Anthraquinones and Their Analogues from Marine-Derived Fungi: Chemistry and Biological Activities

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Abstract: Anthraquinones are an interesting chemical class of polyketides since they not only exhibit a myriad of biological activities but also contribute to managing ecological roles. In this review article, we provide a current knowledge on the anthraquinoids reported from marine-derived fungi, isolated from various resources in both shallow waters such as mangrove plants and sediments of the mangrove habitat, coral reef, algae, sponges, and deep sea. This review also tentatively categorizes anthraquinone metabolites from the simplest to the most complicated scaffolds such as conjugated xanthone–anthraquinone derivatives and bianthraquinones, which have been isolated from marine-derived fungi, especially from the genera Apergillus, Penicillium, Eurotium, Altenaria, Fusarium, Stemphylium, Trichoderma, Acremonium, and other fungal strains. The present review, covering a range from 2000 to 2021, was elaborated through a comprehensive literature search using the following databases: ACS publications, Elsevier, Taylor and Francis, Wiley Online Library, MDPI, Springer, and Thieme. Thereupon, we have summarized and categorized 296 anthraquinones and their derivatives, some of which showed a variety of biological properties such as enzyme inhibition, antibacterial, antifungal, antiviral, antitubercular (against Mycobacterium tuberculosis), cytotoxic, anti-inflammatory, antifouling, and antioxidant activities. In addition, proposed biogenetic pathways of some anthraquinone derivatives are also discussed.

Keywords: anthraquinones; hydroanthraquinones; bianthraquinones; marine-derived fungi; Apergillus sp.; Penicillium sp.; antibacterial activity; cytotoxicity

1. Introduction

Phylogenetically and functionally, fungi are ubiquitous organisms living in associations with almost all viable resources such as plants and animals to complement the nutrient cycling in various ecosystems on Earth [1]. Currently, marine mycology has been somewhat neglected, and most of the fungal diversity normally refers to their terrestrial counterparts. To this respect, although ca. 75% of the Earth’s surface is occupied by seas and oceans, harboring small organisms to the largest ones, there are still only about 1000 fungal species that are derived from terrestrial ancestors [2]. Marine-derived fungi are found in diverse habitats and have significant ecological functions. According to Kohlmeyer et al., the filamentous fungi in the marine environment are generally divided into two groups and ecotypes: (i) obligate species, which are originally living in the salt-free waters or estuarine, and (ii) facultative species, which transited from terrestrial and freshwater milieux needing
to have a physiological adaptation for survival [3]. Therefore, the marine fungal habitats involve deep-sea sediments, hydrothermal vents, arctic ice and snow, sandy and tidal regions, driftwood, seagrasses, mangroves, and coastal salt marshes. These organisms are more likely to adapt to live on or inside other living organisms such as phytoplanktons, marine mammals, algae, corals, sponges, invertebrates and even dinoflagellates and diatoms (primary producers) to either balance or manage the global carbon cycles [1]. The first report of marine-derived fungi, collected in marine environments, dates back to 19th-century research when the use of microscopes and culture media blossomed [4]. Over the last few decades, the interest in mycochemistry of marine-derived fungi has increased dramatically since the 1990s due to the discovery of bioactive compounds with possible pharmaceutical applications [5]. To date, a large number of fungi that are isolated from the marine ecosystems belong to a few genera including *Aspergillus*, *Penicillium*, *Cladosporium*, *Aureobasidium*, *Cryptococcus*, and *Malassezia*, which were isolated from various environmental niches ranging from the deep sea all the way to surface waters [6]. Furthermore, marine-derived fungi have a versatile biosynthetic machinery capable of biosynthesizing a myriad of secondary metabolites of different chemical classes such as alkaloids, polyketides, meroterpenoids, terpenoids, steroids, and peptides [7,8]. Among fungal secondary metabolites, polyketides are the most structurally diverse and pharmacologically relevant natural products with low toxicity and high efficacy, many of which exhibit cytotoxic effects on cancer cells [9,10]. These include anthraquinones, hydroxyanthraquinones, naphthalenes, naphthoquinones, macrolides, polyenes, tetracyclines, and tropolones that are responsible for a broad range of bioactivities viz. antimicrobial, antifungal, antiviral, antioxidant, anti-inflammatory, anti-fouling, cytotoxicity, inhibition of various enzymes including protein kinases and enzymes related to diabetes [11,12].

By increasing the body of marine-derived fungi literature, this comprehensive review aims to present an update of the previous reviews [11,13], providing the latest classification of all the anthraquinones isolated thus far from the marine-derived fungi. In the following subsections, the review starts with the biosynthesis of anthraquinones. Subsequently, chemistry and some relevant structural features, and species-specific anthraquinones from marine-derived fungi are discussed. The databases used to search for anthraquinone metabolites and the keywords were Google Scholar, PubMed, Scopus, and Web of Science.

2. Biosynthesis of Anthraquinone Scaffold

The biosynthesis of anthraquinones in plants is different from that in fungi since there are two distinct pathways in plants, i.e., the shikimate and the acetate–malonate pathways, while the acetate–malonate pathway is a uniquely reported pathway in fungi for the biosynthesis of these polyketides. The biosynthesis of anthraquinones is regulated by non-reducing polyketide synthases (NR-PKs) comprising the acyl carrier protein (ACP), which provides the regioselective cyclization of a β-polyketide chain to yield various aromatic metabolites. The polyketide pathway providing anthraquinones consists of successive Claisen condensations of malonyl-CoA units (extender units) with acetyl-CoA (a starter unit), leading to the β-ketoacyl-S-ACP intermediate as the product template (PT) domain. Depending on the regioselectivity of the cyclization of the first ring and the size of the final product, PT undergoes either C4-C9 or C6-C11 cyclizations, followed by aldol reaction, enolization, oxidation, and decarboxylation, resulting in the formation of the anthraquinone scaffold (Figure 1) [14,15].
Figure 1. Plausible biosynthetic pathways of fungal anthraquinones.

By using suitable cultivation methods, many fungal species have been isolated from the submerged areas such as sea water, sediments, sponges, algae, mangrove plants, etc., that are routinely producing anthraquinone compounds. Some of the predominant fungal strains viz. Aspergillus sp., Penicillium sp., Eurotium sp., Fusarium sp., and Alternaria sp. have been reported in aquatic ecosystems [6]. To a lesser extent, other species that are able to biosynthesize biologically active anthraquinones such as Acremonium sp., Amorosia sp., Chaetomium sp., Cladosporium sp., Guignardia sp., Curvularia sp., Engyodontium sp., Geotrichum sp., Gliocladium sp., Halorosellinia sp., Microsphaeropsis sp., Microsporum sp., Monodictys sp., Neosartorya sp., Nigrospora sp., Paeilomyces sp., Phoma sp., Phomopsis sp., Scopulariopsis sp., Sporendonema sp., Stemphylium sp., Talaromyces sp., Thermomyces sp., Trichoderma sp., and Xylaria sp. have also been isolated from the marine environments ranging from decayed plants to living macro-organisms. In the following sections, we have tentatively categorized marine fungal anthraquinones from the simplest to the most complex structures.

3. Anthraquinoid Polyketides and Their Analogues from Marine-Derived Fungi

A comprehensive literature survey of anthraquinoid polyketides covering the period from 2000–2021 was undertaken. In order to facilitate the discussion of the reported anthraquinones from marine-derived fungi, they are classified according to the complexity of the substituents on the anthracene-9,10-dione scaffold as follows: anthraquinones (I), tetrahydroanthraquinones (II), 5,8-anthraquinones (III), tetrahydro-5,8-anthraquinones (IV), anthrones (V), tetrahydro-9-hydroxyanthrones (VI), anthrols (VII), 9,10-dihydroxyanthracenes (VIII), azaanthraquinones (IX) (Figure 2), dimeric anthraquinones, and anthraquinone analogues fused with xanthone and chromone derivatives.
3.1. Anthraquinones

3.1.1. Simple Anthraquinones

In general, anthraquinones (9,10-dioxoanthracene or anthracene-9,10-dione) represent the type of pigments possessing a \( p \)-quinone moiety as a central ring of the anthracene scaffold. Replacing each hydrogen atom of the benzene rings with simple substituents such as hydroxyl, methoxy, methyl or its oxidation analogs (hydroxymethyl, formyl and carboxyl groups), prenyl group, and other substituents leads to diverse anthraquinoid compounds [11].

Buttachon et al. reported the isolation of emodin (1) (Figure 3) from the culture extract of *Aspergillus candidus* KUFA0062, isolated from a marine sponge *Epipolasis* sp., which was obtained from the coral reef at the Similan Island National Park, Phang-Nga province, Thailand [16]. Compound 1 was also obtained from the ethyl acetate (EtOAc) extract of the culture of *Penicillium ochrochloron*, isolated from the underwater sea sand, which was collected from the North Sea in St. Peter-Ording, Germany [17]. In another study, Wang et al. isolated 1 and questin (2) (Figure 3) from a solid culture extract of *A. flavipes* HN4-13, obtained from a Lianyungang coastal sediment from Jiangsu Province, China [18]. Liu et al. also isolated 1 from the culture extract of a marine-derived *Aspergillus* sp. LS57, isolated from a marine sponge *Haliclona* sp., which was collected at Lingshui, Hainan Province, China [19]. The mycelial extract of *A. terreus* DTO 403-C9, isolated from the leaves of an unidentified mangrove tree, which was collected at Khanh Hoa Province, Vietnam, furnished 2 and a new naturally occurring 1,2,5-trihydroxy-7-methyl-9,10-anthraquinone (3) (Figure 3) [20].
A DPPH• radical scavenging activity-guided fractionation of the culture extract of *A. europaeus* WZXY-SX-4-1, isolated from a marine sponge *Xestospongia testudinaria*, which was collected on Weizhou Island, Guangxi Province, China, resulted in the isolation of 1-methyl emodin (*4*) and dermolutein (*5*) (Figure 3) [21]. The culture extract of *A. glaucus* HB1-19, isolated from a marine sediment collected in Fujian Province, China, furnished 1 and 2, together with physcion (*6*), catenarin (*7*), and rubrocristin (*8*) (Figure 3) [22]. Compound 6 is a common fungal anthraquinone since it was obtained from several sources such as the culture extract of *A. wentii* EN-48, isolated from a marine brown alga *Sargassum* sp. [23], the EtOAc extract of the culture of *Eurotium repens*, isolated from a marine sponge *Suberites domuncula*, collected near Zelenyi Island (Kuril Islands) [24], the fermentation extract of *E. cristatum*, isolated from a marine sponge *Mycale* sp., which was collected from Wonnapa Beach, Bangsaen, Chonburi Province, Thailand [25], the culture broth extract of *Microsporum* sp. MPSYL, isolated from a marine red alga *Lomentaria catenata*, which was collected from Guryongpo, NamGu, PoHang, Republic of Korea [26], and the fermentation extract of *Penicillium* sp. ZZ901, isolated from a sample of a wild bivalve *Scapharca broughtonii* (Schrenck), which was collected from the Sea Shoal, China [27].

The culture extract of *Aspergillus tritici* SP2-8-1, isolated from a soft coral, *Galaxea fascicularis*, which was collected at Port Dickson, Malaysia, yielded besides 1, 3-hydroxy-1,2,5,6-tetramethoxyanthracene-9,10-dione (*9*), 3-hydroxy-2-hydroxymethyl-1-methoxyanthracene-9,10-dione (*10*) and 1,2,3-trimethoxy-7-hydroxymethylanthracene-9,10-dione (*11*) (Figure 3) [28].

The culture extracts of the algicolous fungi, viz. *Aspergillus wentii* (pt-1), *A. ustus* (cf-42), and *A. versicolor* (dl-29 and pt-20), possessing algicidal property, afforded algicidal property, afforded 1,5-dihydroxy-3-methoxy-7-methylanthraquinone (*12*), 1,3,5-trihydroxy-7-methylanthraquinone (*13*), and 5-hydroxy-2,4-dimethoxy-7-methylanthraquinone (emodin-6,8-dimethyl ether; *14*) (Figure 3) [29]. Compound 14 was also reported from the culture extract of the strain *A. wentii* EN-48, isolated from a marine macroalga *Sargassum* sp. [30].

The culture extract of *Eurotium chevalieri* KUFA0006, isolated from the inner twig of a mangrove plant, *Rhizophora mucronata* Poir, which was collected in the Eastern Seaboard of Thailand, yielded 1, 2, 6 and questinol (*15*) (Figure 3) [31]. Fractionation of the culture extract of an algicolous fungus, *Chaetomium globosum*, isolated from the inner tissue of a marine red alga, *Polysiphonia urceolata*, which was collected from the Qingdao coastline, resulted in the isolation of 7 and erythroglaucin (*16*) (Figure 3) [32].
Fallacinol (17) (Figure 3) was isolated, together with 1 and 15 (Figure 3), from the fermentation extract of *Talaromyces stipitatus* KUFA 0207, obtained from a marine sponge *Stylissa flabelliformis*, which was collected at a depth of 10–15 m from the coral reef at Samaesarn Island in the Gulf of Thailand [33].

The culture extract of *Aspergillus versicolor*, isolated from the inner tissue of a green alga, *Halimeda opuntia*, which was collected at a depth of 5–8 m from the coast of Rass Mohamed of Red Sea (South Sinai, Egypt), furnished evariquinone (18) and 7-hydroxyemodin-6,8-dimethyl ether (19) (Figure 3), in addition to 1 and 4 (Figure 3) [34].

2-(Dimethoxymethyl)-1-hydroxyanthracene-9,10-dione (20), 1-hydroxy-2-methylanthracene-9,10-dione (21), 2-methylanthracene-9,10-dione (22), damnacanthal (23), rubiadin (24), xanthopurpurin (25), rubianthraquinone (26) and 6-hydroxyrubiadin (27) (Figure 4) were isolated, together with 1 (Figure 3), from the fermentation extract of *A. versicolor*, obtained from a deep-sea sediment [35].

Further anthraquinones viz. citreorosein (28), chrysophanol (29) and aloe-emodin (30) (Figure 4) were isolated, together with 1 (Figure 3), from the mycelial extract of *Penicillium oxalicum* 2HL-M-6, which was obtained from a sea mud in Bohai Bay, China [36].

Khamthong et al. reported the isolation of 1, 28 and 29 (Figure 4) from the fermentation extract of *P. citrinum* PSU-F51, which was obtained from a gorgonian Sea fan (*Annella* sp.), collected at the Similan Islands, Phangnga Province, Thailand [37].

Figure 4. Structures of 20–43.
Ren et al., in the screening for cytotoxic agents against human myeloid leukemia K562 cell line, described the isolation of 1 and 28 from the culture extract of Gliocladium sp. T31, which was isolated from a marine lichen collected from the South Pole [38]. Compounds 1 (Figure 3), 28, and 29 (Figure 4) were reported from the culture broth extract of a gorgonian coral-derived Penicillium sp. SCGAF0023 [39], whereas 28 and 29 were also reported from the fermentation extract of Fusarium equiseti, isolated from a brown alga, Padina pavonica, collected from the Red Sea [40].

Chemical investigation of the fermentation extract of an endophytic fungus, Penicillium citrinum HL-5126, isolated from the mangrove plant, Bruguiera sexangula var. rhynchopetala, which was collected in the South China Sea, resulted in the isolation of 2 (Figure 3) and 28 (Figure 4) [41]. Compounds 1 (Figure 3) and 29 (Figure 4) were also reported from the EtOAc extract of the mycelial extract of Paecilomyces sp. (Tree1-7), isolated from a mangrove saprophytic bark from the Taiwan Strait [42], and from the culture extract of Aspergillus candidus KUFA0062, isolated from a marine sponge, Epipolasis sp., which was obtained from the coral reef at the Similan Island National Park, Phang-Nga province, Thailand [16].

Purification of the culture broth extract of Trichoderma sp. (H-1), isolated from a surface muscle of a sea cucumber, which was collected from Chengshantou Island, Yellow Sea, China, also afforded 1 (Figure 3) and 29 (Figure 4) [43]. Compound 29 (Figure 4) was also reported from the culture extract of an unidentified marine red alga-derived fungus (strain F-F-3C), which was collected at the coast of Tarama Island, Okinawa, Japan [44].

The chloroform-soluble portion of the methanol (MeOH) extract of a culture of Penicillium sp. strain F01V25, isolated from a marine alga, Dictyosphaeria versluyii, collected near Dravuni, Fiji, yielded carviolin (31) (Figure 4) [45]. Purification of a MeOH-soluble extract of Penicillium sp. SCSIsosolf101, isolated from sediment samples, collected in the South China Sea (2448 m depth), also afforded an emodin derivative, named emodic acid (32) (Figure 4) [46]. Compounds 1 (Figure 3) and 32 (Figure 4) were also isolated from the culture extract of Eurotium rubrum, which was obtained from the inner tissue of a semi-mangrove plant, Hibiscus tiliaceus, collected from Haiinan island, China [47].

Macrosporin (33), 1,7,8-trihydroxy-3-methoxy-6-methylanthraquinone (34), and 1-hydroxy-3-methoxy-6-methylanthraquinone (35) (Figure 4) were isolated from the mycelial extract of Penicillium sp., obtained from a soft coral, Sarcophyton tortuosum, which was collected in the South China Sea [48]. Compound 33 was also reported from the culture extract of a marine-derived fungus, Alternaria sp. ZJ-2008003, which was isolated from a soft coral, Sarcophyton sp., collected from the South China Sea [49], as well as from the solid-rice culture extract of an endophytic fungus, Stemphylium sp. 33231, isolated from a mangrove plant, Burguiera sexangula var. rhynchopetala, which was collected in the South China Sea [50], as well as from the solid-rice culture extract of S. lycopersici, isolated from the inner tissue of a gorgonian soft coral, Dichotella gymnaca, collected from the South China Sea [51]. Compounds 33 and 35 (Figure 4) were also isolated from the fermentation extract of Phomopsis sp. PSU-MA214, which was obtained from the leaves of a mangrove plant, Rhizophora apiculata Griff. Ex T. Anderson, collected from Songkhla province, Thailand [52].

Chemical investigation of Eurotium chevalieri MUT2316, isolated from the Atlantic sponge, Grantia compressa, afforded cinnalutein (36) (Figure 4), together with 6 (Figure 3) [53], while the culture extract of E. chevalieri KUFA0006, isolated from the inner twig of a mangrove plant, Rhizophora mucronata Poir, which was collected in the Eastern Seaboard of Thailand, yielded acetylquestinol (37) (Figure 4), in addition to 1, 2, 6 and 15 (Figure 3) [31]. Compound 37 was also obtained from the culture extract of Neosartorya spinosa KUFA 1047, isolated from a marine sponge, Mycale sp., which was collected from a coral reef at Samae San Island, Chonburi province, Thailand [54].

Pachybasin (38), phomarin (39), 1-hydroxy-3-hydroxymethylanthraquinone (40), and ω-hydroxydigitoeminodin (41) (Figure 4) were isolated, together with 1 (Figure 3) and 29 (Figure 4), from the fermentation extract of Trichoderma harzianum (XS-20090075), isolated from the inner tissue of a soft coral, which was collected from the coral reef at Xisha Island in the South China Sea [55]. A defatted culture extract of Trichoderma sp. strain...
SCSIO41004, isolated from a marine sponge, *Callyspongia* sp., which was collected from the sea area near Xuwen County, Guangdong province, China, furnished 1,3,6-trihydroxy-8-methylanthraquinone (42) (Figure 4) [56].

She et al. described the isolation of 1,4-dihydroxy-2-methoxy-7-methylanthracene-9,10-dione (43) (Figure 4) from the culture extract of an estuarine fungus, *Halorosellinia* sp. (no. 1403). The structure of 43 was confirmed by a single-crystal X-ray diffraction analysis [57].

Mycelial and broth extracts of a mangrove endophytic fungus, *Halorosellinia* sp. (no. 1403), isolated from a decayed woody tissue of a mangrove tree, *Kandelia candel* (L.) Druce., which was collected from Mai Po, Hong Kong, yielded 1,4,6-trihydroxy-2-methoxy-7-methylanthracene-9,10-dione (44), demethoxyaustrocortirubin (45), 1-hydroxy-3-methyl-9,10-anthraquinone (46), and austrocortinin (47) (Figure 5) [58]. Compound 47 (Figure 5) was also isolated from the broth culture extract of *Fusarium* sp. PSU-F14, isolated from a gorgonian sea fan, which was collected near Koh Hin Ran Pet, Suratthani Province, Thailand [59].

Figure 5. Structures of 44–59.

El-Beih et al., reported the isolation of monodictyquinone A (48) (Figure 5), together with 1 (Figure 3), 29 and 38 (Figure 4), from the EtOAc-soluble fraction of the ethanol (EtOH) extract of *Monodictys* sp., which was isolated from a sea urchin, *Anthocidaris crassispina*, collected from Toyama Bay in the Sea of Japan [60].

