (70), Q (76) and S (79) were reported to have phytotoxic activity [59, 60]. Compounds 56, 59 and 70 exhibited higher activity than 65 and 76, which could be attributed to the existence of a tetrahydrofuran moiety. Moreover, 70 showed more powerful activity than 56, 59 and 79, suggesting that the lactone rings may reduce the phytotoxic effects [60]. The discovery indicated that chaetomugilins could be utilized for developing natural eco-friendly herbicides. Chaetomugilins I (64) and 11-epi-chaetomugilin I (78) were reported to have anti-inflammatory activity. They could remarkably suppress TNF-induced NF-κB activity with an IC₅₀ value of 0.9 μM [61]. Chaetoviridin E (87) was demonstrated as showing antimalarial activity against Plasmodium falciparum with an IC₅₀ value of 2.9 μg/ml [62]. And finally, chaetoviridin A (86) was indicated to have noticeable antioxidant potential on TLC [63].

Fig. 5. Azaphilones produced by marine-derived Chaetomium species.

Fig. 6. Xanthone derivatives produced by marine-derived Chaetomium species.
Xanthone Derivatives

Xanthones are a class of oxygen-heterocycles containing a γ-pyrone moiety with two aromatic rings. This family of compounds has shown a variety of biological activities, such as α-glucosidase inhibitory activity, antimicrobial activity, anti-inflammatory activity and cytotoxicity [64-69]. Xanthones derived from marine Chaetomium species are shown in Fig. 6.

Three new natural xanthone derivatives, chaetocyclinone A–C (101–103), were produced by the marine alga-derived Chaetomium sp. Gö 100/2. Among them, chaetocyclinone A (101) exhibited inhibitory activity against phytopathogenic fungi Phytophthora infestans [70]. Investigations of the marine fungus Chaetomium sp. 620/GrK 1a led to the discovery of three new fungal polyketide metabolites, chaetoxanthones A–C (104–106). Their antiparasitic activity was tested, and compound 105 showed selective activity against Plasmodium falciparum, while compound 106 displayed a moderate activity against Trypanosoma cruzi [71].

Others

Cultivation of the marine red alga-derived fungus C. globosum revealed a new benzaldehyde secondary metabolite chaetopyranin (110), together with ten known compounds, including two benzaldehyde congeners, 2-(2,3-epoxy-1,3'-heptadienyl)-6-hydroxy-5-(3-methyl-2-butenyl)benzaldehyde (111) and isotetrahydroauroglucin (112), two anthraquinone derivatives, erythroglucin (113) and parietin (114), five asperentin derivatives including asperentin (115), 5'-hydroxy-asperentin-8-methylether (116), asperentin-8-methylether (117), 4'-hydroxyasperentin (118) and 5'-hydroxyasperentin (119) (Fig. 7). Compounds 110–113 were evidenced to have moderate DPPH radical-scavenging properties. Compound 110 was also found to have cytotoxicity toward several tumor cell lines [72]. Successive fractionation of the marine fungal Chaetomium sp. resulted in obtaining a novel benzonaphthyridinedione derivative, chaetominedione (120), and two known fungal metabolites, 2-furancarboxylic acid (121) and 5-(hydroxymethyl)-2-furancarboxylic acid (122) (Fig. 7). Compounds 120 and 122 showed significant inhibitory activity toward TK p56lck tyrosine kinase [73].

Conclusion

This review summarized 122 secondary metabolites with potent bioactivities derived from marine environment species, reported from 2001 to 2021, and which will benefit future drug development and innovation. As for the structure types of the compounds, we covered cytochalasans (29.51%), dioxopiperazines (3.28%), indole alkaloids (12.30%), azaphilones (36.89%), xanthone derivatives (4.92%) and others (13.11%), indicating the chemical diversity of marine Chaetomium. The natural products originating from marine-derived Chaetomium species also showed a multiplicity of biological activity, including cytotoxicity, enzyme inhibitory activity, radical-scavenging activity, antiparasitic, antibacterial, and antifungal activity.

It is noteworthy that most of the metabolites were isolated from C. globosum strains. When compared to the large number of species (more than 100) contained in Chaetomium, very few have been screened for the production of interesting secondary metabolites. This situation may be attributed to the difficulty in cultivating marine microorganisms, especially certain deep-sea-derived fungi that cannot survive under normal laboratory conditions and therefore must be cultured using nontraditional techniques [74, 75]. As a result, the potential of Chaetomium genus derived from marine Chaetomium remains virtually untapped.

Fig. 7. Other compounds produced by marine-derived Chaetomium species.
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Conflict of Interest

The authors have no financial conflicts of interest to declare.

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