Rheoemodin (49) (Figure 5) was isolated, together with 1, 15, 17 (Figure 3) and 28 (Figure 4) from the fermentation extract of *Talaromyces stipitatus* KUFA 0207, which was obtained from a marine sponge, *Stylissa flabelliformis*, collected from the coral reef at Samaesarn Island in the Gulf of Thailand [33].
Marcrospin (50) (Figure 5) and 6 (Figure 3) were isolated from the mycelial extract of Altenaria sp. ZJ9-6B, isolated from fruits of a mangrove tree, Aegiceras corniculatum, collected in Zhanjiang mangrove, Guangdong province, China [61]. Chemical investigation of the broth culture extract of Altenaria sp. (SK11), isolated from the root of a mangrove tree, Excoecaria agallocha, from Shankou, Guangxi province, China, yielded 6-methylquinizarin (51) (Figure 5), together with 47 [62]. 6-O-Methylalaternin (52) (Figure 5) was obtained from a culture extract of Altenaria tenuissima DFFCS013, which was isolated from a sediment collected at a depth of 2403 m from the South China Sea [63].

Jadulco et al. reported the isolation of lunatin (53) (Figure 5) from the culture extract of Curvularia lunata, which was isolated from a marine sponge, Niphates olemda, collected in the Bali Bata National Park in Indonesia [64]. By using bioactivity-guided purification approach, Ren et al. also isolated 1 (Figure 3), 28 (Figure 4), and 53 (Figure 5) from the fermentation extract of Gliocladium catenulatum T31, isolated from marine sediment samples [65].

1,3-Dihydroxy-6-hydroxymethyl-7-methoxyanthraquinone (54) and 1,3-dihydroxy-6-methyl-7-methoxyanthraquinone (55) (Figure 5) were isolated from a defatted culture extract of Thermomyces lanuginosus Tsikl KMM 4681, obtained from a marine sediment from the South China Sea, Vietnam [66], while 7-methoxymacrosorpin (56) and 7-(γ,γ)-dimethylallylamacrosorpin (57) (Figure 5) were isolated from the culture extract of an endophytic fungus, Phoma sp. L28, obtained from the roots of a mangrove plant, Myoporum bontioides A. Gray, which was collected in Leizhou peninsula, Guangdong province, China [67].

3,5,8-Trihydroxy-7-methoxy-2-methylanthracene-9,10-dione (58) and 47 (Figure 5) were obtained from the culture extract of Nigrospora sp. ZJ-2010006, isolated from an unidentified sea anemone, which was collected from the Weizhou coral reef in the South China Sea. In order to evaluate the antibacterial activity of their analogs, 47 and 58 were acetylated to give a series of acetylated antraquinones viz. 8-acetoxyaustrocortirubin (47a), 8-acetoxy-3,5-dihydroxy-7-methoxy-2-methylanthracene-9,10-dione (58a), 5-acetoxy-3,8-dihydroxy-7-methoxy-2-methylanthracene-9,10-dione (58b), 3-acetoxy-5,8-dihydroxy-7-methoxy-2-methylanthracene-9,10-dione (58c), 5,8-diacetoxy-3-hydroxy-7-methoxy-2-methylanthracene-9,10-dione (58d), 3,8-diacetoxy-5-hydroxy-7-methoxy-2-methylanthracene-9,10-dione (58e), 3,5-diacetoxy-8-hydroxy-7-methoxy-2-methylanthracene-9,10-dione (58f), and 3,5,8-triacetoxy-7-methoxy-2-methylanthracene-9,10-dione (58g) (Figure 5) [68]. The fermentation extract of the same fungus, isolated from the inner tissue of the zoathid, Palythoa haddoni (GX-WZ-20100026), collected from coral reefs in the South China Sea, also furnished both 47 and 58 (Figure 5) [69].

1,6,8-Trihydroxy-4-benzoyloxy-3-methylanthraquinone (59) (Figure 5) was isolated, together with 2, 6 and 7 (Figure 3), from the culture extract of Eurotium sp. SCSIO F452, obtained from sediment samples collected from the South China Sea [70].

Brauers et al. reported the isolation of three 1,3,6,8-tetrahydroxyanthraquinone analogues, 60–62 (Figure 6), from the culture extract of Microsphaeropsis sp., obtained from fresh samples of a marine sponge, Aplysina aerophoba, which was collected from Banyuls-sur-Mer in Southern France. The absolute configuration of the stereogenic carbon of the substituent on C-2 of 60–62 was established as R by comparison of their calculated and experimental electronic circular dichroism (ECD) spectra [71,72]. Fractionation of a defatted culture extract of a marine sponge-associated fungus, Trichoderma sp. strain SCSIO41004, led to the isolation of 7-acetyl-1,3,6,8-tetrahydroxyanthracene-9,10-dione (63) and ZSU-H85 (64) (Figure 6) [56].
Zhao et al., in their screening program to search for metabolites with anti-phytopathogenic bacterial and fungal activities, as well as cytotoxicity, found that the culture extract of *Fusarium equiseti*, isolated from the intertidal marine plants of the Yellow Sea in Qingdao, China, showed interesting bioactivities. Further fractionation of the culture extract led to the isolation of 63 and (11S)-1,3,6-trihydroxy-7-(1-hydroxyethyl) anthracene-9,10-dione (65) (Figure 6). The absolute configuration of the stereogenic center (C-11) in 65 was determined as S by comparison of its calculated and experimental ECD spectra [73]. Compound 65 (Figure 6) was also isolated from the culture extract of *Cladosporium* sp. HNWSW-1, isolated from fresh roots of a mangrove plant, *Ceriops tagal*, which was collected from Dong Zhai Gang Mangrove Reserve in Hainan province, China [74].
The mycelial extract of *Fusarium sp.* (strain no. b77), obtained from the Shenzhen coast, Guangzhou, China, provided 5-acetyl-2-methoxy-1,4,6-trihydroxyanthraquinone (66) and 1-acetoxy-5-acetyl-2-methoxy-4,6-trihydroxyanthraquinone (67) (Figure 6) [75], while isorhodoptilometrin (68) (Figure 6) was isolated from the mycelial extract of a sea mud-derived *Penicillium oxalicum* 2HL-M-6 [36]. Ren et al. isolated 68 from the active extract of a marine lichen-derived *Gliocladium* sp. T31 [38]. Compound 68 was also obtained from the fermentation extract of a sea-sediment-derived *G. catenulatum* T31, using antitumor activity-guided purification approach [65].

The isorhodoptilometrin derivative, (−)-2′R-1-hydroxyisorhodopilometrin (69) (Figure 6), was obtained from the culture extract of *Penicillium* sp. OUCMDZ-4736, isolated from a sediment surrounding the roots of a mangrove plant, *Acanthus ilicifolius*, collected at Wenchang, Hainan Province, China. The absolute configuration of the stereoergic carbon in 69 was determined as 12R, based on a comparison of the experimental ([α]_{D}^{25} − 56.0) and calculated optical rotation values, which was in contrast with that of (+)-2′S-1-hydroxyisorhodopilometrin ([α]_{D}^{25} + 30) [76]. Isorhodoptilometrin-1-methyl ether (70) (Figure 6) was isolated from the EtOAc extract of a culture of an algicolous fungus, *A. versicolor* [34].

(+)-2′S-Isorhodoptilometrin (71) (Figure 6) was isolated, together with 1 (Figure 3), 29, and 38–41 (Figure 4), from the fermentation extract of a soft coral-associated *Trichoderma harzianum* (XS-20090075) [55]. Nalgiovensin (72) (Figure 6), an anthraquinone with a 2′-hydroxypropyl substituent on C-5, was reported from a defatted EtOAc extract of the culture of the asexual morph of a marine alga-associated *A. alliaceus* (teleomorph: *Petromyces alliaceus*). The absolute configuration of the hydroxyl-bearing stereoergic carbon of the side chain was determined as 2′S by X-ray crystallographic analysis [77].

1-Methyl ether of nalgiovensin (73) (Figure 6) was also isolated, together with 14, 19 (Figure 3) and 28 (Figure 4), from the MeOH fraction of the mycelial extract of a deep-sea-derived fungus, *Emericella* sp. SCSIO 05240, which was isolated from sediment samples collected from the South China Sea at a depth of 3258 m [78].

Chemical investigation of the culture extract of a marine sponge-associated fungus, *Neosartorya spinosa* KUFA 1047, led to the isolation of two alkylated anthraquinones, penipurdin A (74) and acetylpenipurdin A (75) (Figure 6). The absolute configuration of C-2′ in 75 was suggested to be the same as that of 74, i.e., 2′S, on the basis of the biogenic consideration [54].

1,3,6-Trihydroxy-7-(dihydroxypropyl)-anthraquinone (76) (Figure 6) was isolated from a defatted culture extract of a marine sediment-derived fungus, *Thermomyces lanuginosus* Tsikl KMM 4681. The relative configurations of C-15 and C-16 of a diol side chain in 78 were determined by the observed correlations in the NOESY (Nuclear Overhauser Effect Spectroscopy) spectrum and the value of the coupling constant of the vicinal protons, as well as the presence of magnetically non-equivalent methyl groups of its acetone (76a) (Figure 6). The absolute configurations of C-15 and C-16 in 76 and 76a were established as 15R,16S by comparison of their calculated and experimental ECD spectra [66].

6,8-Dimethoxy-1-methyl-2-(3-oxobutyl)-anthrakunthone (77) (Figure 6) was isolated from the culture extract of a marine mangrove endophytic fungus, *Fusarium* sp. ZZF60, from the South China Sea [79], whereas norsolorinic acid (78) (Figure 6), a tetrahydroxyanthraquinone with a hexanoyl substituent on C-2, was purified by ethanol stress strategy from a combination of EtOAc and acetone/water extracts of the culture of *Aspergillus nidulans* MA-143, isolated from fresh leaves of a mangrove plant, *Rhizophora stylosa* [80].

The acetone/EtOAc extract of mycelia of *A. punicus* SCSIO Z021, isolated from a deep-sea sediment, which was collected from Okinawa Trough (1589 m depth), afforded the undescribed anthraquinones, 8-O-methyl versiconol (79), 2′,3′-dihydroxy versiconol (80), and the previously reported methyl averantin (81) and versiconol (82) (Figure 7). The stereoergic carbon (C-2′) of the 1,4-dihydroxy-butan-2-yl substituent of 79 was determined as 2′S based on the highly similarity of the cotton effects (CEs) at 388, 314, and 235 nm, as well as of its ECD spectrum to those of aspergilol I. However, the absolute configurations of
the stereogenic carbons, C-2' and C-3', of the 1',2',3',4'-tetrahydroxybutan-2-yl substituent in 80 remained unassigned [81].

Figure 7. Structures of 79–95.

The undescribed 6,8-di-O-methylaverantin (83) and the previously reported 6,8-di-O-methylversiconol (84) (Figure 7) were obtained from the combined MeOH and EtOAc extracts of *A. versicolor* EN-7, isolated from a brown alga, *Saragassum thunbergii*, which was collected from the Qingdao coastline of Shandong Province, China. The absolute configuration of the stereogenic carbon of the side chain of 83 (C-1') was determined as S by comparison of its optical rotation ([α]_D^20 = 92.2) with that of (−)-averantin ([α]_D^22 = −138°) [82]. Compound 84 was also isolated from the culture extract of a mangrove endophytic fungus, ZSUH-36, isolated from the Shenzhen mangrove, *Acanthus ilicifolius* Linn. [83].
Averantin (85) was isolated, together with 81 and 82 (Figure 7), from the culture extract of *A. versicolor*, isolated from a marine sponge, *Petrosia* sp., which was collected at the depth of 20 m at Jeju Island, Korea [84]. Compounds 82 and 85 (Figure 6) were also isolated from a culture broth of a marine-derived *Penicillium falvum* SHK1-27 by bioassay-guided isolation approach [85].

6,8,1'-Tri-O-methylaverantin (86) (Figure 7) was isolated, together with 81, from the mycelial extract of a mangrove endophytic fungal strain ZSUH-36, which was isolated from the Shenzhen mangrove, *Acanthus ilicifolius* Linn. [86]. Compound 86 was also obtained from the culture extract of a marine-derived fungus, *Aspergillus* sp. SF-6796, isolated from a marine organism collected from the Ross Sea, Antarctica [87].

Averythrin (87) (Figure 7) was obtained, together with 80 and 85, from the culture broth extract of *A. versicolor* INF 16–17, isolated from the inner tissue of an unidentified marine clam [88]. Compounds 81, 85, and 87 (Figure 7) were also obtained from the culture extract of *A. versicolor* A-21-2-7, isolated from a deep-sea sediment from the South China Sea [89]. Compound 87 was also obtained from the fermentation extract of a mangrove endophytic fungus, *Aspergillus* sp. 16-5C, which was isolated from the leaves of a mangrove tree, *Sonneratia apetala*, collected at Hainan Island, China [90].

The combined acetone and EtOAc culture extracts of *Aspergillus* sp. SCSIO F063, isolated from a deep-sea sediment from the South China Sea, furnished (1'S)-6,1’-O,O-dimethylaverantin (88), (S)-(−)-averantin (89), 6-O-methylaverantin (90), and averantin-1'-butyl ether (91) (Figure 7), in addition to 81 and 87 (Figure 7). The absolute configuration of the stereogenic center at C-1’ in 88 was assigned as S based on its negative value of rotation ([α]D25 = −140°), which was the same as that of the previously described 89 ([α]D25 = −138°) and 90 [91].

Aspergilol I (92), SC3-22-3 (93), and coccoquinone A (94) (Figure 7) were isolated, together with 81 and 82, from the culture broth extract of *A. versicolor* SCSIO-41502, which was obtained from marine sediment samples collected from the South China Sea. The absolute configuration of C-16 in 92 was determined as S by comparison of its circular dichroism (CD) spectrum with that of the previously described (1'S)-7-chloroaverantin, while the absolute configuration of C-19 was established by the modified Mosher’s method. Moreover, the absolute configuration of C-16 in 93 and 94 was also determined as S by comparison of their CD spectra and optical rotations ([α]D25 = 30.6° for 93 and −11.1° for 94) with those of (1’S)-7-chloroaverantin [92].

Versiconol B (95) (Figure 7) was isolated, together with 81, from the culture extract of *Aspergillus* sp. F40, isolated from a marine sponge, *Callyspongia* sp., which was collected from the sea area near Xwumen County, Guangdong Province, China. The absolute configuration of a stereogenic carbon (C-1’) in 95 was established as S by comparison of its optical rotation ([α]D25 = −38.6°) with that of 82 ([α]D25 = 101.5°) [93].

The culture extract of a marine sponge-associated fungus, *A. europaeus* WZXY-SX-4-1, furnished (+)-1-O-demethylvariecolorquinone A (96) and (+)-variecolorquinone A (97) (Figure 8) [21]. The NMR data of 96 were identical to those of the previously described (2S)-2,3-dihydroxypropyl-1,6,8-trihydroxy-3-methyl-9,10-dioxoanthracene-2-carboxylate, a demethylated analogue of variecolorquinone A. Since the specific rotation of 96 was dextrorotatory ([α]D22 + 25° in MeOH), while that of the previously reported (2S)-2,3-dihydroxypropyl-1,6,8-trihydroxy-3-methyl-9,10-dioxoanthracene-2-carboxylate was levorotatory ([α]D22 = −23° in MeOH) [94], the absolute configuration 2'R was assigned for 96 [21]. The same authors also reported the isolation of 97 from the culture extract of *A. glaucus* HBI-19, isolated from a marine sediment collected in Fujian Province, China. Similar to 96, the specific rotation of 97 was also dextrorotatory ([α]D20 + 16.8°), which is opposite to that of variecolorquinone A ([α]D20 = −18.0°); thus, the absolute configuration of C-2’ of 97 was assigned as R [22]. Compound 97 was also reported from the fermentation extract of *Eurotium cristatum* EN-220, which was isolated from the marine alga, *Sargassum thunbergii*, collected from the coast of Qingdao, China [95].
Four anthraquinone derivatives, 6-O-methylaverufin (98), 6,8-di-O-methylaverufin (99), aversin (100) and 8-O-methylversicolorin A (101) (Figure 9), were obtained from a defatted culture extract of *Aspergillus nidulans* MCCC 3A00050, which was isolated from a deep-sea sediment collected from the western Pacific ocean [96]. Compound 99 was also reported from the culture extract of a marine-derived fungus, *Aspergillus* sp. SF-6796 [87], while 100 was reported from the culture extract of a mangrove endophytic fungus ZSUH-36 [83] and from a fermentation extract of *A. versicolor* MF359, isolated from a marine sponge, *Hymeniacidon perleve*, which was collected from the Bohai Sea, China [97].

The ethanol-stress culture of the mangrove endophytic fungus, *A. nidulans* MA-143, furnished isoversicolorin C (102), versicolorin C (103), averufin (104), paeciloquinone E (105), and averufanin (106) (Figure 9). The absolute configurations of C-1′ and C-2′ in 102 were established as 1′S,2′R by comparison of calculated and experimental ECD spectra [80]. Compound 104 was also isolated from the culture extract of a deep-sea sediment-derived *A. versicolor* SCSIO-41502 [92].

![Figure 8. Structures of 96 and 97.](image_url)

![Figure 9. Structures of 98–121.](image_url)
Nidurufin (107) (Figure 9) was reported, together with 104, from the mycelial extract of A. niger strain MF-16#, isolated from the sea water collected in Quanzhou Gulf, Fujian Province, China [98]. Compounds 104 and 107 were also isolated from the culture extract of a marine sponge-associated fungus, A. versicolor [84]. Compound 107 was also isolated from a liquid culture extract of Penicillium flavidorsum SHK1-27, obtained from marine sediment samples, collected from Weizhou Island, China [99].

The liquid culture extract of a mangrove endophytic fungal strain (isolate 1850), isolated from a leaf of a mangrove plant, Kandelia candel, collected at the estuarine mangrove in Hong Kong, also furnished 103, 104 and 107 (Figure 9) [100], while the fermentation extract of a deep-sea sediment-derived fungus, A. puniceus SCSIO z021, yielded 3'-hydroxy-8-O-methyl versicolorin B (108), versicolorin B (109), and 8-O-methylnidurufin (110) (Figure 9), in addition to 104, 106 and 107 [81]. The absolute configurations of C-1′, C-2′ and C-3′ in 108 were established as 1′R,2′R,3′R by comparison of its calculated and experimental ECD spectra [81]. Compounds 104 and 109 (Figure 9) were also isolated from the culture extracts of a marine sponge-associated fungus, Aspergillus sp. F40 [93], and of A. versicolor MF18051, isolated from a sediment collected from Bohai Sea, China [101].

2′-Hydroxyversicolorin B (111) and noraverufanin (112) (Figure 9) were isolated, together with 104, 107 and 109, from the culture extract of a marine sponge-associated fungus, A. versicolor SCSIO 41016 [102], whereas 98–100, 6,8-di-O-methylnidurufin (113) and 6,8-di-O-methylversicolorin A (114) (Figure 9) were reported from the fermentation extract of an algicolous fungus, A. versicolor EN-7 [82]. The culture extract of a deep-sea sediment-derived A. versicolor A-21-2-7 furnished UCT1072M (115) (Figure 9), in addition to 104, 106, 107, and 109 [89], whereas a mangrove endophytic fungus, Aspergillus sp. strain 16-5C, yielded asperquinone A (116) (Figure 9), along with 99, 100, and 113. The absolute configurations of the stereogenic carbons, C-1′, C-4′, C-5′, in 116 were established as 1′S,4′R,5′S by comparison of its calculated and experimental ECD spectra [90].

The culture extract of Aspergillus sp., isolated from the inner part of a fresh tissue of a gorgonian, Dichotella gemmacea, which was collected from the South China Sea, furnished 8-O-methylaverufanin (117) and 8-O-methylaverufanin (118) (Figure 9), in addition to 104, 106, 107, and 110. The relative configuration of 110 was established by 1H-1H coupling constants and analysis of NOESY correlations, whereas the absolute configurations of its stereogenic carbons were proposed as 1′R,2′S,5′S on the basis of the biogenic consideration as well as by comparison with those of 107, whose stereostructure was unambiguously established [103]. Versicolorin A (119) (Figure 9), together with 100, 104, 107, 109 and 118, were isolated from the culture extract of a marine-derived Penicillium flavidorsum SHK1-27 by bioassay-guided isolation approach [85].

Insecticidal activity-guided fractionation of a solid-rice culture extract of an endophytic fungus, Acremonium vitellinum, isolated from a fresh inner tissue of an unidentified marine red alga, collected from Qingdao, China, led to the isolation of 6,8-di-O-methylbipolarin (120) (Figure 9), in addition to 99, 100, and 113. The absolute configuration at C-1′ of 120 was established as S by comparison of its calculated and experimental ECD spectra [104]. 6,8-Di-O-methyl averufin (121) (Figure 9) was isolated, together with 99, 103 and 104, from the mangrove endophytic fungal strain ZSUH-36 [86].

Chemical investigation of a deep-sea sediment-derived fungus, A. versicolor SCSIO-41502, resulted in the isolation of four aspergilol analogs, i.e., aspergilols (±)-A (122), (±)-B (123), (±)-G (124), and (±)-H (125) (Figure 10). Since 122–125 displayed no optical rotation, and because the HPLC (high performance liquid chromatography) analysis with a chiral column showed the presence of two peaks with a ratio of 1:1 for each of them, it was concluded that the compounds were isolated as racemic mixtures. By using HPLC equipped with a CHIRALPAK IA column and n-hexane/isopropanol/trifluoroacetic acid (80:20:0.05) as eluent, (±)-122 was further purified to give pure (+)- and (−)-optical isomers [92].
Figure 10. Structures of 122–134 and a plausible biosynthesis of 133 and 134.
Two anthraquinone-citrinin derivatives, penicillanthrains A (126) and B (127) (Figure 10), were obtained from the mycelial extract of a gorgonian-associated fungus, *Penicillium citrinum* PSU-FS1. The relative configurations of the stereogenic carbons of a dihydrofuran ring (C-1’, C-3’, C-4’) in 126 were assigned by NOEDIFF (Nuclear Overhauser Enhancement Difference) results. The absolute configurations of the stereogenic carbons in 127 were assumed to be the same as those of 126 since they showed similar optical rotations [37].

Emodacidamides A (128), B (129), D (130), E (131), and H (132) (Figure 10), anthraquinones with amino acid-containing amide side chains, were obtained from the culture extract of a deep-sea sediment-derived *Penicillium* sp. SCSIO sof101. The absolute configurations of the amino acid residues were determined by Marfey’s method or by a combination of Marfey’s method with chiral-phase HPLC analysis. L-Val was identified as the amino acid in the amide side chain of 128 and 129, whereas L-Ile was the amino acid of the amide side chain of 130 and 131, and L-Ala was identified for 132 [46].

Two anthraquinones containing a 1-hydroxy-2(2R)-2-(methoxycarbonyl)-5-oxopyrrolidin-1-yl substituent, anthrininones B (133) and C (134) (Figure 10), were obtained from the culture extract of a deep-sea sediment-derived fungus, *Altenaria teniuissima* DFFSCS013. In order to determine the absolute configurations of C-13 and C-18, the ECD spectra of two diastereomers (13R,18S)-133 and (13S,18S)-134 were calculated, which also generated the ECD spectra of their enantiomers for (13S,18R)-133 and (13R,18R)-134. Comparison of the calculated and experimental ECD spectra of 133 and 134 showed that the mirror imaged-ECD spectra for (13S,18R)-133 and (13R,18R)-134 and the experimental ECD spectra of 133 and 134 had accordant strong positive CEs near 220 nm, thus confirming the absolute configurations of C-18 in 133 and 134 as R. However, because both of the experimental ECD spectra of 133 and 134 showed weak CEs around 250–460 nm, the complete absolute configurations of 133 and 134 could not be accurately determined by ECD calculations. Therefore, the absolute configurations of C-18 in 133 and 134 were determined by 13C NMR calculations using density functional theory (DFT) at the mPW1PW91/6-311G(d,p) level. The results strongly suggested that the absolute configurations of C-13 and C-18 in 133 and 134 were 135,18R and 13R,18R, respectively. Compounds 133 and 134 were epimers at C-13 and that the C-18R was derived from a cyclization of D-glutamate to form a butylaminolate moiety as shown in Figure 10 [63].

### 3.1.2. Halogenated Anthraquinones

Although a number of chlorinated anthraquinone derivatives have been isolated, together with non-haloginated anthraquinones, from the culture of marine-derived fungi with normal culture media, the brominated counterparts were only isolated from marine-derived fungi cultured in bromide-enriched media. Eze et al. described the isolation of 2-chloro-1,3,8-trihydroxy-6-(hydroxymethyl)anthracene-9,10-dione (136) (Figure 11) from the EtOAc extract of the culture of an underwater sea sand-derived *Penicillium ochrochloron* [17], while Luo et al. reported the isolation of 2-chloro-1,3,8-trihydroxy-6-(hydroxymethyl)anthracene-9,10-dione (136) (Figure 11) from the culture extract of a sea sediment-derived *Penicillium* sp. SCSIO sof101 [46].

The culture extract of a mangrove endophytic fungus, *P. citrinum* HL-5126, furnished 2’-acetoxy-7-chlorocitreorosein (137) (Figure 11) [41], whereas the fermentation extract of *Penicillium* sp. SCSIO sof101, isolated from sediment samples collected in the South China Sea, furnished 7-chloro-1’-hydroxyisorhodoptilometrin (138) (Figure 11) [105].

The halogenated derivatives of averantin, including (1’S)-7-chloroaverantin (139), (1’S)-6-O-methyl-7-chloroaverantin (140), (1’S)-1’-O-methyl-7-chloroaverantin (141), (1’S)-6,1’-O, O-dimethyl-7-chloroaverantin (142), (1’S)-7-chloroaverantin-1’-butyl ether (143), 7-chloroaverethrin (144), and 6-O-methyl-7-chloroaverethrin (145) (Figure 11), were isolated from the organic extract of a sea salt-containing culture of a deep-sea sediment-derived *Aspergillus* sp. SCSIO F063, while (1’S)-6,1’-O,O-dimethyl-7-bromoaverantin (146) and (1’S)-6-O-methyl-7-bromoaverantin (147) (Figure 11) were isolated from the fungal mycelia using a sodium bromide-containing culture medium. The absolute configurations of the stereogenic carbon (C-1’) in 139–143, 146 and 147 were established as S by comparison of
the CD spectra of 139, 140 and 147 with that of (S)-(−)-averantin (89) (Figure 7), as well as the same sign of optical rotations of 139–147 [91].

Figure 11. Structures of 135–152.

Nalgiolaxin (148) and 7-chloro versicolorin A (149) (Figure 11) were isolated from the culture extract of an algicolous fungus, A. alliaceus [77], and the fermentation extract of a deep-sea sediment-derived A. puniceus SCSIO z021 [81], respectively. The absolute configurations at C-1' and C-2' of the furofuran ring system were established as 1'R,2'S by comparison of the calculated and experimental ECD spectra of 149 [81].

The chlorinated anthraquinones containing amide side chain, viz. emodacidamides C (150), F (151), and G (152) (Figure 11), were also reported from the fermentation extract of a deep-sea sediment-derived fungus, Penicillium sp. SCSIOsof101. The absolute configurations of the amino acids in the amide side chains were assigned by Marfey’s method and chiral-phase HPLC analysis as L-Val in 150, L-Ile in 151, and L-Leu in 152 [46].

3.1.3. Sulphated Anthraquinones

Only three anthraquinones containing a sulfate group have been reported from cultures of marine-derived fungi. Macroposprin-7-O-sulfate (153) (Figure 12) was reported from the solid-rice culture extract of a mangrove endophytic fungus, Stemphylium sp. 33231 [50], whereas emodin-3-O-sulphate (154) and citreorosein-3-O-sulphate (155) (Figure 12) were isolated from the mycelia extract of a sea mud-derived Penicillium oxalicum 2HL-M-6 [36].
3.1.4. Glycosylated Anthraquinones

Although anthraquinones containing a sugar moiety are not common, some of them have been reported from the cultures of marine-derived fungi. The fermentation extract of Eurotium rubrum, obtained from the inner tissue of a stem of the mangrove plant, Hibiscus tiliaceus, from Hainan Island, China, furnished 6-O-(α-D-ribofuranosyl)-questin (156) (Figure 13) [106], while the culture extract of an algicolous fungus, E. cristatum EN-220, yielded 157 and 6-O-(α-D-ribofuranosyl)-questinol (157). The sugar moiety was identified as D-ribose by acid hydrolysis of the glycosides and by subsequent measurement of its optical rotation ([α]_D^{20} − 17.6°) [95].

3.1.5. Seco-Anthraquinones

Seco-anthraquinones are proposed to derive from an oxidative cleavage of the p-benzoquinone ring of the anthraquinone scaffold, followed by recyclization to form a 7-membered lactone ring. The seco-anthraquinones, wentiquinones A (160) and B (161), and 1,8-dihydroxy-10-methoxy-3-methyl dibenz[\textit{b,e}]oxepin-6,11-dione (162) (Figure 14) were isolated from the culture extract of an algicolous fungus, Aspergillus wentii EN-48 [30]. The culture extract of a marine sponge-associated fungus, A. europaeus WZXY-SX-4-1, yielded 162 and wentiquinone C (163) (Figure 14) [21]. The proposed biogenetic pathways of 161 and 162 suggested that emodin is a precursor, which, after oxidative cleavage and lactonization of the anthraquinone core, generates 162 and 163 [21]. Compound 163 was also isolated from the fermentation extract of an algicolous fungus, A. wentii EN-48 [23].
9-Dehydroxyeurotinone (164) and 2-O-methyl-9-dehydroxyeurotinone (165) (Figure 14) were isolated from the culture extract of a mangrove endophytic fungus, *Eurotium rubrum* [47], while a marine sediment-derived *Eurotium* sp. SCSIO F452 also furnished 165 [70]. Compound 165 was isolated, together with 2-O-methyleurotinone (166) and 2-O-methyl-4-O-(α-D-ribofuranosyl)-9-dehydroxyeurotinone (167) (Figure 14), from the culture extract of a mangrove endophytic fungus, *E. rubrum* [106].

![Figure 14. Structures of 160–167.](image)

3.2. Tetrahydroanthraquinones

The culture extract of a soft coral-associated fungus, *Aspergillus tritici* SP2-8-1, furnished aspetritone B (168) (Figure 15). The relative configurations of the stereogenic carbons (C-2 and C-3) in 168 were established by NOESY correlations from H-1 to H-3 and H-2 to H$_{ax}$-4, while the absolute configurations were established as 2R,3S by comparison of the calculated and experimental ECD spectra [28].

(3R)-1-Deoxyaustrocortilutein (169) and altersolanol B (or dactylarin; 170) (Figure 15) were obtained from the culture extract of a deep-sea sediment-derived *Altenaria tenuissima* DFFSCS013 [63]. Compound 170 was also obtained from a marine-derived fungus, *Altenaria* sp. ZJ-2008003, isolated from a soft coral, *Sarcophyton* sp., which was collected from the South China Sea [107].

The solid-rice culture extract of a mangrove endophytic fungus, *Stemphylium* sp., yielded altersolanol C (171) (Figure 15), together with 170, altersolanol A (172), auxarthrol C (173), and 2-O-acetylaltersolanol B (174) (Figure 15). The absolute configurations of the stereogenic carbons in 173 were established as 1R,2R,3R,4R,1aS,4aR by X-ray analysis of the product resulting from the epoxide ring-opening reaction to obtain a suitable crystal for X-ray crystallography. The absolute configurations of the stereogenic carbons in 174 were established as 2R,3S by X-ray analysis of a crystal obtained from a hydrolysis reaction, followed by a preparation of its 2,3-O-acetonide [50]. Compounds 170, 172 and 173 (Figure 15) were also isolated from the solid-rice culture extract of a gorgonian-associated fungus, *S. lycopersici* [51].

Antibacterial activity-guided fractionation of the culture extract of a sea cucumber-associated fungus, *Trichoderma* sp. (H-1), resulted in the isolation of lentisone (175) (Figure 15) [43], whereas SZ-685C (also known as 1403C; 176) (Figure 15) was isolated from the culture extract of a mangrove endophytic fungus, *Halorosellinia* sp. (no. 1403) [108].
Phomopsantraquinone or (2R,3S)-7-ethyl-1,2,3,4-tetrahydro-2,3,8-trihydroxy-6-methoxy-3-methyl-9,10-anthracenedione (177) (Figure 15) was reported from the broth culture extract of Phomopsis sp. PSU-MA214, isolated from the leaves of a mangrove tree, Rhizophora apiculata Griff. Ex T. Anderson. The relative configurations of C-2 and C-3 in 177 were established by NOEDIFF experiment, while their absolute configurations were suggested to be the same as those of 170, i.e., 2R,3S since the specific rotation of 177 ([α]_D^{25} = 58°, c 0.05, EtOH) was almost identical to that of 170 ([α]_D^{25} = 63°, c 0.05, EtOH) [52].

Figure 15. Structures of 168–180.

Ge et al. reported the isolation of auxarthrol D (178), a chlorine-containing auxarthrol G (179), and 4-dehydroxyaltersolanol A (180) (Figure 15), in addition to 170, from the culture extract of Sporendonema casei HDN16-802, isolated from sediment samples collected from Zhangzi Island, Liaoning province, China. The relative configurations at C-2, C-3 and C-4 in 178 and 179 were established based on NOESY correlations, while their absolute configurations were established as 2S,3R,4S,1aR,4aR by comparison of the calculated and experimental ECD spectra [109].

3.3. Tetrahydro-5,8-anthraquinones

Chemical investigation of the culture extract of a soft coral-associated fungus, Aspergillus tritici SP2-8-1, resulted in the isolation of aspetritone A (181) (Figure 16). The relative configurations at C-1, C-2 and C-3 were established based on NOESY correlations, while their absolute configurations were determined as 1S,2S,3R by comparison of the calculated and experimental ECD spectra [28].

The culture extract of Aspergillus sp. strain 05F16, isolated from an unidentified alga collected in the coral reef at Manado, Indonesia, yielded bostrycin (182) (Figure 16) [110]. Compound 182 was also isolated from the culture extract of a mangrove endophytic fungus strain no. 1403, collected from the South China Sea [111].
Nigrosporins A (183), B (184) and a spiro dihydronaphthoquinone/tetrahydroantharquinone derivative, fusarnaphthoquinone C (185) (Figure 16), were isolated, together with 182, from the extracts of the culture broth and mycelia of a gorgonian-associated fungus, Fusarium sp. PSU-F14 and PSU-F135. The NOEDIFF experiment was used to locate the methyl group on the tetrahydro-5,8-antharquinone moiety and the 2-oxopropyl group on the dihydronaphthoquinone portion. However, neither relative nor absolute configurations of the stereogenic carbons in 185 were determined [59].

![Figure 16. Structures of 181–189.](image)

Deoxybostrycin (186) (Figure 16) was obtained, together with 182, from the culture extract of a mangrove endophytic fungus, Nigrospora sp. (strain no. 1403), isolated from a decayed wood of a mangrove plant, Kandelia candel (L.) Druce, collected from Mai Po, Hong Kong [112]. 10-Deoxybostrycin (187) (Figure 16) was isolated, together with 182, 184 and 186, from the culture extract of Nigrospora sp. ZJ-2010006, isolated from an unidentified sea anemone. Acetylation of 182 and 186 gave 3-acetoxybostrycin (182a) and 3-acetoxy-4-deoxybostrycin (186a) (Figure 16), respectively. The 1D NOE data of 188 showed that all asymmetric carbons had the same relative configurations as those of 182. The absolute configurations of the stereogenic carbons in 187 were tentatively assigned as 2S,3R,4S on the ground that 187 shared a biogenesis with 4α-epi-9α-methoxydihydrodeoxybostrycin whose absolute structure had already been established [68]. Compound 187 was also reported from the same fungal strain but was isolated from the inner tissue of the zoathid, Palythoa haddoni [69]. A bostrycin derivative, hydroxybostrycin (188) (Figure 16), was isolated from the culture broth extract of a mangrove endophytic fungus, Altenaria sp. (SK11) [62], whereas 1403P-3 (189) (Figure 16) was reported from a mangrove endophytic fungus, strain no. 1403 [113].
3.4. Anthrones

Anthrone derivatives reported from marine-derived fungi occur as complex structures with the anthrone or modified anthrone scaffolds. These compounds can be considered to derive from a condensation of the anthraquinone scaffold, such as physcion (6) and catenarin (7) (Figure 3) with polyketides of diketopiperazine derivatives.

Du et al., in their search for antitumor compounds from marine-derived microorganisms, have isolated anthraquinone derivatives from *Aspergillus glaucus* HB1-19, isolated from a marine sediment around the mangrove roots, collected in Fujian Province, China. Fractionation of the culture extract furnished aspergiolide A (190) (Figure 17), an anthraquinone derivative with naphtha[1,2,3-de]chromene-2,7-dione skeleton [114], whereas aspergiolide B (191) (Figure 17) was isolated from the culture extract of *A. glaucus* HB1-19, isolated from a marine sediment, collected in Fujian Province, China [22].

Further investigation of the mycelial extract of *A. glaucus* HB1-19, isolated from the marine sediment-surrounding mangrove roots collected in Fujian Province (China), by the same authors led to the isolation of aspergiolides C (192) and D (193) (Figure 17), two spiro[5,5]undecane scaffold-containing anthrones. Although 192 and 193 possess a stereogenic center at a spiro junction of the ring system (C-19), both compounds displayed no optical rotation and CD effects. Therefore, both compounds were assumed to be a 1:1 mixture of enantiomers. By using HPLC with a Lux-Amylose-2 column, each compound gave a baseline-separated peaks in a 1:1 ratio for both compounds, confirming their racemic nature. Of these peaks, HPLC-CD spectra were recorded in the stopped-flow mode and the resulting opposite CD curves confirmed the assumption that the two peaks represent their enantiomers. Comparison of the online and calculated CD spectra and the configurations of both enantiomers of 192 and 193 were established [115].

Biosynthetically, 190 was proposed to arise from a condensation of catenarin (7) (Figure 3) with aromatic pentaketide, as depicted in Figure 17 [114], while 192 was proposed to derive from catenarin (7) with an aromatic heptaketide as shown in Figure 17 [115].

Three pairs of anthrone-based racemic spirocyclic diketopiperazine enantiomers, variecolortins A (194), B (195) and C (196) (Figure 18), were obtained from *Eurotium* sp. SCSIO F452, isolated from the South China Sea sediment samples. Compounds 194–196 represented a 6/6/6/6 tetracyclic cyclohexene–anthrone skeleton. The relative configurations of the stereogenic carbons in 194 were unambiguously determined as (12R,21S,32R) by X-ray analysis. However, the lack of optical rotation of 194 suggested its racemic nature. The enantiomers were subsequently separated by a chiral HPLC to give (+)-194 and (−)-194. Conversely, the relative configurations of 195 and 196 were established by NOESY experiments. In each compound, the diagnostic NOESY correlations between NH-11 and H-21b, as well as between OH-22 and H-21a, resulted in the identification of α- and β-orientations, respectively. In addition, the geometry of the Δ8 double bond was assigned as Z-configuration via the deshielding effect of H-8 caused by the carbonyl group on the β-vinyl proton. The baseline ECD curves of 195 and 196 revealed that they were racemic mixtures. Therefore, 195 and 196 were separated by a chiral-phase HPLC, and the calculated ECD spectra for the individual enantiomer assigned them as 12S,22R-195 and 12S,22R-196, which were in agreement with the experimental ECD spectra of (+)-195 and (−)-196, respectively.
Figure 17. Structures of 190–193 and plausible biosynthetic pathways of 190 and 192.
Figure 18. Structures of 194–196 and plausible biosynthetic pathways of 194–196.
Hydroxyviocristin (Figure 18) was proposed to be a biosynthetic precursor of (±)-194, while physcion (6) (Figure 3) was proposed as a biosynthetic precursor of (±)-195 and (±)-196 [116]. The proposed biosynthetic pathways leading to the formation of 194–196 are depicted in Figure 18.

3.5. Tetrahydro-9-hydroxyanthrones

Tetrahydro-9-hydroxyanthrones are considered to derive from a reduction of the carbonyl group on C-10 of tetrahydroanthraquinones to a hydroxyl group. This group of anthraquinone derivatives are widely isolated from culture extracts of marine-derived fungi.

The culture extract of an algicourous Aspergillus sp. strain 05F16 furnished tetrahydrobostrycin (197) and 1-deoxytetrahydrobostrycin (198) (Figure 19). The relative configurations of the stereogenic carbons of 197 were assigned by analysis of the $^1$H-$^1$H coupling constants and NOESY correlations [110].

Figure 19. Structures of 197–227.
The fermentation extract of an endophytic fungus, Talaromyces islandicus EN-501, isolated from the inner tissue of a marine red alga, Laurencia okamura, collected in Qingdao, China, yielded 8-hydroxyconiothyrinone B (199), 8,11-dihydroxyconiothyrinone B (200), 4R,8-dihydroxyconiothyrinone B (201), 4S,8-dihydroxyconiothyrinone B (202), and 4S,8-dihydroxy-10-O-methylidendrolyl E (203) (Figure 19). The relative stereochemistry of 199 was determined by analysis of \(^1\)H–\(^1\)H coupling constants as well as by NOESY correlations. The large coupling constant value \((J = 8.8\ \text{Hz})\) between H-9 and H-9a revealed a trans orientation. The important NOE correlations were observed between H-9 and H-4a, indicating a co-facial orientation of the two protons, while the NOE correlations between H-2 and H-9a showed that they were on the opposite sides of the molecule. The absolute configurations of the stereogenic carbons of 199 were established as 2S,4aS and 9R,9aS by X-ray analysis. The relative and absolute configurations of the stereogenic carbons of 200 and 201 were deduced to be the same as those in 199. However, the measured ECD spectrum of 201 suggested the \(R\) absolute configuration at C-9 in 199–201. The \(^1\)H and \(^13\)C NMR data revealed that 202 is a C-4 epimer of 201. The absolute configurations of the stereogenic carbons in 202 were determined as 2R,4S,4aR,9R,9aS by comparison of its calculated and experimental ECD spectra. The relative configuration of 203 was established on the basis of NOESY correlations, while the absolute configurations of its stereogenic carbons were established as 2S,4S,4aS,10S,9aS by comparison of the calculated and experimental ECD spectra [117].

Fusauquinons A (204), B (205), and C (206) (Figure 19) were isolated from the fermentation extract of Fusarium sp. (no. ZH-210), obtained from a mangrove sediment from Zhuhai, China. The relative configurations at C-6, C-7, C-8a, C-9 and C-10a of 204 were established based on NOESY correlations. The structures of 205 and 206 were elucidated as 1,4,5,6,7,9-hexahydro-2-methoxy-7\(\alpha\)-methyl-5\(\alpha\)-hydroxydihydrodesoxybostrycin (205) and 1,4,6,7,9-pentahydroxy-2-methoxy-7\(\alpha\)-methyl-5\(\alpha\)-hydroxydihydroanthracen-10-one and 1,4,6,7,9-pentahydroxy-2-methoxy-7\(\alpha\)-methyl-5\(\alpha\)-hydroxydihydroanthracen-10-one, respectively [118].

Fusaransatrquinone (207), 9\(\alpha\)-hydroxydihydrodesoxybostrycin (208), 9\(\alpha\)-hydroxyhalorosellinia A (209) (Figure 19) were isolated from the culture broth and mycelia extracts of a gorgonian sea fan-associated fungi, Fusarium sp. PSU-F14 and PSU-F135 [59]. 4a-Epi-9\(\alpha\)-methoxydihydrodesoxybostrycin (210) (Figure 19), together with 208, were reported from the culture extract of a sea anemone-associated fungus, Nigrospora sp. ZJ-2010006. The absolute configurations of the stereogenic carbons in 210 were established as 2S,3R,9R,1aS,4aR by X-ray crystallographic analysis. Based on the absolute structure of 210, the absolute configuration of the stereogenic carbons of 208, whose relative configuration was previously determined, was unambiguously established as 2S,3R,9R,1aS,4aS [68].

Dihydroaltersolanol A (211), altersolanol L (212) and ampelanol (213) (Figure 19) were obtained from the culture extract of a deep-sea sediment-derived fungus, Alternaria tenussima DFFSCS013 [63], whereas 213 was also isolated from the fermentation extract of a gorgonian soft coral-associated fungus, Stemphylium lycopersici [51]. Tetrahydroaltersolanol B (214) (Figure 19) was isolated from the mycelia extract of a mangrove endophytic fungus, Alternaria sp. ZJ9-6B. The absolute configurations of the stereogenic carbons in 214 were established by X-ray diffraction analysis [61].

Halarosellinia A (215), or 1,4,5,6,7,9-hexahydroxy-2-methoxy-7-methyl-5\(\beta\),9\(\beta\),8\(\alpha\),6\(\alpha\),10\(\alpha\)-hexahydroanthracen-10(10H)-one, was isolated, together with 197 and 208 (Figure 19), from the culture broth extract of a mangrove endophytic fungus, Alternaria sp. (SK11) [62]. Compound 215 was also reported from the culture extract of a mangrove endophytic fungus, Halorosellinia sp. (no. 1403). The relative stereochemistry of 215 was established by NOE correlations and \(^1\)H–\(^1\)H coupling constants [38].

Tetrahydroaltersolanols C (216), D (217), E (218), and F (219) (Figure 19) were isolated, together with 211–213, from the culture extract of a soft coral-associated fungus, Alternaria sp. ZJ-2008003. The relative configuration of 219 was determined by observation of the correlations from the ROESY spectrum, while the absolute configurations of its stereogenic carbons were established as 2S,3R,4aS,9R,9aS by a modified Mosher’s method. Based on
the absolute configurations of the stereogenic carbons of 219 and a shared biogenesis, the absolute configurations of the stereogenic carbons of 211 and 216–218 were established as 1R,2R,3R,9R,9aS-211, 2S,3R,4aS,9S,9aS-216, 2S,3R,4aR,9R,9aR-217, and 2S,3S,4aS,9R,9aS-218, respectively [49]. Compounds 213, 214, and 216 (Figure 19) were also reported from the culture extract of a mangrove endophytic fungus, Phomopsis sp. PSU-MA214 [52].

2-O-Acetylaltersolanol L (220) (Figure 19) was isolated, together with 211–214, from the culture extract of a mangrove endophytic fungus, Stemphylium sp. 33231. The absolute configurations of the stereogenic carbons of 220 were established as 1R,2S,3R,4aS,9R,9aS by X-ray analysis of the deacetylated product [50].

Harzianummones A (221) and B (222) (Figure 19) were isolated from the culture extract of a soft coral-associated fungus, Trichoderma harzianum (XS-20090075). The absolute configurations of the stereogenic carbons in 221 and 222 were established as 7R,8R,8aR,10S,10aS-221, and 7R,8R,8aR,10R,10aS, respectively, by comparison of their calculated and experimental ECD spectra. Compounds 221 and 222 are C-10 epimers [55].

Xylanthraquinone (224) (Figure 19) was isolated from the culture extract of a mangrove endophytic fungus, Xylaria sp. 2508. The absolute configurations of the stereogenic carbons in 224 were determined as 2S,3R,4aS,9R,9aS by single-crystal X-ray diffraction using Cu Kα radiation [119]. Auxarthrols E (225), F (226), and H (227) (Figure 19), were isolated from the fermentation extract of a sediment-derived fungus, Sporendonema casei HDN16. The relative stereochemistry of 225, 226, and 227 was determined by NOESY correlations, while their absolute structures were determined as 2R,3R,4S,9S,1aR,4aR-225, 2S,3R,4R,9R,1aS,4aR-226, and 2S,3R,4S,9S,1aS,4aS-227, respectively, by comparison of their calculated and experimental ECD spectra [109].

### 3.6. Tetrahydroanthrols

Asperflavin (228) (Figure 20) was obtained, as the main pigment, from the fermentation extract of a marine sponge-associated fungus, Eurotium repens. Since 228 did not display an optical rotation, it was suggested to be a racemic mixture [24]. Compound 228 and isoasperflavin (229) (Figure 20) were isolated from the culture extract of a mangrove sediment-derived Aspergillus glaucus HB1-19. The relative configurations of C-3 and C-4 in 229 were determined by the value of the coupling constant between H-3 and H-4 (J3,4 7.7 Hz), while the absolute configurations at C-3 and C-4 were established as 3R,4S on the basis of maximal-negative and minimal-positive CEs at 281.0 and 223.4 nm, respectively, in the CD spectrum [22]. 3,4-Dihydro-3,9-dihydroxy-6,8-dimethoxy-3-methylanthracen-1(2H)-one (230) (Figure 20) was isolated from the fermentation extract of an algicolous fungus, A. wentii EN-48 [30].
Eurorubrin (231) (Figure 20), a bisdihydroanthracenone derivative, was obtained, together with 228, from the culture extract of a mangrove endophytic fungus, *Eurotium rubrum*. Since both 231 \( [\alpha]_D^{25} + 21.1^\circ \) and 228 were dextrorotatory, they were suggested to have the same stereochemistry at C-3 [106]. The culture extract of an algicolicus fungus, *E. cristatum* EN-220, furnished asperflavin ribofuranoside (232) (Figure 20), in addition to 228 and 231 [95].

3.7. 9,10-Dihydroxyanthracenes

Anthrininone A (233) (Figure 21) was obtained from the culture extract of a deep-sea sediment-derived fungus, *Altenaria tenuissima* DFFCS013. The absolute configurations of its stereogenic carbons were established as 4R,6S,7R,15R,17S,18R by a single-crystal X-ray diffraction analysis using Cu Kα radiation [63]. The proposed biosynthetic pathway leading to a formation of a hexacyclic spiro-fused ring system in 233 was shown in Figure 21. A condensation of the intermediate (i), derived from a cyclization of an octaketide, with the intermediate (ii), which is derived from a nucleophilic addition of D-xylose by acetoacetyl CoA, led to a formation of a spiro ketal in 233.

![Figure 21](image_url)

*Figure 21.* Plausible biosynthetic pathway for 233.

3.8. 2-Aza-anthraquinones

2-Aza-anthraquinones consist of a naphthoquinone moiety fused with a pyridine ring. These compounds are synthesized in nature by either fungi or lichens. Van Wagoner et al. reported the isolation of scorpinone (234) (Figure 22) from the extract of a rare fungus, *Amorosia littoralis*, collected from an inertial sediment in the Bahamas. The biosynthetic pathway of 234 was studied using [2-\(^13\)C]-acetate and [1,2-\(^13\)C]-acetate, and was followed to verify if its biosynthesis was similar to that of bostrycoidin (235) (Figure 22). The labeling results showed that a linear heptaketide is a precursor in the biosynthesis of 234, and consequently the incorporation of a nitrogen atom produced 2-aza-anthraquinones [120]. *A. littoralis* gen. sp. nov., also isolated from the littoral zone in the Bahamas, was capable of
producing 234 (Figure 22) and caffeine [121]. Chemical investigation of the CHCl₃-MeOH extract of cultured mycelia of Bispora-like tropical fungus, collected from the intertidal zone surrounding the Bahamas Island, also led to the isolation of 234 (Figure 22) [122].

![Figure 22. Structures of 234–236.](image)

The culture extract of an endophytic fungus, *Aspergillus terreus* (no. GX7-3B), isolated from a branch of a mangrove tree, *Bruguiera gymnolhiza* (Linn.) Savigny, which was collected from the salt coastline of the South China Sea in Guangxi province, yielded 8-O-methylbostrycoidin (236) (Figure 22) [123].

### 3.9. Dimeric anthraquinones

The compounds of this group include two anthraquinoid units, one anthraquinone and one tetrahydroanthraquinone, two tetrahydroanthraquinones, one anthrone and one tetrahydro-5,8-anthraquinone, or one anthraquinone and one seco-anthraquinone, linked together by C-O-C or C-C bonds.

6,6′-Oxybis(1,3,8-trihydroxy-2-((S)-1-methoxyhexyl)anthracene-9,10-dione) (237) and 6,6′-oxybis(1,3,8-trihydroxy-2-((S)-1-hydroxyhexyl)anthracene-9,10-dione) (238) (Figure 23) were reported from the culture broth extract of a marine clam-associated fungus, *Aspergillus versicolor*. The $^1$H and $^{13}$C NMR data of 237 resembled those of 81, except for the signals of H-2 and H-4. Based on the sign of their optical rotations ($[\alpha]_{D}^{23} = -72.4^\circ$ for 237, and $-51.4^\circ$ for 238), the absolute configurations of the stereogenic centers at C-11 and C-11′ in 237 and 238 were determined as S [88].

![Figure 23. Structures of 237 and 238.](image)

2,2′-Bis-(7-methyl-1,4,5-trihydroxyanthracene-9,10-dione) (239) (Figure 24) was obtained from the fermentation extract of a marine sponge-associated fungus, *Talaromyces stipitatus* KUFA 0207 [33].
Alterporriols K (240), L (241), and M (242) (Figure 24) were obtained from the mycelial extract of a mangrove endophytic fungus, *Altenaria* sp. ZJ9-6B. The relative configurations at C-5 and C-8 in 240 were established as $5S^*,8R^*$ on the basis of NOESY correlations and the value of a coupling constant between H-5 and H-6$\alpha$, whereas the relative configurations of H-6, H-7 and H-8 in 241 and 242 were established as $6S^*,7R^*,8R^*$ and $6S^*,7R^*,8R^*$, respectively, by the NOE experiment and the value of a coupling constant between H-5$\alpha$ and H-6. Compound 241 is, therefore, a C-7 epimer of 242 [61].

Xia et al. reported the isolation of alterporriol S (243) and (+)-$aS$-alterporriol C (244) (Figure 24) from the culture broth extract of a mangrove endophytic fungus, *Altenaria* sp. (SK11). The relative stereochemistry of 243 was determined as $6S^*,7R^*,8S^*,8aS^*,10R^*,10aR^*$ and $6R^*,7'S^*$ by the $^1H-^1H$ coupling constant values as well as by NOESY correlations, while the absolute configurations of the stereogenic carbons were established as $6S,7R,8S,8aS,10R,10aR$ and $6'R,7'S$ by comparison of calculated and experimental ECD spectra. The planar structure of 244, elucidated by high-resolution mass spectrometry (HRMS) and 1D and 2D NMR analyses, was the same as that of alterporriol C. The relative configurations of the stereogenic carbons of 244 were also established by $^1H-^1H$ coupling constants and the correlations ob-
served in the NOESY spectrum as 5′R,6′S,7′R,8′S. Since 244 displayed the specific rotations \([\alpha]_D^2 + 75^\circ\) and +208°, it was suggested to be an atropisomer of alterporriol C. Comparison of the calculated and experimental ECD spectra of 244 revealed the absolute configuration of its stereogenic carbons as 5′R,6′S,7′R,8′S. Thus, the axial configuration of 244 was confirmed as \(\alpha S\), also called M helicity [62].

The culture extract of a soft coral-associated fungus, Alténaria sp. Zj-2008003, also afforded besides the previously reported alterporriol C (245), another five alterporriol-type anthraquione dimers, i.e., alterporriols N (246), O (247), P (248), Q (249), and R (250) (Figure 24) [49].

The liquid culture extract of a zoanthid Palythoa haddoni-associated fungus, Nigrospora sp. (ZJ-20100026), afforded a hydroanthrone dimer, nigrodiquinone A (251) (Figure 24). The relative configurations of the stereogenic carbons of 251 were assigned as 1αR,2S,3R,4αR,9R,10R,2′S,3′R,4′S, which were the same as those of 4α-epi-9α-methoxydihydrodeoxybostrycin (210) and 10-deoxybostrycin (187). The absolute configurations of the stereogenic carbons of 251 were established as 1R,2S,3R,4αR,9R,2′S,3′R,4′S by comparison of the calculated and experimental ECD spectra as well as of the values of the calculated and experimental optical rotations [69].

The previously described cytoskyrin A (252) (Figure 24) was isolated from the culture broth and mycelial extracts of a marine sponge-associated fungus, Curvularia lunata [64].

The solid-rice culture extract of a mangrove endophytic fungus, Stemphylium sp. 33231, furnished alterporriols A (253), B (254), D (255), E (256), T (257), U (258), V (259), and W (260) (Figure 25), in addition to 245, 246, 249 and 250 (Figure 24). Compound 257 is a heterodimer consisting of 170 and 171 linked by C-5—C-7′, whereas 258 is a homodimer of 170 linked by C-5 and C-7′, and 260 is a heterodimer of 170 and 33 linked by C-1 and C-5′. The configurations of the stereogenic carbons of 257 were tentatively assigned as 2R,3R,4αR,2′R,3′S, whereas those of 258 and 260 were also assigned as 2R,3S,2′R,3′S and 2′R,3′S,4′R. However, the absolute configurations for the axes of chirality in 258–260 were not determined. Since the CD spectrum of 260 showed the same spectral feature in the 205–340 nm range as 256, the overall absolute configuration of 260 was tentatively assigned as \(\alpha R,2′R,3′R,4′S\) [50].

Alterporriol Y (261) (Figure 25) was isolated from the EtOAc extract of a liquid culture of a gorgonian soft coral-associated fungus, S. lycopersici. Compound 261 is a homodimer of 171 linked by C-8—C-8′. The relative configurations of the stereogenic carbons of 261 were determined as 25S,3R on the basis of NOE experiment. The ECD spectrum of 261 presented two negative CEs at 252 and 227 nm and two positive CEs at 306 and 272 nm, which was a mirror image of the ECD spectra of 246 and 255, with \(\alpha S\) axial chirality, and close similarity to that of \(\alpha R\)-256. Therefore, the absolute structure of 261 was assigned as \(\alpha R,2′R,3′R,4′S\) [51].

Alterporriols F (262), G (263), Z1(264), Z2 (265), and Z3 (266) (Figure 25), along with 246 (Figure 24), were isolated from the MeOH extract of the solid-rice culture of Stemphylium sp. FJ006, obtained from an unidentified sponge, which was collected at the coast of Jeju Island, Korea. The relative configurations of the stereogenic carbons of 264 were assigned as 1′R,2′R,3′S,4′S on the basis of the \(^1\)H—\(^1\)H coupling constants and NOESY correlations. Since the experimental ECD spectrum showed significant CEs at 269 (\(\Delta \varepsilon 35.79\)) and 285 (\(\Delta \varepsilon -36.06\) nm, the \(\alpha R\) (also defined as P helicity) configuration at C-6-C-6′ was assigned to 264. However, the calculated ECD spectra did determine the absolute configuration of C-1-C-4. The 1D and 2D NMR analysis revealed that the planar structure and relative stereochemistry of 265 were the same as those of 264. However, the experimental ECD spectrum of 265 was quasi-mirror image of 264, indicating that 265 is an atropisomer of 264. The relative configurations of the stereogenic carbons in 266 were determined as 1′R,2′R,3′S,4′S on the basis of the \(^1\)H—\(^1\)H coupling constants and NOESY correlations, whereas the absolute configurations of the C-1/C-6′ chiral axis was assigned as \(\alpha R\), based on the similarity of its ECD spectrum to that of 264. Moreover, the ECD spectrum of 262 also assigned the configuration of a C-5/C-5′ chiral axis as \(\alpha R\) [124].
Figure 25. Structures of 253–269.
Antibacterial activity-guided fractionation of the culture extract of an unidentified marine red alga-derived fungal strain F-F-3C led to the isolation of rubellin A (267), 14-acetoxyrubellin A (268), and 14-acetoxyrubellin C (269) (Figure 25). The structures of 268 and 269 were elucidated by 1D and 2D NMR analysis and comparison of their NMR data with those of the previously reported 267; however, the relative and absolute configurations of their stereogenic carbons were not described [44].

3.10. Bianthrones

Trans- and cis-emodin-physcion bianthrones (271 and 272) (Figure 26) were isolated, together with 270, from the culture extract of a marine sediment-derived fungus, Aspergillus glaucus HB1-19. The cis and trans relationship between C-10/C-10′ of 271 and 272 was determined based on a comparison of their NMR data with those from the literature [22]. Two atropisomers of 8,8′-dihydroxy-1,1′,3,3′-tetramethoxy-6,6′-dimethyl-10,10′-bianthrone (273 and 274) (Figure 26) were obtained, together with 270, from the culture extract of an algicolous fungus, Aspergillus wentii EN-48 [30].

![Figure 26. Structures of 270–278 and a plausible biosynthetic pathway of 278.](image-url)
Three chlorinated bianthrone, allianthrone A (275), B (276), and C (277) (Figure 26), were isolated from the EtOAc extract of the co-culture of two different developmental stages of a marine alga-derived Aspergillus alliaceus. The structures of 275–277 were elucidated by 1D and 2D NMR spectral analysis. The absolute configurations of the stereogenic carbons of 275 were established as 10R,10′S,12S,12′S by X-ray analysis, whereas those of the pseudo-enantiomers, 276 and 277, were determined as 10R,10′R,12R,12′S and 10S,10′S,12S,12′S, respectively, by comparison of their calculated and experimental ECD spectra [125].

Eurotine A (278) (Figure 26) was isolated from the culture extract of a marine sediment-derived fungus, Eurotium sp. SCSIO F452. X-ray diffraction analysis not only confirmed its planar structure, elucidated by 1D and 2D NMR analysis, but also determined the relative configuration of its stereogenic carbons as 10S*,10′S*. However, the crystal of 278 occupied a Pccn space group, indicating its racemic nature, which was also supported by its lack of optical activity. Separation of (+)-278 by chiral HPLC yielded (+)-278 and (−)-278, whose absolute configurations were established as 10S,10′S and 10R,10′R, respectively, by comparison of their calculated and experimental ECD spectra [70]. The proposed biosynthetic pathway of 278 from physcion (6) (Figure 3) as a precursor was depicted in Figure 26.

3.11. Anthraquinone Analogues Fused with Xanthone and Chromone Derivatives

The previously described anthraquinone–xanthone derivatives, JBIR-97/98 (279) and JBIR-99 (280) were isolated, together with engyodontochoenes A (281), B (282), C (283), D (284), E (285), and F (286) (Figure 27) from the mycelia and culture broth extracts of Engyodontium album strain LF069, which was isolated from a tissue of a marine sponge, Cacospinga scalaris, collected from the Limski Fjord, Croatia. The relative configurations of 279–286 were determined by NOESY correlations and 1H–1H coupling constants. The absolute configurations of 279, 280 and 282 were established as 9R,10S,12S,24R,25S–279, 9R,10S,12S,24R,25R–280 and 9R,10S,12S,24S,25S–282, whereas the absolute configurations of the stereogenic carbons in 281 were established, based on its common biogenesis with 279 and 280, as 9R,10S,12S,24R,25S. The calculated ECD spectra of 283–286 only determine the absolute configurations of C-9, C-10, C-12 and C-24, but not C-25. Consequently, the absolute configurations of these compounds were established as 9R,10S,12S,24R–283, 9R,10S,12S,24R–284, 9R,10S,12S,24R–285, and 9R,10S,12S,24S–286 by comparison of the calculated and experimental ECD spectra [125].

By using UPLC-ESI-QToF/MS analysis, Martins et al. identified acremonidins A (287), B (288), C (289), G (290) and acremonoxanthones A (291), B (292), D (293), F (294), and G (295) (Figure 27) from the EtOAc extracts of a culture broth and mycelia of Acremonium camptosporum, isolated from a marine sponge, Aplysina fulva, which was collected from the mid-Atlantic Saint Peter and Saint Paul Archipelago, Brazil [126].

Ayers et al. described the isolation of the previously described anthraquinone-xanthone derivatives i.e., 287, 289, and 294, together with acremonoxanthone C (296) (Figure 27), from the solid-rice culture extract of an unidentified fungus of the order Hypocreales (MSX 17022), which was obtained from leaf litter from a beech tree community in Hillsborough, NC, USA [127].
Figure 27. Structures of 279–296.
4. Biological Activities

4.1. Antibacterial and Antifungal Activities

Compounds 1, 9–11 (Figure 3), 168 (Figure 15) and 181 (Figure 16), isolated from a culture extract of a soft coral-associated fungus, Aspergillus tritici SP2-8-1, were assayed for antibacterial activity against MRSA Staphylococcus aureus (ATCC 43300 and CGMCC 1.12409), Vibrio vulnificus MCCC E1758, V. rotiferianus MCCC E385, and V. campbellii MCCC E333. Compound 181 showed potent activity against all the tested strains, with minimum inhibitory concentration (MIC) values of 7.53, 7.63, 31.47, 31.17, and 15.53 \( \mu \text{g/mL} \), while 168 exhibited weaker activity, with MIC values of 15.27, 15.63, 15.47, 31.33, and 15.77 \( \mu \text{g/mL} \) against MRSA. S. aureus (ATCC 43300 and CGMCC 1.12409), V. vulnificus MCCC E1758, V. rotiferianus MCCC E385, and V. campbellii MCCC E333, respectively. Compound 1 showed similar activity to 168, with MIC values of 15.65, 15.53, 15.73, 62.67, and 31.35 \( \mu \text{g/mL} \). Compound 9 only exhibited activity against both strains of MRSA, with MIC values of 31.32 and 31.33 \( \mu \text{g/mL} \). The positive control, chloramphenicol, displayed MIC values of 7.67 and 7.87 \( \mu \text{g/mL} \) against MRSA-ATCC 43300 and CGMCC 1.12409, respectively. Compound 10 selectively inhibited the growth of V. rotiferianus MCCC E385 (MIC = 31.28 \( \mu \text{g/mL} \)), while the positive control, erythromycin, showed MIC = 3.93 \( \mu \text{g/mL} \) [28].

Compounds 1, 15 (Figure 3) and 37 (Figure 4), isolated from the culture extract of a mangrove-derived endophytic fungus, Eurotium chevalieri KUFA 0006, were tested for antibacterial and antifungal activities. Compound 1 showed antibacterial activity against Enterococcus faecalis ATCC29212 and S. aureus ATCC25923, with an MIC values = 64 and 32 \( \mu \text{g/mL} \), respectively (the positive control, cefotaxime, has MIC values ranging from 0.031 to 16 \( \mu \text{g/mL} \)). Compounds 15 and 37, at a concentration of 64 \( \mu \text{g/mL} \), caused a significant reduction in biofilm formation in Escherichia coli ATCC25922 (percentage of biofilm production; 56.1% and 50.6%, respectively), while 1 and 6 (Figure 3) displayed an inhibition of a biofilm formation in S. aureus ATCC25923 [31].

Compounds 1 (Figure 3) and 20 (Figure 4), isolated from the fermentation extract of a marine sediment-derived fungus, A. versicolor, were tested against MRSA-ATCC 43300 and MRSA-CGMCC 1.12409, V. vulnificus, V. rotiferianus, and V. campbellii. Compound 20 showed potent antibacterial activity against MRSA-ATCC 43300 and MRSA-CGMCC 1.12409, with MIC values = 3.9 and 7.8 \( \mu \text{g/mL} \), respectively (The positive control, chloramphenicol, displayed MIC = 7.78 \( \mu \text{g/mL} \) against both MRSA ATCC 43300 and CGMCC 1.12409), and moderate antibacterial activity against V. vulnificus, V. rotiferianus, and V. campbellii, with MIC values ranging from 15.6 to 62.5 \( \mu \text{g/mL} \). Conversely, 1 showed moderate activity against MRSA-ATCC 43300 and MRSA-CGMCC 1.12409 with MIC = 15.6 \( \mu \text{g/mL} \) for both strains, and weak activity against V. vulnificus, V. rotiferianus, and V. campbellii, with MIC values ranging from 15.6–62.5 \( \mu \text{g/mL} \). The positive control, erythromycin, displayed MIC values of 2, 3.9 and 7.8 \( \mu \text{g/mL} \) against V. vulnificus, V. rotiferianus, and V. campbellii, respectively. Molecular docking studies showed that 20 also bound to the AmpC \( \beta \)-lactamase receptor with good least binding energy of −4.45 kcal/mol, indicating hydrogen bond interactions of OH-1 and CH(OCH\(_3\))\(_2\)-O in 20 with Arg148, a \( \pi-\pi \) interaction of the fused ring system with the benzene ring of Tyr150, and hydrophobic interactions with Lys290, Ala292, Leu293, Ala294, Lys315, and Thr316 residues [35].

Wang et al., in their screening for compounds produced by marine-derived fungi that inhibit biofilm formation in S. aureus, have found that 1 (Figure 3) and 28 (Figure 4), isolated from Penicillium sp. SCSGAF 0023 (CCTCC M 2012507), exhibited antibiofilm activity. Compound 1, at a concentration of 12.5 \( \mu \text{g/mL} \), was able to inhibit a biofilm formation more than 50%, while 28 was less active, inhibiting biofilm formation less than 37% at a concentration of 25 \( \mu \text{g/mL} \) [128].

Compounds 1 (Figure 3), 29 (Figure 4), 175 (Figure 15) and 223 (Figure 19), isolated from a sea cucumber-associated fungus, Trichoderma sp. (H-1), were evaluated for their antibacterial activity against three marine pathogenic bacteria, V. parahaemolyticus, V. anguillarum, and Pseudomonas putida. Compound 223 showed pronounced antibacterial activity against V. parahaemolyticus, V. anguillarum and P. putida, with MIC values of 6.25, 1.56, and 3.13 \( \mu \text{M} \),
respectively. Compound 175 exhibited significant inhibitory activity against *V. anguillarum* and *P. putida*, with MIC values of 1.56 and 6.25 µM, respectively. Compound 1 displayed moderate activity against *P. putida* with a MIC value of 25.0 µM, whereas 29 showed activity against *V. parahaemolyticus* with a MIC value of 25.0 µM. The positive control, ciprofloxacin, showed MIC values of 2.50, 0.625, and 0.625 µM, against *V. parahaemolyticus*, *V. anguillarum*, and *P. putida*, respectively [43].

Compounds 1, 40 (Figure 4) and 71 (Figure 6), isolated from a soft coral-associated fungus, *Trichoderma harzianum* (XS-20090075), selectively exhibited the growth of *S. aureus* with MIC values of 6.25, 25.0, and 25.0 µM, respectively [55].

Compound 6 (Figure 3), isolated from a marine sponge-associated fungus, *Europium chevalierii* MUT2316, showed inhibitory activity against four bacterial species including *Halomonas aquamarina* ATCC14400, *Polaribacter irgensii* ATCC700398, *Vibrio aestuarii* ATCC 35048, and *Pseudoalteromonas citrea* ATCC 29720 with low observable effect concentration (LOEC) values of 0.01, 1, 10, and 0.01 µg/mL, respectively [53].

Compounds 28 (Figure 4) and 137 (Figure 11), isolated from a mangrove endophytic fungus, *Penicillium citrinum* HL-5126, showed weak antibacterial activity against *S. aureus* ATCC29213 with the same MIC values of 22.8 µM. Compound 137 also exhibited antibacterial activity against *V. parahaemolyticus* ATCC17802 with a MIC value of 10 µM. The positive control, ciprofloxacin, showed MIC values of 0.31 and 1.25 µM against *S. aureus* ATCC29213 and *V. parahaemolyticus* ATCC17802, respectively [41].

Although 29 (Figure 4), isolated from the culture extract of a marine sponge-associated fungus, *Aspergillus candidus* KUPA0062, did not exhibit antibacterial activity against Gram-positive (*S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, MRSA *S. aureus* 66/1, and VRE *E. faecalis* B3/101) and Gram-negative bacteria (*E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, a colistin-resistant *E. coli* 1418/1 strain, and a clinical isolate ESBL *E. coli* SA/2), it induced a significant reduction in biofilm formation (67.7% of the control) in *E. coli* ATCC 25922 (the background absorbance was used as a control) [16].

Compounds 29, 267, 268, and 269 (Figure 25), isolated from a red alga-associated fungal strain F-F-3C, showed antibacterial activity against pathogenic bacteria *E. coli* and *S. aureus* at a concentration of 50 µg/disk with inhibition zones ranging from 13 to 15.5 mm [44].

Compounds 33 (Figure 4), 171 (Figure 15), and 245 (Figure 24), isolated from the culture extract of a soft coral-associated fungus, *Alternaria* sp. ZJ-2008003, showed antibacterial activity against *E. coli*, *V. parahaemolyticus*, and *Staphylococcus albus*. Compound 33 inhibited the growth of all three bacterial strains with MIC values of 2.30, 5.0, and 15 µM. The positive control, ciprofloxacin, displayed MIC values of 0.62, 0.16, and 0.31 µM. Compound 171 showed the same potency as ciprofloxacin against *E. coli* with MIC value of 0.62 µM, followed by *V. parahaemolyticus* and *S. albus* (MIC values of 1.25 and 12 µM, respectively). Compound 245 inhibited antibacterial activity against *E. coli* and *V. parahaemolyticus* with the same MIC value of 2.5 µM, while no antibacterial activity against *S. albus* was recorded (IC₅₀ > 20 µM) [49].

Compounds 33, 170, 172, 173, 174 (Figure 15), 214 (Figure 19), 245, 254–256, 258, and 259 (Figure 25), isolated from a mangrove endophytic fungus, *Stemphylium* sp. 33231, were assayed for antibacterial activity against seven terrestrial pathogenic bacteria viz. *Micrococcus tetragenus* (ATCC13623), *E. coli* (ATCC 25922), *S. albus* (ATCC 8799), *Bacillus cereus* (ATCC 14579), *S. aureus* (ATCC 6538), *Kocuria rhizophila* (ATCC 9341), and *B. subtilis* (ATCC 6633). Compounds 173 and 214 selectively inhibited the growth of *E. coli* (MIC = 9.8 and 7.3 µM), while 245 selectively inhibited the growth of *S. albus* (MIC = 8.9 µM). Compounds 254, 258, and 259 also showed selective antibacterial activity against *B. cereus* with MIC values of 7.9, 8.3, and 8.1 µM, respectively. Compound 174 displayed better antibacterial activity against *E. coli*, *B. cereus*, *B. subtilis*, and *S. aureus* with the same MIC value of 3.9 µM, and against *M. tetragenus* with MIC value of 7.8 µM. Compound 170 had the same MIC value of 7.8 µM against *E. coli*, *S. aureus*, *K. rhizophila*, and *B. subtilis*, whereas 33, 172, 255, and 256 inhibited the growth of *M. tetragenus*, *E. coli*, *B. cereus*, *S. aureus*, and *B.
subtilis with MIC values ranging from 2.07 to 10 µM. The positive control, ciprofloxacin, showed MIC = 0.3, 0.3, 0.6, 0.6, 0.16, 0.3, and 0.6 µM [50].

Compound 48 (Figure 5), isolated from the culture extract of a sea urchin-derived Monodictys sp., at a concentration of 2.5 µg/disk, inhibited the growth of B. subtilis and E. coli, with the inhibition zones of 7 and 8 mm, respectively [60].

Compounds 53 (Figure 5) and 252 (Figure 24), isolated from the culture extract of a marine sponge-associated fungus, Curvularia lunata, at a concentration of 5 µg/mL, inhibited the growth of S. aureus ATCC 25923, E. coli ATCC 25922 and E. coli HBI 101 in the agar plate diffusion assay with the same inhibition zones of 8.5, 9.0, and 8.0 mm, respectively. Both 53 and 252 were also active against B. subtilis 168, with MIC values of 7.5 and 8.0 mm, respectively [64].

Compounds 58 (Figure 5), 182, 184, 186, 187 (Figure 16), 208, 209 and 210 (Figure 19), isolated from a sea-anemone-associated fungus, Nigrospora sp., were tested for antibacterial activity against a panel of pathogenic bacteria including B. subtilis, B. cereus, Micococcus luteus, M. tetragenus, S. aureus, S. albus, E. coli, V. anguillarum, and V. parahaemolyticus. Although 58 did not show any antibacterial activity, its acylated derivative, 58d, inhibited the growth of B. subtilis, B. cereus, M. tetragenus, V. anguillarum, and V. parahaemolyticus with MIC values of 5.00, 37.5, 9.40, 4.70, and 75.0 µM, respectively. Compound 182 was active against V. anguillarum (MIC = 0.39 µM) (the positive control, ciprofloxacin, showed MIC = 0.0780 µM), whereas 182a (Figure 16) displayed a pronounced inhibitory activity against B. cereus with MIC = 0.0488 µM (25 times more potent than ciprofloxacin whose MIC = 1.25 µM). Compound 184 exhibited potent antibacterial activity against B. subtilis and B. cereus with the same MIC values of 0.313 µM, respectively, which were comparable with the reference drug, ciprofloxacin, whose MIC values were 0.313 and 1.25 µM, respectively. Compounds 186, 208 and 209 inhibited the growth of all the tested bacterial strains, with the exception of M. luteus, with MIC values ranging from 1.56–3.12 µM for 186, and 0.780 to 25 µM for 208 and 209. Compound 187 showed strong antibacterial activity against B. subtilis with an MIC value of 0.625 µM [68].

Compounds 63 and 65 (Figure 6), isolated from the culture extract of a marine plant-associated fungus, Fusarium equiseti, displayed antibacterial activity against Pseudomonas syringae pv. lachrymans, Acidovorax avenae, and Erwinia carotovora. While 63 showed strong inhibition against the three bacterial strains, with MIC values of 3.91, 3.91, and 7.81 µg/mL, 65 displayed weak activity with MIC values of 15.6, 15.6, and 7.81 µg/mL, respectively (the positive control, streptomycin, showed MIC values of 0.24, 0.98, and 0.98 µg/mL, respectively) [73].

Compound 70 (Figure 6), isolated from a green alga-associated fungus, A. versicolor, at a concentration of 50 µg/disk, inhibited the growth of B. cereus, B. subtilis, and S. aureus with the inhibition zones of 11, 12, and 14 mm, respectively (the reference drug, oxytetracycline, showed the inhibition zones of 17, 20, and 17 mm, at a concentration of 50 µg/disk) [34].

Compound 73 (Figure 6), isolated from a deep-sea sediment-derived Emericella SCISO 05240, showed moderate antibacterial activity against E. coli ATCC29922, Klebsiella pneumonia ATCC13883, S. aureus ATCC29213, E. faecalis ATCC29212, Acinetobacter baumannii ATCC19606, and Aeromonas hydrophila ATCC7966 with inhibition zones ranging from 9 to 11 mm. The inhibition zone produced by the reference drug, ciprofloxacin, ranged between 35 and 40 mm [78].

Compounds 81, 85 (Figure 7), 104 and 107 (Figure 9), isolated from a marine sponge-associated fungus, A. versicolor, were evaluated for antibacterial activity against clinically isolated Gram-positive strains viz. Streptococcus pyogenes 308A, S. pyogenes 77A, S. aureus SG511, S. aureus 285, and S. aureus 503. Compound 81 selectively inhibited the growth of S. pyogenes 308A with MIC = 6.25 µg/mL, while 104 displayed antibacterial activity against S. pyogenes 308A and S. aureus 503, with the same MIC value of 6.25 µg/mL. Conversely, 85 and 107 inhibited the growth of all strains, with MIC values ranging from 0.78 to 6.25 µg/mL. The positive control, meropenam, showed MIC values of 0.01, 0.01, 0.10, 0.10, and 0.05 µg/mL. Since 107 displayed stronger antibacterial activity than 104, the OH-2' group was suggested to play a key role in antibacterial activity in 107 [84].
Compounds 82 and 95 (Figure 7), isolated from a marine sponge-associated fungus, *Aspergillus* sp. F40, were evaluated for antibacterial activity against *S. aureus* ATCC25923 and *V. parahaemolyticus* ATCC17802. Compound 82 selectively inhibited the growth of *V. parahaemolyticus* with MIC value of 12 µg/mL, whereas 97 showed weak antibacterial activity with MIC values of 48 and 24 µg/mL, respectively. The positive control, tobramycin, displayed MIC values of 0.75 and 0.38 µg/mL, respectively [93].

Compounds 83, 84 (Figure 7) and 113 (Figure 9), isolated from an algicolous fungus, *A. versicolor* EN-7, exhibited weak antibacterial activity against *E. coli*, at a concentration of 20 µg/disk, with inhibition zones of 7.0, 6.5, and 6.5 mm. Compound 113 also weakly inhibited the growth of *S. aureus* with an inhibition zone of 7.0 mm. The positive control, chloramphenicol, showed inhibition zones of 25 and 22 mm, at a concentration of 20 µg/disk [82].

Compounds 102 and 103 (Figure 9), isolated from a mangrove endophytic fungus, *A. nidulans* MA-143, displayed the antibacterial activity against some human and aquatic pathogenic bacteria viz. *E. coli, M. luteus, V. vulnificus, V. anguillarum, V. parahaemolyticus*, and *Edwardsiella ictaluri* with MIC values ranging from 1–64 µg/mL. Compound 102 showed potent antibacterial activity toward *V. alginolyticus* (MIC = 1 µg/mL), while 103 showed strong activity against *E. coli* and *V. parahaemolyticus*, with the same MIC value of 1 µg/mL. The positive control, chloramphenicol, showed MIC values of 1, 2, 8, 1, 0.5, 2, and 0.5 µg/mL [80].

Compounds 104 and 109 (Figure 9), isolated from a deep-sea sediment-derived *A. versicolorin* MF180151, displayed antibacterial activity against *S. aureus*, with MIC = 6.25 µg/mL. Compounds 104 and 109 also showed moderate activity against MRSA *S. aureus* with MIC = 25 and 12.5 µg/mL, respectively. The positive control, vancomycin, showed MIC = 1 µg/mL for both bacterial strains [101].

Compounds 104, 106, 107, 110, 117 and 118 (Figure 9), isolated from a gorgonian-associated fungus, *Aspergillus* sp., inhibited the growth of *S. albus* with MIC values ranging from 12.5–50 µM. Compounds 110 and 117 showed stronger antibacterial activity (MIC = 6.25 µM) than 106, 107 and 104 (MIC values of 25, 25 and 50 µM, respectively) against *M. luteus*, suggesting that the methoxy group on C-8 might play an important role for this activity. The positive control, ciprofloxacin, showed MIC values of 3.13 and 0.780 µM, respectively [103].

Sharma et al. [129], in their search for novel potent inhibitor(s) against β-ketoacyl-ACP reductase (MabA) and polyketide synthase18 (PKS18), which are involved in mycolic acid biosynthesis in *Mycobacterium tuberculosis*, by virtual screening of anthraquinones from marine-derived fungi, have found that among 100 marine-derived anthraquinones retrieved from the PubChem database, only three fulfilled all ADMET (absorption, distribution, metabolism, excretion, and toxicity) descriptors after the filtering through Lipinski’s rule of five (for drug likeness) and in silico ADME/Tox analysis (for pharmacokinetic properties). Compound 104 showed the highest human intestinal absorption among all anthraquinones tested and the controls (isoniazid and ethambutol). Molecular docking studies using AutoDock 4.2 revealed that 104 showed the best docking conformation with binding affinities of −8.84 and −8.23 kcal/mol with MabA and PKS18, respectively, and Ki values of 1.79 and 3.12 kcal/mol, respectively. Further analysis of 104 to identify its best docking pose revealed three binding pockets and interacting residues of active sites in the respective pockets of MabA. Compound 104 showed interactions with amino acids Arg25, Gly28, Gly26, Met190, Thr191, Ile186, Pro183, Tyr185, Gly184, Gly139, Val141, Ser140, Tyr153, Asn88 in the first binding pocket and hydrogen bond formation with three amino acids, i.e., Ser140, Ile27, Thr188. In PKS18, 149 showed the interaction with Tyr188, His192, Gly136, Ser166, Gln255, Glu295, Phe253, Ser252, Ser251, Glu295, in the first binding pocket and established hydrogen bonds with five amino acid residues, i.e., Ser254, Gln255, Met296, Ser164, Asp299 [129].

Compounds 156, 157 (Figure 13), and 231 (Figure 20), isolated from an algicolous fungus, *Eurotium cristatum* EN-220, were evaluated for their antibacterial activity. Compound 156
inhibited the growth of *E. coli* with MIC value of 32 µg/mL, while 157 was inactive, indicating that the methyl group at C-3 is essential for bioactivity in 156. Compound 231 showed weak activity against *E. coli*, with MIC value of 64 µg/mL. The positive control, chloramphenicol, showed MIC value of 4 µg/mL [95].

Compound 126 (Figure 10), isolated from a sea fan-derived fungus, *Penicillium citrinum* PSU-F51, showed moderate antibacterial activity against *S. aureus* ATCC25923 and MRSA *S. aureus* SK1, with a MIC values of 16 µg/mL. Vincomycin was used as a positive control and showed MIC value of 1 µg/mL [37].

Compounds 170, 178, 179, 180 (Figure 15) and 226 (Figure 19), isolated from the culture extract of a sea sediment-derived fungus, *Sporendonema casei* HDN16-802, displayed antibacterial activity against *Mycoheribacterium phlei*, *Proteus* sp., *B. subtilis*, *V. parahemolyticus*, and *P. aeruginosa*, with MIC values ranging from 12.5 to 200 µM (MIC values of the positive control, ciprofloxacin, ranged from 0.781 to 3.12 µM) [109].

 Compound 177 (Figure 15), isolated from the culture extract of a mangrove endophytic fungus, *Phomopsis* sp. PSU-MA214, showed, in a colorimetric broth microdilution assay, moderate antibacterial activity against *S. aureus* ATCC25923 and methicillin-resistant *S. aureus* SK1, with MIC values of 128 and 64 µg/mL, respectively (the positive control; vancomycin, showed MIC value of 1 µg/mL) [52].

Compounds 182 and 186 (Figure 16), isolated from the mangrove endophytic fungus, *Nigrospora* sp. (strain no. 1403), showed strong antibacterial activity against *S. aureus* ATCC27154, *E. coli* ATCC25922, *P. aeruginosa* ATCC25668, *Sarcina ventriculi* ATCC29168, and *B. subtilis* ATCC6633, with the same MIC values of 3.13 µg/mL. The MIC value of the positive control, ampicillin, ranged from 3.1 to 50 µg/mL [112].

Compounds 184 and 186 (Figure 16), isolated from a mangrove endophytic fungus, *Nigrospora* sp., were tested in an in vitro anti-mycobacterial activity against various strains of *Mycoheribacterium*, such as *M. bovis* BCG (strain Pasteur, ATCC 35734), *M. tuberculosis* H37Rv reference strain (ATCC 27294), clinical multidrug-resistant (MDR) *M. tuberculosis* strain (K2903531, resistant to SM, INH, RFP and EMB), clinical MDR *M. tuberculosis* strain (0907961, resistant to SM and EMB), clinical drug-resistant *M. tuberculosis* strain (K0903557, resistant to INH), clinical drug-sensitive *M. tuberculosis* strain (0907762). Compound 186 displayed potent activity against two MDR *M. tuberculosis* clinical isolates, K2903531 and 0907961, and even better than that of the first line anti-tuberculosis agents. Moreover, treatment of *M. tuberculosis* H37Rv with 186 caused a significant difference of 119 genes, with 52 being significantly increased and 67 significantly decreased [130].

Compounds 184 (Figure 16), 208 and 209 (Figure 19), isolated from a sea fan-associated *Fusarium* sp. PSU-F14 and PSU-F135, exhibited a growth inhibition of *M. tuberculosis* H37Ra, with MIC values of 41, 87, and 38.57 µM, respectively (MIC values of the positive control, isoniazid, ranging from 0.17–0.34 µM) [59].

Compounds 197 and 198 (Figure 19), isolated from a coral-associated *Aspergillus* sp. strain 05F16, showed antibacterial activity against *S. aureus* IAM 12544T and *E. coli* IAM 12119T. Compound 197, at a concentration of 100 µg/disc, weakly inhibited the growth of *S. aureus* IAM 12544T and *E. coli* IAM 12119T (inhibition zones = 15 and 9.2 mm, respectively), while 198 was only active against *S. aureus* (inhibition zone = 12 mm). It was suggested that the presence of the quinone core is necessary for the bioactivity [110].

Compounds 199, 200, 201, 202 and 203 (Figure 19), isolated from the culture extract of an algicolic fungus, *Talaromyces islandicus* EN-501, showed pronounced antibacterial activity against *S. aureus* EMBLC-2 with MIC values ranging from 2 to 8 µg/mL. Compounds 200-203 showed weak inhibitory activity against *E. coli* EMBLC-1 and *E. tarda* QDIO-2, with MIC values ranging from 16 to 64 µg/mL. Compound 199 also exhibited weak activity against *E. coli* with MIC value of 64 µg/mL. The positive control, chloramphenicol, showed MIC = 2, 4, and 2 µM, against *S. aureus*, *E. coli*, and *E. tarda*, respectively [117].

Compounds 237 and 238 (Figure 23), isolated from a marine clam-associated fungus, *A. versicolor*, selectively inhibited *S. aureus* (inhibition zones 14 and 19 mm) at a concentra-
tion of 30 µg/well by a radial dilution assay. The positive control, tetracycline, displayed an inhibition zone of 30 mm at a concentration of 30 µg/well [88].

Compounds 243 and 244 (Figure 24), isolated from a mangrove endophytic fungus, *Alternaria* sp. (SK11), showed an inhibitory activity against *M. tuberculosis* protein tyrosine phosphatase B (MptpB), which is an essential virulence factor when *M. tuberculosis* hosts macrophages. Compound 244 (IC$_{50} = 8.7$ µM) was more active than 243 (IC$_{50} = 64.7$ µM). The IC$_{50}$ value of the positive control, sodium orthovanadate, was 0.05 µM [62].

Compounds 279, 283, 285 and 286 (Figure 27), isolated from a marine sponge-associated fungus, *Engyodontium album* strain LF069, were examined against clinically relevant bacterial strains viz. *Staphylococcus epidermidis* DSM 20044, methicillin-resistant *S. aureus* (MRSA) DSM 18827, and *Propionibacterium acnes* DSM 1897. Compounds 279–282 (Figure 27) showed strong antibacterial activity against *S. epidermidis* and methicillin-resistant *S. aureus* (MRSA) with IC$_{50}$ values of approximately 0.2 µM, which were 10 times more active than chloramphenicol (IC$_{50}$ value of 1.8 and 2.9 µM, respectively), and against *P. acnes* with IC$_{50}$ values of 11.0, 13.8, 14.1, and 11.7, respectively. Conversely, 283, 285, and 286 inhibited the growth of *S. epidermidis* and methicillin-resistant *S. aureus* (MRSA) with IC$_{50}$ ranging from 1.80 to 6.77 µM [125].

### 4.2. Antifungal Activity

Compounds 33 (Figure 4), 56, 57 (Figure 5), 212 and 214 (Figure 19), isolated from a mangrove endophytic fungus, *Phoma* sp. L28, showed an in vitro antifungal activity against *Fusarium oxysporum* Schlecht. f. sp. *lycopersici* (Sacc.) W.C. Snyder et H. N. Hansen, *F. graminearum* Schw, *Colletotrichum musae* (Berk. & M. A. Curtis) Art., *C. gloeosporioides* (Penz) Sacc., *Penicillium italicum* Wehme, and *Rhizoctonia solani* Kuhn. Compound 33 exhibited a broad-spectrum antifungal activity with MIC values of 3.75, 60, 30, 60, 100, and 60 µg/mL, respectively (the positive control, carbendazim; showed IC$_{50}$ values ranging from 4.1 to 13.5 µM). Conversely, 56 and 57 only showed moderate to weak (MIC values ranging from 80 to 200 µg/mL) or no (MICs > 200 µg/mL) antifungal activity against all the assayed fungal strains, while 214 was inactive against all the tested pathogens with the exception of *P. italicum* (MIC = 80 µg/mL). Compound 212 moderately inhibited the growth of *P. italicum* and *R. solani* (MIC = 35 and 50 µg/mL) and weakly inhibited the growth of *F. graminearum* and *C. gloeosporioides* (MIC = 100 and 200 µg/mL) [67].

Compounds 63 and 65 (Figure 6), isolated from the culture extract of a marine plant-derived fungus, *Fusarium equiseti*, displayed a moderate inhibitory activity against *Pestalozzia theae* with MIC value of 31.3 µg/mL. The fungal inhibitor, carbendazim, showed MIC = 7.81 µg/mL [75].

Compound 182 (Figure 16), isolated from a mangrove endophytic fungus strain no. 1403, inhibited, in a yeast-based assay on *Saccharomyces cerevisiae*, cell proliferation through the cell cycle at G1 phase, leading to cell death in a time- and dose-dependent manner [111].

Compounds 182 and 186 (Figure 16), isolated from the mangrove endophytic fungus, *Nigrospora* sp. (strain no. 1403), moderately inhibited the growth of *Candida albicans* ATCC10231 with the same MIC values (12.5 µg/mL). The MIC value of the positive control, nystatin, was 1.56 µg/mL [112].

Compound 268 (Figure 25), isolated from an algicolous fungal strain F-F-3C, inhibited the growth of *Choanephora cucurbitarum* at a concentration of 50 µg/disk, with an inhibition zone of 11–12.5 mm [44].

Compounds 279–282 (Figure 27), isolated from a marine sponge-associated fungus, *Engyodontium album* strain LF069, exhibited weak antifungal activity against *C. albicans* and *Trichophyton rubrum* with IC$_{50}$ values ranging from 4.1 to 13.5 µM. The IC$_{50}$ values of positive controls, nystatin and clotrimazol, were 1.5 and 0.16 µM, respectively [125].

### 4.3. Antiviral Activity

Compounds 1 and 4 (Figure 3), isolated from a green alga-derived fungus, *Aspergillus versicolor*, showed inhibitory activity against hepatitis C virus (HCV) protease (HCV-PR)
with IC₅₀ values of 22.5 and 40.2 µg/mL, respectively. The positive control, HCV I2, showed an IC₅₀ value of 1.5 µg/mL [34].

The fermentation extract of *Fusarium equiseti*, isolated from a brown alga, *Padina pavonica*, potently inhibited the HCV NS3-NS4A protease with an IC₅₀ value of 27.0 µg/mL. Compounds 28 (Figure 4), isolated from this extract, also inhibited HCV NS3-NS4A protease with an IC₅₀ value of 10.7 µg/mL, which was comparable to the positive control, HCV-I₂ (IC₅₀ = 1.5 µg/mL). Conversely, the co-isolate 29 was void of activity. It was suggested that the substituent CH₂OH at C-3 is essential for the bioactivity of 28 [40].

Compounds 47 and 58 (Figure 5), isolated from a zoanthid-derived fungus, *Nigrospora* sp., were evaluated for antiviral activity. Compound 47 exhibited antiviral activity against respiratory syncytial virus (RSV) with an IC₅₀ value of 74.0 µM, while 58 showed a moderate inhibitory activity against coxsackie virus (Cox-B3) with an IC₅₀ value of 93.7 µM. The positive control, ribavirin, showed antiviral activity against RSV and Cox-B3 with IC₅₀ values of 78.0 and 39.0 µM, respectively [69].

Compound 64 (Figure 6), isolated from a marine sponge-associated fungus, *Trichoderma* sp. strain SCSIO41004, showed significant antiviral activity against enterovirus 71 (EV71) on Vero cells by CCK-8 assay (IC₅₀ value of 25.7 µM). The positive control, ribavirin, showed an IC₅₀ value = 13.3 µM [56].

Compound 69 (Figure 6), isolated from the acidic fermentation extract of a mangrove sediment-derived fungus, *Penicillium* sp. OUCMDZ-4736, displayed anti-hepatitis B virus (HBV) activity by inhibiting the secretion of both HBeAg and HBsAg by HepG2.2.15 cells, in a dose-dependent manner. Compound 69 inhibited both HBeAg and HBsAg more efficiently than the positive control, 3TC [76].

Compounds 92, 94 (Figure 7), and 125 (Figure 10), isolated from a deep-sea sediment-derived fungus, *Aspergillus versicolor* SCSIO 41502, showed antiviral activity toward HSV-1, in a plaque reduction assay, with half maximal effective concentration (EC₅₀) values of 6.25, 3.12, and 4.68 µM, and 50% inhibitory concentration (CC₅₀) values of 50.7, 65.1, and 108.6 µM, respectively. The corresponding IC₅₀ and CC₅₀ values of the positive control acyclovir, were 3.0 and >1000 µM, respectively [92].

Compounds 104 and 107 (Figure 9), isolated from the culture extract of a sea water-derived fungus, *Aspergillus niger* (MF-16), showed inhibitory activity against Tobacco Mosaic virus (TMV) replication at a concentration of 0.2 mg/mL (inhibition 58.1% and 64.9%, respectively), with EC₅₀ values of 0.101 and 0.122 mg/mL, respectively [98].

Compounds 107 and 112 (Figure 9), isolated from the culture extract of a marine sponge-associated fungus, *A. versicolor*, reactivated the latent human immunodeficiency virus (HIV)-1 expression in an in vitro model of 2D10 cells, at a concentration of 10 µM, with reactivation of 39.1% and 43.3%, respectively. The positive control, prostratin, exhibited reactivation of 79.4% at a concentration of 2.5 µM [102].

Compound 216 (Figure 19), isolated from the culture extract of a marine alga-derived endophytic fungus, *Talaromyces islandicus* EN-501, significantly inhibited a replication of the porcine reproductive and respiratory syndrome virus (PRRSV), in a dose-dependent manner, with EC₅₀ = 12.11 µM, CC₅₀ = 395.31 µM, and selective index (SI) = 32.64. Further experiments revealed that 216 effectively inhibited virus entry, but did not block adsorption to the host cell surface [107].

### 4.4. Antiparasitic Activity

Compounds 182, 184 (Figure 16), and 209 (Figure 19), isolated from a sea fan-associated fungus, *Fusarium* sp. PSU-F14 and PSU-F135, were assayed for antiparasitic activity against *Plasmodium falciparum* K1 by the microculture radioisotope technique. Compounds 182 (IC₅₀ = 9.8 µM) and 184 (IC₅₀ = 13 µM) showed better antimalarial activity than 209 (IC₅₀ = 24.5 µM). The positive control, dihydroartemisinin, showed IC₅₀ = 0.004 µM [59].

Compounds 192 and 193 (Figure 17), isolated from modified cultures of a mangrove sediment-derived fungus, *Aspergillus glaucus* HB 1-19, were examined for its activity against the pathogens of leishmaniasis and African sleeping sickness. Compound 192 showed no
activity against Leishmania major (promastigote form) or Trypanosoma cruzi (IC_{50b} > 50 mm) but weak activity against T. brucei brucei and L. donovani (amastigote form) with IC_{50} values of 29 and 17 µM, respectively, while 193 had no activity against both parasites (IC_{50} > 50 µM) [115].

4.5. Cytotoxic Activity

Compounds 1 (Figure 3) and 164 (Figure 14), isolated from the culture extract of a mangrove endophytic fungus, Eurotium rubrum, were assayed for their cytotoxic activity against seven human tumor cell lines viz. breast adenocarcinoma (MCF-7), cholangiocarcinoma (SW1990), hepatoma (HepG2), non-small cell lung cancer (NCI-H460), hepatoma (SMMC7721), cervical cancer (Hela), and prostate cancer (Du145). Compound 1 showed selective cytotoxicity against DU145 (IC_{50} = 15 µg/mL), while 164 displayed selective cytotoxicity toward SW1990 (IC_{50} = 25 µg/mL) [47].

Compounds 1 (Figure 3), 28 (Figure 4), 53 (Figure 5) and 68 (Figure 6), isolated from a marine sediment-derived fungus, Gliocladium catenulatum T31, showed cytotoxicity against human leukemia cell line (K562) with IC_{50} values of 1.09, 1.24, 8.92, and 13.60 µmol/L, respectively [65].

Compounds 1, 10, 11 (Figure 3), 168 (Figure 15) and 181 (Figure 16), isolated from the culture extract of a soft coral-associated fungus, Aspergillus tritici SP2-8-1, were assayed against human cancer cell lines viz. HeLa, lung carcinoma (A549), and HepG2, using Cell Counting Kit-8 (CCK-8) assay. Compounds 1, 168, and 181 displayed cytotoxicity against HeLa, A549, and HepG2 cells with IC_{50} = 25.07, 22.17, and 30.20 µM; for 1, IC_{50} = 10.57, 4.67, and 8.57 µM; for 168, and IC_{50} = 2.67, 3.13, and 3.87 µM; for 181, respectively. Compound 10 selectively inhibited the growth of A549 cells with IC_{50} value of 45.63 µM, while 11 selectively inhibited the growth of HepG2 with IC_{50} value of 42.07 µM. The positive control, doxorubicin, showed cytotoxicity with IC_{50} values of 0.5, 0.09, and 1.06 µM, respectively [28].

Compound 6 (Figure 3), isolated from the culture extract of a wild bivalve-derived fungus, Penicillium sp. Z9901, displayed antiproliferative activity against glioma C6 and U78MG cells with IC_{50} values of 30.22 and 34.68 µM, respectively. The positive control, doxorubicin, showed IC_{50} values of 0.47 and 1.2 µM, respectively [27]. Compound 6, isolated from a red alga-associated fungus, Micosporum sp., showed cytotoxic and anti-proliferative activities against HeLa cells through apoptosis. The Western blot analysis revealed that 6 downregulated Bcl-2 expression, upregulated Bax expression, and activated the caspase-3 enzyme [26].

Compounds 40 (Figure 4) and 71 (Figure 6), isolated from a marine coral-associated fungus, Trichoderma harzianum, showed cytotoxicity toward HepG2 cells, in a sulforhodamine B (SRB) assay, with IC_{50} values of 9.39 and 2.10 µM, respectively. Compound 71 also exhibited cytotoxicity against HeLa cells with an IC_{50} value of 8.59 µM [55].

Compound 46 (Figure 5), isolated from a decayed wood-derived fungus, Haloarcula limicola sp. (no. 1403), was tested against human nasopharyngeal epithelial tumor (KB and KBv200) cell lines using a 2,5-diphenyl-2H-tetrazolium bromide (MTT) colorimetric method. Compound 46 showed remarkable cytotoxicity against both cell lines with IC_{50} values of 1.40 and 2.58 µg/mL, respectively [58]. Zhang et al., in the screening of 14 anticancer anthraquinone metabolites against KB and KBv-200 cell lines, have found that 46 was the most active anthraquinone that inhibited the growth of both cancer cell lines with IC_{50} values of 3.17 and 3.21 µM, respectively (IC_{50} values of the positive control, adriamycin, were 0.034 and 1.894 µM, respectively). The authors suggested that the mitochondrial dysfunction might be responsible for the apoptosis caused by this compound [131].

Compounds 47 (Figure 5), 182, 184 (Figure 16), 208 and 209 (Figure 19), isolated from a sea fan-derived fungus, Fusarium sp. PSU-F14 and PSU-F135, were evaluated for cytotoxic activity against KB, MCF-7, and non-cancerous Vero (African green monkey kidney fibroblasts) cell lines. Compounds 182, 184, 208, and 209 showed cytotoxicity against all the tested cell lines (IC_{50} = 0.9, 2.7, and 4.2 µM; for 182, IC_{50} = 88, 5.4, and 29 µM; for 184, IC_{50} = 19, 15, and 57 µM; for 208, and IC_{50} = 49, 6.2, and 54 µM; for 209, respectively), while 47 selectively inhibited MCF-7 cells (IC_{50} value of 6.3 µM). The positive
control, doxorubicin, showed IC$_{50}$ values of 0.33 and 2.18 µM against KB and KBMCF-7 cells, respectively, whereas the IC$_{50}$ of ellipticine (the positive control for Vero cells) was 4.47 µM [59].

Compound 55 (Figure 5), isolated from a marine sediment-derived fungus, *Thermonomyces lanuginosus* Tsikl. KMM 4681, displayed cytotoxic activity toward drug-resistant human prostate cancer, 22Rv1, cells. The cell viability, at a concentration of 100 µM for 48 h, was reduced by 35% following treatment with 55. Compound 55 also did not show high cytotoxicity on human prostate non-cancer PNT-2 cells. Treatment with 55 suppressed the formation of a colony in prostate cancer 22Rv1 cells by 70% at the non-cytotoxic concentration of 50 µM [66].

Compound 77 (Figure 6), isolated from a mangrove endophytic fungus, *Fusarium* sp. ZZF60, exhibited cytotoxicity against human larynx carcinoma (Hep2) and HepG2 cancer cell lines, in a cell-based MTT assay, with IC$_{50}$ values of 16 and 23 µmol/L, respectively [79].

Compounds 81, 82, 85 (Figure 7), 104 and 107 (Figure 9), isolated from a marine sponge-associated fungus, *A. versicolor*, were assessed against five human solid tumor cell lines, viz. A549 (lung), SK-OV-3 (ovarian), SK-MEL-2 (skin), XF498 (CNS), and HCT15 (colon). Compounds 81, 85, and 107 showed significant cytotoxic activity with IC$_{50}$ values ranging from 0.41–3.88 µg/mL, while 82 and 104 exhibited weak cytotoxicity toward the assayed cell lines, with IC$_{50}$ ranging from 15.29–23.73 µg/mL. The positive control, doxorubicin, showed IC$_{50}$ values of 0.004, 0.019, 0.002, 0.01, and 0.034 µg/mL, respectively [84].

Compounds 82, 85, 99, 104, 107, 109, 118 and 119 (Figure 9), isolated from a marine-derived *Penicillium flavidorsum* SHK1-27, were examined for their antiproliferative activity against K562 cells by SRB method. Compound 107 was the most potent, followed by 82, 104, 109, 85, and 119 with IC$_{50}$ values of 12.6, 27.7, 72.4, 91.0, 93.4, and 98.7 µM, respectively. Conversely, 99 and 118 weakly inhibited the proliferation of K562 cells with IC$_{50}$ values > 100 µM [85].

Compounds 81, 85, 87, 88, 91 (Figure 7), 139–147 (Figure 11), isolated from a marine sediment-derived fungus, *Aspergillus* sp. SCSIO F063, were tested for their cytotoxic activity against three human tumor cell lines viz. SF-268 (brain), MCF-7, and NCI-H460 (non-small cell lung cancer) by SRB method. Compound 140 showed pronounced cytotoxicity against all tested cell lines, with IC$_{50}$ values of 7.11, 6.64, and 7.42 µM, respectively, while 81, 141, and 147 showed moderate cytotoxicity against all the tested cell lines with IC$_{50}$ values ranging from 18.91 to 44.22 µM. Compounds 85, 87, 139, 143, and 145 selectively inhibited the growth of MCF-7 cells, with IC$_{50}$ values of 45.47, 29.69, 36.41, 49.53, and 24.38 µM, respectively. Compound 91 weakly inhibited the growth of SF-268 and MCF-7 cells with IC$_{50}$ values of 47.19 and 40.47 µM, respectively. The positive control, cisplatin, showed IC$_{50}$ values of 4.59, 10.23, and 1.56 µM, respectively [91].

Compounds 107 and 109 (Figure 9), isolated from a deep-sea sediment-derived fungus, *A. versicolor*, weakly inhibited A549 cell lines with IC$_{50}$ values of 25.6 and 25.97 µM, respectively. Compound 107 also displayed a weak cytotoxicity against human ovary (A2780) cell line (IC$_{50}$ value of 38.76 µmol/L) [89]. Compound 107, isolated from a gorgonian-associated fungus, *Aspergillus* sp., showed significant growth inhibitory effects on K562 and HL-60 cell lines, in the MTT assay, with IC$_{50}$ values of 0.87 and 1.46 µM, respectively [103]. Further in vitro antitumor activity investigation revealed that 107 caused a significant induction in cell cycle arrest at G$_2$/M transition in K562 cell line in a concentration- and time-dependent manners (IC$_{50}$ = 12.6 µM) [99].

Compound 128 (Figure 10), isolated from a sea fan-associated fungus, *Penicillium citrinum* PSU-F51, displayed mild cytotoxicity against KB cells with IC$_{50}$ value of 30 µg/mL [37].

Compounds 170 and 172 (Figure 15), isolated from a soft coral-associated fungus, *Stemphylium lycopersici*, were assayed against HTC-116, MCF-7, and Huh7 cancer stem cell-like cells using CCK-8 assay. Compound 172 showed significant growth inhibitory activity against all tested cell lines with IC$_{50}$ values of 1.3, 7.2, and 38.0 µM, respectively, while 170 exhibited cytotoxic affects toward HTC-116 and MCF-7 cancer cells with IC$_{50}$
values of 3.5 and 9.0 µM, respectively. The positive control, Adriamycin, showed IC\(_{50}\) values of 5.4, 6.2, and 15.4 µM, respectively, for HTC-116, MCF-7, and Huh7 cancer cells [51].

Compounds 171 (Figure 15), 245 and 248 (Figure 24), isolated from the culture extract of a soft coral-associated fungus, *Altenaria* sp., were evaluated for cytotoxic activity against human colon carcinoma (HCT-116), human breast cancer (MCF-7/ADR), human prostatic cancer (PC-3), and human hepatoma (HepG2 and Hep3B) cell lines, using MTT method. Compound 171 exhibited potent cytotoxicity against all the tested cell lines, with IC\(_{50}\) values of 2.2, 3.2, 7.6, 8.9, and 8.2 µM, respectively, while the IC\(_{50}\) values for 245 and 248 ranged from 24–98 and 6.4–23 µM, respectively. IC\(_{50}\) values of the positive control, epirubicin, were 0.82, 1.65, 0.46, 1.65, and 0.96 µM, respectively [49].

Compound 176 (Figure 15), isolated from a mangrove endophytic fungus, *Halorosellina* sp. no. 1403, showed a broad-spectrum anti-proliferative activity against six human cancer cell lines viz. breast cancer (MCF-7 and MDA-MB-435), prostate cancer (PC-3), glioma cancer (LN-444), and hepatoma cancer (Hep-3B and Huh-7), in a cell-based MTT assay, with IC\(_{50}\) values ranging from 3.0 to 9.6 µM. This compound also suppressed the growth of breast cancer xenografts in mice [108]. In order to investigate the mechanism underlying the anticancer activity, Chen et al. evaluated the effects of 176 on rat prolactinoma cell line, MMQ, using MTT assay, flow cytometry, real-time polymerase chain reaction (RT-PCR) and immunoblotting assays. Compound 176 inhibited cell growth of MMQ in a dose-dependent manner (IC\(_{50}\) = 13.2 mM) and displayed weak toxicity against rat pituitary cells (RPCs) with an IC\(_{50}\) value of 49.1 mM. The apoptotic cells in MMQ cells treated with 176 were enhanced through downregulation of miR-200c, and the expression level of prolactin (PRL) was inhibited without any changes in PRL mRNA levels [132]. Compound 176 also stimulated apoptosis in human nonfunctioning pituitary adenoma (NFPA) cells through the inhibition of the Akt pathway [133].

Compound 177 (Figure 15), isolated from the culture extract of a mangrove endophytic fungus, *Phomopsis* sp. PSU-MA214, selectively inhibited the growth of MCF-7 cells with an IC\(_{50}\) value of 27 µg/mL but was not cytotoxic to Vero cells. Doxorubicin (IC\(_{50}\) = 8.57 µg/mL) and tamoxifen (IC\(_{50}\) = 89.47 µg/mL) were used as positive controls [52].

Compounds 178 (Figure 15) and 226 (Figure 19), isolated from a sediment-derived fungus, *Sporella* sp. HDN16-802, were assayed against ten human cancer cell lines, including Hela, K562, HL-60 (leukemia), HCT-116 (colon), MGC-803 (gastric), HO8910 (ovarian), MDA-MB-231 (breast cancer), SH-SYSY (neuroblastoma), PC-3, BEL-7402 (liver), and L-02 (human normal liver cell line) using MTT and SRB assays. Compounds 178 and 226 displayed moderate cytotoxicity toward all cancer cell lines tested, with IC\(_{50}\) values ranging from 4.5 to 22.9 µM. IC\(_{50}\) values of the positive control, doxorubicin, ranged from 0.1 to 1.0 µM [109].

Compounds 182 and 186 (Figure 16), isolated from a mangrove endophytic fungus, *Nigrospora* sp. (strain no. 1403), showed significant cytotoxicity against six human cancer cell lines, viz. A549, Hep-2, HepG2, KB, MCF-7, and MCF-7/Adr, with IC\(_{50}\) values ranging from 2.44 to 6.68 µM/mL [112]. In another research, 186, isolated from the same marine-derived fungus, also exhibited the anticancer activity against MDA-MB-435, HepG2, and HCT-116 cancer cell lines, with IC\(_{50}\) values of 3.19, 9.99, and 5.69 µM, respectively. The positive control, epirubicin, showed IC\(_{50}\) values of 0.56, 0.96, and 0.48 µM, respectively [134].

Compounds 184, 187 (Figure 16) and 209 (Figure 16), isolated from a sea anemone-associated fungus, *Nigrospora* sp. ZJ-2010006, as well as 182a and 186a (Figure 16), showed cytotoxic activity against A549 cells with IC\(_{50}\) values of 3.32, 4.56, 41.5, 2.72, and 5.25 µM, respectively. The positive control, mitomycin, showed IC\(_{50}\) = 3.00 µM [68].

Compound 189 (Figure 16), isolated from a mangrove endophytic fungus no. 1403, exhibited a potent cytotoxicity against KB and KBv200 cells in the MTT assay, with IC\(_{50}\) values of 19.66 and 19.27 µM, respectively. Compound 189 caused apoptosis in KB and KBv200 cells through non-related reactive oxygen species (ROS) generation in mitochondria and activation of caspase-8 in death receptor pathways [113].
Compound 190 (Figure 17), isolated from a marine sediment-derived fungus, *A. glaucus*, showed selective cytotoxicity against A-549 and BEL-7402 cell lines (by SRB method), as well as HL-60 and P388 (mouse lymphoma) cell lines (by MTT assay), with IC<sub>50</sub> values of 0.13, 0.28, 7.5, and 35.0 µM, respectively [114].

Compounds 191, 271 and 272 (Figure 26), isolated from a marine sediment-derived fungus, *A. glaucus*, were also assayed for cytotoxicity toward HL-60 and A-549 cell lines. Compound 191 displayed a potent cytotoxicity against both HL-60 and A-549 cell lines (IC<sub>50</sub> values of 0.51 and 0.24 µM, respectively), while 271 (IC<sub>50</sub> values against HL-60 and A-549 cell lines = 7.8 and 9.2 µM) and 272 (IC<sub>50</sub> values against HL-60 and A-549 cell lines = 44.0 and 14.2 µM, respectively) were less cytotoxic. However, the trans congener (271) was more potent than the cis congener (272) [22].

Compounds 195 and 196 (Figure 18), isolated from a deep-sea sediment-derived fungus, *Eurotium* sp. SCSIO F452, showed moderate (IC<sub>50</sub> = 12.5 and 15.0 µM, respectively) and weak (IC<sub>50</sub> = 30.1 and 37.3 µM, respectively) cytotoxicity against SF-268 and HepG2 cancer cell lines [116].

Compound 200 (Figure 19), isolated from the culture extract of a red alga-derived fungus, *Talaromyces islandicus* EN-501, displayed weak cytotoxicity against sensitive (A2780) and cisplatin-resistant (A2780 CisR) human ovarian cancer cell lines, at a concentration of 100 µM [117].

Compounds 240 and 241 (Figure 24), isolated from a mangrove endophytic fungus, *Altentaria* sp. ZJ9-6B, displayed cytotoxicity against MDA-MB-435 (higher metastasizing cells) and MCF-7 (lower metastasizing cells) cell lines (by MTT assay), with IC<sub>50</sub> values of 26.97 and 29.11 µM (for 240), and 13.11 and 20.04 µM (for 241), respectively [61]. Compound 241 was further investigated for its underlying mechanism for cytotoxicity in MCF-7 cells. It was found that 241 mainly induced cell necrosis, and only a portion of cells was in the state of apoptosis. Compound 241 also caused a significant increase in ROS production, a significant increase in intracellular calcium and alteration of cell morphology of the MCF-7 cells, which is characteristic of apoptosis [135].

Compounds 275, 276, and 277 (Figure 26), isolated from an algicolous fungus, *A. alliaceus*, were tested for cytotoxicity against HCT-116 and SK-Mel-5 (melanoma) cell lines. Compound 275 showed higher cytotoxicity toward HCT-116 and SK-Mel-5 cells (IC<sub>50</sub> values = 9.0 and 11.0 µM, respectively) than 276 (IC<sub>50</sub> values = 10.5 and 12.2 µM, respectively) and 277 (IC<sub>50</sub> values = 13.7 and 19.7 µM, respectively) [77].

Compounds 279–283 (Figure 27), isolated from a marine sponge-associated fungus, *Engyodontium album* strain LF069, displayed weak cytotoxicity toward a mouse fibroblasts cell line (NIH-3T3) with IC<sub>50</sub> values of 14.0, 11.0, 13.2, 14.4, and 34.3 µM, respectively. The IC<sub>50</sub> of the positive control, tamoxifen citrate, was 16.5 µM [125].

Compounds 287, 289, 293 and 296 (Figure 27), isolated from the culture extract of an unidentified fungus of the order Hypocreales (MSX 17022), were assayed against MCF-7, H460, and SF268 (human astrocytoma) cancer cell lines. Compound 287 (IC<sub>50</sub> values = 18.1, 13.6, and 21.4 µM, respectively) and 296 (IC<sub>50</sub> values = 21.0, 10.9, and 16.1 µM, respectively) exhibited moderate cytotoxicity against MCF-7, H460, and SF268 cells. Compound 289 (IC<sub>50</sub> values = 20.6 and 21.0 µM) and 293 (IC<sub>50</sub> values = 14.0 and 21.4 µM, respectively) displayed moderate cytotoxicity against H460 and SF268 cells. The positive control, camptothecin, showed IC<sub>50</sub> values of 0.06, 0.01, and 0.05 µM toward MCF-7, H460, and SF268 cells, respectively [127].

Compounds 104, 106, 109 (Figure 9) and 149 (Figure 11), isolated from a deep-sea sediment-derived fungus, *A. puniceus* SCSIO z021, showed toxicity against brine shrimps (*Artemia salina* larvae) with a lethal concentration 50% (LC<sub>50</sub>) values of 15, 21, 5.3, and 2.7 µM, respectively. Compounds 109 also showed strong toxicity against Vero cells with a median toxic concentration (TC<sub>50</sub>) value of 4.3 µM [81].

Compound 158 (Figure 13), isolated from a mangrove endophytic fungus, *Stemphylium* sp. 33231, showed a moderate lethality effect in brine shrimp lethality assay, with LD<sub>50</sub> = 10 µM [50].
Compound 231 (Figure 20), isolated from a brown alga-derived fungus, Eurotium cristatum EN-220, also displayed moderate cytotoxicity in brine shrimp lethality assay (41.4% rate) at a concentration of 10 µg/mL [95].

Compounds 6 (Figure 3) and 228 (Figure 20), isolated from a marine sponge-associated fungus, Eurotium repens, showed cytotoxicity against sex cells of the sea urchin (Strongylocentrotus intermedius) at a concentration of 25 and 10 µg/mL, respectively [24].

4.6. Enzyme Inhibitory Activity

4.6.1. Inhibition of α-Glucosidase Activity

Compounds 1 and 2 (Figure 3), isolated from a deep-sea sediment-derived fungus, Aspergillus flavipes HN4-13, were assayed for α-glucosidase inhibitory activity. Compound 1 was a non-competitive α-glucosidase inhibitor, with a Ki/IC$_{50}$ value of 0.79/19 µM, whereas 2 was void of activity [18].

Compound 65 (Figure 6), isolated from a mangrove endophytic fungus, Cladosporium sp. HNWSW-1, effectively inhibited α-glucosidase enzyme with an IC$_{50}$ value of 49.3 µM, which was almost 5.5-fold more active than the positive control, acarbose (IC$_{50}$ = 275.7 µM) [74].

4.6.2. Inhibition of Trypsin Activity

Compounds 1 and 4 (Figure 3), isolated from a green alga-derived fungus, A. versicolor, displayed a non-competitive inhibitory activity against the human trypsin, with IC$_{50}$ values of 450.5 and 50.1 µg/mL, respectively. The soybean trypsin–chymotrypsin was used as a positive control and showed trypsin inhibitory activity with an IC$_{50}$ value of 0.01 µg/mL [34].

Compound 28 (Figure 4), isolated from the culture extract of an algicolous fungus, Fusarium equiseti, inhibited trypsin activity with an IC$_{50}$ value of 48.5 µg/mL, which was comparable with the positive control (soybean trypsin-chemotrypsin inhibitor; T-I, IC$_{50}$ = 0.01 µg/mL). Compound 29 (Figure 4), isolated from the same extract, did not show any inhibitory activity. Therefore, it was proposed that the CH$_2$OH group at C-3 of the anthraquinone scaffold was essential for the bioactivity of 28 [40].

4.6.3. Inhibition of Tyrosinase Activity

Compound 74 (Figure 6), isolated from a marine sponge-associated fungus, Neosartorya spinosa KUFA 1047, displayed weak antityrosinase activity, at the maximum concentration of 200 µM (% inhibition = 11.56%). The positive control, kojic acid, inhibited tyrosinase activity at 95.04% of the same maximum concentration [54].

4.6.4. Inhibition of Indoleamine 2,3-dioxygenase (IDO1) Activity

Compounds 52 (Figure 5), 133, 134 (Figure 10) and 233 (Figure 21), isolated from a deep-sea sediment-derived fungus, Alternaria tenuissima DFFSCS013, showed inhibitory activity against indoleamine 2,3-dioxygenase (IDO1). Compounds 52, 133, and 134 displayed a significant inhibition, with IC$_{50}$ values of 1.7, 4.2, and 0.5 µM, respectively, while 233 showed weak inhibition with IC$_{50}$ value of 32.3 µM. The positive control, NLG919, displayed IC$_{50}$ = 0.08 µM [63].

4.6.5. Inhibition of Protein Tyrosine Phosphatases and Protein Kinases Activity

Compounds 52 (Figure 5), 133 and 134 (Figure 10) were also assayed against five recombinant human protein tyrosine phosphatases (PTPs), viz. T cell protein tyrosine phosphatase (TCPTP), Src homology region 2 domain-containing phosphatase 1 (SHP1), Src homology region 2 domain-containing phosphatase 1 (SHP2), megakaryocyte protein tyrosine phosphatase 2 (MEG2), and protein tyrosine phosphatase 1B (PTP1B). Compound 52 inhibited all the tested PTPs, with IC$_{50}$ values of 3.5, 3.4, 14.6, 29.6, and 2.1 µM, respectively. Compounds 133 and 134 selectively inhibited TCPTP, SHP1, and MEG2, with IC$_{50}$ values ranging from 26.2 to 68.2 µM [63].

Compounds 60–62 (Figure 6), isolated from a marine sponge-associated fungus, Microsphaeropsis sp., displayed inhibitory activity against protein kinase C (PKC-ε), cyclin-
dependent kinase 4 in complex with its activator cyclin D1 (CDK4/cyclin D1), and epidermal growth factor receptor (EGF-R), with IC₅₀ values ranging from 18.5 to 54 µM [71,72].

Compounds 79, 81, 82 (Figure 7), 104, 106-109 (Figure 9) and 149 (Figure 11), isolated from a deep-sea sediment-derived fungus, *A. puniceus* SCSIO z021, inhibited activities of seven PTPs, which are involved in cancer and type 2 diabetes, i.e., TCPTP, SHP1, SHP2, MEG2, PTP1B, CDC25B, and CD45. Compounds 81, 104, and 106 showed inhibitory activity against all the tested PTPs, with IC₅₀ values ranging from 0.2 to 19 µM. Compounds 107 and 109 inhibited the activity of TCPTP, SHP1, MEG2, CDC25B, and CD45, with IC₅₀ values ranging from 1.0 to 18 µM. Compound 79 exhibited inhibition of TCPTP, SHP1, SHP2, MEG2, CDC25B, and CD45, with IC₅₀ values of 8.6, 19, 18, 1.9, 18, and 18 µM, respectively. While compound 108 inhibited the activity of SHP1, SHP2, MEG2, PTP1B, and CDC25B, with IC₅₀ values of 5.4, 5.4, 2.2, 18, and 18 µM, respectively, 149 displayed inhibition of TCPTP, SHP1, SHP2, MEG2, and PTP1B with IC₅₀ values of 4.8, 4.9, 13, 8.0, and 8.0 µM, respectively. Compound 82 selectively inhibited the activity of MEG2, with IC₅₀ value of 6.9 µM. The positive control, Na₃VO₄, showed an inhibitory activity against TCPTP, SHP1, SHP2, MEG2, and PTP1B with IC₅₀ values of 2.4, 4.4, 6.2, 3.2, and 1.6 µM, respectively, while the positive control, menadione AACQ, inhibited CDC25B and CD45 activities with IC₅₀ values of 14 and 0.29 µM, respectively [81].

Compounds 192 and 193 (Figure 17), isolated from modified cultures of *A. glaucus*, showed an inhibitory activity of receptor tyrosine kinases (RTKs) viz. c-Met, Ron, and c-Src, with IC₅₀ of 4.3, 7.5, and 7.5 µM (for 192), and 1.8, 9.4, and 5.7 µM (for 193), respectively [115].

4.6.6. Inhibition of Acetylcholinesterase (AChE) Activity

Compounds 29, 38, 41 (Figure 4) and 71 (Figure 6), isolated from a soft coral-associated fungus, *Trichoderma harzianum*, exhibited weak anti-acetylcholinesterase (AChE) activity, by Ellman method, at a concentration of 100 µM [55], whereas 236 (Figure 22), isolated from the culture extract of a mangrove endophytic fungus, *A. terreus* (no. GX7-3B), showed stronger anti-AChE activity with IC₅₀ = 6.71 µM. The IC₅₀ value of the positive control, huperazine A, was 0.003 µM [123].

4.7. Anti-Inflammatory Activity

Compounds 4 and 5 (Figure 3), isolated from a marine sponge-associated fungus, *A. eurupaeus* WZXY-SX-4-1, were assayed for their anti-inflammatory activity. Compounds 4 and 5 were found to significantly downregulate Nuclear factor kappa B (NF-κB) in a human colon carcinoma cell line (SW480) induced by lipopolysaccharide (LPS) with the inhibitory rates of 75.9% and 73.1%, respectively, which were comparable with NF-κB inhibitor, MG132, (88.9% inhibition) [21].

Compound 86 (Figure 7), isolated from a marine-derived fungus, *Aspergillus* sp. SF6796, was assayed for its anti-neuroinflammatory activity. Compound 86 induced the expression of heme oxygenase (HO)-1 protein in BV2 microglial cells through activation of a nuclear transcription factor erythroid-2 related factor 2 (Nrf2), regulation of p38 mitogen-activated protein kinase, and phosphatidylinositol 3-kinase/protein kinase B signaling pathways. The pro-inflammatory mediators including nitric oxide (NO), prostaglandin E2, inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 in LPS-stimulated BV2 microglial cells were also suppressed by treatment with 86 [87].

Compounds 128, 130, 131 (Figure 10) and 150 (Figure 11), isolated from the fermentation extract of a marine sediment-derived fungus, *Penicillium* sp. SCSIO sof101, were evaluated for their abilities to inhibit interleukin 2 (IL-2) secretion by Jurkat cells. Compared with FK506 (the interleukin 2 inhibitor; IC₅₀ = 5.8 µM), 128, 131, and 150 strongly inhibited the IL-2 secretion with IC₅₀ values of 4.1, 5.4, and 5.1 µM, respectively, while 130 moderately inhibited the IL-2 secretion with IC₅₀ = 12 µM [46].

Compounds 246 (Figure 24) and 262-265 (Figure 25), isolated from the culture extract of a marine-derived fungus, *Stemphylium* sp., were assayed for their anti-inflammatory capacity
through suppression of LPS-induced NO production in RAW 264.7 mouse macrophages. Compounds 246 and 262–265 exhibited moderate anti-inflammatory activity with IC\textsubscript{50} values of 10.7, 11.6, 16.1, 1.6, and 8.4 \(\mu\)M, respectively [124].

4.8. Anti-Obesity Activity

Compounds 1, 15, 17 (Figure 3), 28 (Figure 4) and 49 (Figure 5), isolated from the culture extract of a marine sponge-associated fungus, Talaromyces stipitatus KUFA 0207, were evaluated for their anti-obesity activity using the Zebrafish Nile red assay. However, only 15 and 28 exhibited a significant anti-obesity activity, reducing the stained lipids more than 60% and 90%, respectively, with IC\textsubscript{50} values of 0.95 and 0.17 \(\mu\)M, respectively. The positive control, resveratrol, showed IC\textsubscript{50} = 0.6 \(\mu\)M. Compound 1 caused death of all zebrafish larvae after 24 h of treatment [33].

4.9. Anticoagulant Activity

Compounds 179 and 180 (Figure 15), isolated from a marine sediment-derived fungus, Sporendonema casei HDN16-802, were assayed for anticoagulant activity and showed moderate inhibition of thrombin and Factor Xa, with inhibition ratios of 47.8% and 51.5%, respectively. The positive control, argatroban, showed an inhibition ratio of 65.0% [109].

4.10. Antiangiogenic Activity

Compounds 175 (Figure 15) and 223 (Figure 19), isolated from a sea cucumber-associated fungus, Trichoderma sp. (H-1), exhibited a weak antiangiogenic activity, with 23.80 and 24.60% inhibition of the growth of intersegmental vessels (ISV) of Zebrafish, respectively. The % inhibition of control (0.1% DMSO) was 25.80, and the positive control, PTK787 (0.5 \(\mu\)g/mL), was 0.2 [43].

4.11. Antifouling Activity

Compounds 1 (Figure 3), 28 (Figure 4) and 68 (Figure 6), isolated from the culture extract of a gorgonian coral-associated fungus, Penicillium sp. SCSGAF0023, showed significant antifouling activity against Balanus amphitrite larvae settlement, with EC\textsubscript{50} values of 6.1, 17.9, and 13.7 \(\mu\)g/mL, respectively [39].

4.12. Algicidal Activity

Fengping et al. have investigated the algicidal activity of crude EtOAc extracts of 49 marine macroalgal endophytic fungi against red-tide phytoplanktons, i.e., Alexandrium tamarense, Prorocentrum donghaiense, Heterosigma akashiwo, and Chattonella marina, and have found that four fungal strains, including Aspergillus wentii (pt-1), A. ustus (cf-42), and A. versicolor (dl-29 and pt-20) potently inhibited algal growth. The secondary metabolites isolated from these fungi, including 12, 13 and 14 (Figure 3) showed high 24 h inhibition rates against the red tide algae with EC\textsubscript{50(24-h)} values ranging from 0.01–14.29 \(\mu\)g/mL. Compound 12 possessed the highest algicidal activity against C. marina, H. akashiwo, and P. donghaiense with EC\textsubscript{50(24-h)} values of 0.17, 0.63, and 4.24 \(\mu\)g/mL, respectively. Compound 12 was also found to decrease chlorophyll a (Chl a) and superoxide dismutase (SOD) contents, while increasing soluble protein, malondialdehyde (MDA), and peroxidase contents, which decreases the photosynthesis process. Compound 13 showed the algicidal activity against C. marina, A. tamarense, and H. akashiwo, with EC\textsubscript{50(24-h)} values of 0.44, 5.24, and 1.22 \(\mu\)g/mL, respectively [29].

Compound 36 (Figure 4), isolated from the culture extract of a marine sponge-associated fungus, Eurotium chevalieri MUT2316, inhibited the growth of two algae, including Halamphora coffeaeformis AC713 and Phaeodactylum tricornutum AC171 with low observable effect concentration (LOEC) values of 0.01 and 1 \(\mu\)g/mL, respectively. This compound also inhibited the adhesion of only two algae, viz. Cylindrotheca closterium AC170 and H. coffeaeformis AC713, with LOEC values of 0.001 and 1 \(\mu\)g/mL, respectively [53].
4.13. Insecticidal Activity

Compounds 99, 100 and 120 (Figure 9), isolated from a red alga-derived fungus, Acremonium vitellinum, possessed moderate inhibitory activity against third-instar larvae of Cotton bollworm (Helicoverpa armigera), with LC$_{50}$ values of 0.87, 0.78, and 0.72 mg/mL, respectively. The positive control, matrine, showed LC$_{50} = 0.29$ mg/mL [104].

4.14. Antioxidant Activity

Compound 6 (Figure 3), isolated from an aligcolous fungus, Aspergillus wentii EN-48, showed weak radical scavenging activity against 2,2-diphenyl-1-picrylhydrazyl (DPPH•) radicals, with an IC$_{50}$ value of 99.4 µg/mL. The positive control, butylated hydroxytoluene (BHT), showed IC$_{50} = 36.9$ µg/mL [23].

Compound 16 (Figure 3), isolated from an aligcolous fungus, Chaetomium globosum, showed moderate DPPH• radical scavenging activity with IC$_{50}$ value of 62 µg/mL. The positive control, BHT, showed IC$_{50}$ value of 18 µg/mL [32].

Compounds 87 (Figure 7), 104, 107, 109 and 115 (Figure 9), isolated from a deep-sea sediment-derived fungus, A. versicolor, were assayed for antioxidant capacity by a Trolox equivalent antioxidant capacity (TEAC) assay. Compounds 87, 104, 107, 109, and 115 scavened the 2,2-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid radical cations (ABTS•+), which were approximately equivalent to that of trolox (1.0 mmol/L). These compounds were further evaluated for their capacity to regulate the nuclear factor E2-related factor 2 (Nrf2), a transcription factor that responds to oxidative stress by binding to the antioxidant response element (ARE) in the promoter of genes coding for antioxidant enzymes and proteins for glutathione synthesis, and its activity can be measured by ARE-driven luciferase reporters using HepG2C8 cells, stably transfected with AREluciferase reporter plasmids. Compounds 87, 104, 107, 109, and 115, at a concentration of 10 µmol/L, caused significant induction of luciferase 1.41–1.58-folds more than that of the blank control (DMSO), and approximately half of the positive control, tBHQ (tertiary butylhydroquinone), at a concentration of 50 µmol/L [89].

Compounds 97 (Figure 8), isolated from a marine sponge-associated fungus, A. europaeus WZXY-SX-4-1, scavenged DPPH• radicals with IC$_{50}$ value of 13.2 µg/mL. The positive control, trolox, quenched DPPH• radicals with IC$_{50}$ value of 5.4 µg/mL [21].

The antioxidant activity of (+)-122, (-)-A (122), (-)-A (122), (±)-123, (±)-124, and (±)-125 (Figure 10), isolated from a deep-sea sediment-derived fungus, A. versicolor SCSIO 41502, were assayed for their antioxidant activity against ABTS•+ radical cations. Compounds 122–125 showed TEAC values of 2.11, 2.07, 2.00, 2.27, 2.18, and 2.03 mmol/g, respectively. These results indicated that the configuration of the stereogenic carbon in 122 (Figure 10) did not influence its antioxidant activity [92].

Compounds 2 (Figure 3), 155 (Figure 12), 165–167 (Figure 14), 228 and 231 (Figure 20), isolated from a mangrove endophytic fungus, Eurotium rubrum, were examined for their DPPH• radical scavenging capacity. Compounds 166 and 231 displayed moderate to potent scavenging activity, with IC$_{50}$ values of 74.0 to 44.0 µM, while 2, 155, 165, 167, and 228 exhibited weak activity. The positive control, BHT, showed IC$_{50} = 82.6$ µM [106].

Compound (+)-194 (Figure 18), isolated from a deep-sea sediment-derived fungus, Eurotium sp. SCSIO F452, showed DPPH• radicals scavenging activity, with an IC$_{50}$ value of 58.4 µM, while the pure (−)-194 scavenged DPPH• radicals with IC$_{50} = 159.2$ µM. Ascorbic acid was used as a positive control and showed IC$_{50} = 45.8$ µM [116].

Compounds 199–203 (Figure 19), isolated from the culture extract of an aligcolous fungus, Talaromyces islandicus EN-501, scavenged DPPH• radicals with IC$_{50}$ values ranging from 12 to 52 µg/mL, which were better than the reference compound, BHT, whose IC$_{50} = 61$ µg/mL. Compounds 199–203 also showed moderate scavenging activity toward ABTS•+ radical cations, with IC$_{50}$ values ranging from 8.3 to 34 µM, which were comparable to ascorbic acid (positive control) whose IC$_{50} = 16$ µM [117].
4.15. Other Biological Activities

Using calcium imaging assay, 233 (Figure 21), isolated from a deep-sea sediment-derived fungus, *Altenaria tenuissima* DFFS013, effectively stimulated intracellular levels of calcium flux in HEK293 (human embryonic kidney) cells, at a concentration of 10 µM, in the calcium imaging assay. However, 233 did not show any effect at a concentration less than 10 µM [63].

Compounds 287, 289, 293 and 296 (Figure 27), isolated from an unidentified fungus of the order Hypocreales (MSX 17022), displayed the 20S proteasome inhibitory activity at a concentration of 20 µg/mL (% inhibition ranging from 13% to 67%) [127].

In order to enhance a readability of this review, we have summarized the anthraquinoid metabolites and their derivatives, obtained from the marine environment in Table 1. This includes the names and numbers of the isolated compounds, the names of fungal producers, the sources from which the fungi were obtained, the reported biological/pharmacological activities and the references.

### Table 1. Anthraquinone metabolites and their analogues reported from marine-derived fungi.

| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity | Ref. |
|----------|--------------------------|--------------------------------|-------------|------|
| Emodin (I) | Aspergillus flavipes HN4-13 | -Marine sponge | Anthraquinone metabolites and their analogues reported from marine-derived fungi. | Table 1. |
| A. terreus DCO3-9 | -Leaves of an unidentified mangrove tree. | - | Non-competitive α-glucosidase inhibitor. | [10] |
| A. glaucus HBI-19 | -Marine sediment. | - | Antibacterial and cytotoxic activities. | [18] |
| Penicillium citrinum HSI-5126 | -Marine sponge | - | Anthraquinone metabolites and their analogues reported from marine-derived fungi. | [19] |
| Eurotium rubrum | -Inner tissue of semi-mangrove plant | - | Antibacterial, reduction of biofilm formation and cytotoxic activities. | [18] |
| E. chevalieri KUFA0006 | -Inner twig of mangrove plant | - | Antibacterial activity. | [34] |
| Talaromyces stipitatus KUFA0027 | -Marine sponge | - | Anti-obesity activity. | [33] |
| Paecilomyces sp. (Tree 1-7) | -Deep-sea sediment. | - | Antibacterial activity. | [35] |
| Trichoderma harzianum (XS-20090075) | -Marine lichen. | - | Antifouling activity. | [47] |
| Trichoderma sp. (E-1) | -Sea mud. | - | Antibacterial activity. | [44] |
| Gloeocladia sp. T31 | -Marine lichen. | - | Antibacterial activity. | [42] |
| G. catenulatum T31 | -Marine sediment. | - | Cytotoxic activity. | [65] |
| Monodictys sp. | -Sea urchin | - | Antitumor activity. | [66] |
| Questin (MT-1) | -Leaves of an unidentified mangrove tree. | - | Anthraquinone metabolites and their analogues reported from marine-derived fungi. | [12] |
| Aspergillus terreus DCO3-9 | -Marine sponge | - | DPPH* radicals scavenging activity. | [106] |
| A. glaucus HBI-19 | -Marine sediment. | - | Reduction of biofilm formation. | [11] |
| Penicillium sp. ZZ901 | -Marine sponge | - | Reduction of biofilm formation. | [11] |
| Eurotium chevalieri MUT2316 | -Marine sponge | - | Reduction of biofilm formation. | [11] |
| E. chevalieri KUFA0006 | -Marine sponge | - | Reduction of biofilm formation. | [11] |
| Eurotium sp. SCISO F452 | -Marine sediment. | - | Reduction of biofilm formation. | [11] |
| E. repens | -Marine sponge | - | Reduction of biofilm formation. | [11] |
| A. repens | -Marine sponge | - | Reduction of biofilm formation. | [11] |
| A. effusus | -Marine sponge | - | Reduction of biofilm formation. | [11] |
| Microsporum sp. MFS-YL | -Marine red alga | - | Anti-proliferative and cytotoxic activities. | [26] |
### Table 1. Cont.

| Compound            | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity                        | Ref. |
|---------------------|---------------------------|--------------------------------|------------------------------------|------|
| Catenarin (7)       | Aspergillus glaucus HB1-19 | Marine sediment.               | -                                  | [23] |
|                     | Eurotium sp. SC50F452     | Marine sediment.               | -                                  | [70] |
| Rubrocristin (8)     | A. glaucus HB1-19         | Marine sediment.               | -                                  | [22] |
| 3-Hydroxy-1,2,5,6-tetramethoxyantrachene-9,10-dione (9) | A. tritici SP-8-1 | Soft coral Galaxea fascicularis. | -Antibacterial activity.           | [26] |
| 3-Hydroxy-2-hydroxymethyl-1-methoxyantrachene-9,10-dione (10)| A. tritici SP-8-1 | Soft coral G. fascicularis.     | -Antibacterial and cytotoxic activities. | [28] |
| 1,2,3-trihydroxy-7-hydroxymethylantrachene-9,10-dione (11) | A. tritici SP-8-1 | Soft coral G. fascicularis.     | -Antibacterial and cytotoxic activities. | [28] |
| 1,5-Dihydroxy-3-methoxy-7-methylnthaquinone (12) | A. wentii (pt-1), A. ustus (cf-42), A. versicolor (dl-29 and pt-20) | - | -Alginicidal activity.           | [29] |
| 1,3,5-trihydroxy-7-methylnthaquinone (13) | A. wentii (pt-1), A. ustus (cf-42), A. versicolor (dl-29 and pt-20) | - | -Alginicidal activity.           | [29] |
| 5-Hydroxy-2,4-dimethoxy-7-methylnthaquinone (or emodin-6,8-dimethyl ether, 14) | A. wentii (pt-1), A. ustus (cf-42), A. versicolor (dl-29 and pt-20) | - | -Alginicidal activity.           | [29] |
| 2-(dimethoxymethyl)-1-hydroxyantrachene-9,10-dione (20) | A. versicolor | Deep-sea sediment.             | -Antibacterial activity.           | [35] |
| 1-Hydroxy-2-methylnthacone-9,10-dione (21) | A. versicolor | Deep-sea sediment.             | -                                  | [35] |
| 2-Methylnthacone-9,10-dione (22) | A. versicolor | Deep-sea sediment.             | -                                  | [35] |
| Damnacanthin (23)   | A. versicolor             | Deep-sea sediment.             | -                                  | [35] |
| Rubiadin (24)       | A. versicolor             | Deep-sea sediment.             | -                                  | [35] |
| Xanthopurpurin (25) | A. versicolor             | Deep-sea sediment.             | -                                  | [35] |
| Rubianthaquinone (26) | A. versicolor             | Deep-sea sediment.             | -                                  | [35] |
| 6-Hydroxynrubadin (27) | A. versicolor             | Deep-sea sediment.             | -                                  | [35] |
| Citreorosin (or ω-hydroxyemodin, 28) | Penicillium oxalicum 2HL-M-6 | Sea mud.                       | -                                  | [36] |
|                     | P. citrinum PSU-F51      | Gorgonian Sea fan (Amellsa sp.) | -Antifouling activity.            | [37] |
|                     | Penicillium sp. SC5GA08023 | Gorgonian coral.               | -                                  | [39] |
|                     | P. citrinum HL-5126      | -                               | -Antibacterial activity.           | [41] |
|                       | Talaromyces stipitatus KUF0006 | Marine sponge Stylosa sibbaldiformis. | -Antibacterial activity.      | [33] |
|                       | Emericella sp. SC50S5240 | Marine sediment.               | -                                  | [75] |
|                       | Fusarium equiseti        | Marine brown alga Padina parvona. | -Antiviral activity; inhibition of human trypsin activity. | [40] |
|                       | Gloeodidym sp. T31      | Marine lichen.                 | -                                  | [38] |
|                       | G. catenulatum T31       | Marine sediment.               | -Anti-tumor activity.             | [65] |
|                       | -                        | -                              | -Anti-biofilm formation.         | [135] |
| Chrysophanol (or chrysophanic acid, 29) | Aspergillus candidus KUF0006 | Marine sponge Epipelas sp.    | -Anti-biofilm formation.         | [16] |
|                       | Penicillium oxalicum 2HL-M-6 | Sea mud.                       | -                                  | [36] |
|                       | P. citrinum PSU-F51      | Gorgonian Sea fan (Amellsa sp.) | -                                  | [37] |
|                       | Penicillium sp. (Tree1-7) | Mangrove saprophytic bark.     | -                                  | [42] |
|                       | Fusarium equiseti        | Marine brown alga Padina parvona. | -Antiviral activity; inhibition of human trypsin activity. | [40] |
|                       | Trichoderma harzianum (NC-20070075) | Inner tissue of soft coral. | -Anti-acetylcholinesterase activity. | [55] |
|                       | Trichoderma sp. (H-1)    | Sea cucumber.                  | -Antibacterial activity.          | [43] |
|                       | Monocystis sp. Strain F-10C | Sea urchin Anthocidaris crassispina. | -                                  | [60] |
|                       | Aloe-emodin (30)         | Marine alga Dictyota vesiculos. | -                                  | [45] |
| Carvulin (31)        | Penicillium sp. strain T01V25 | Marine alga Dictyota vesiculos. | -                                  | [45] |
| Emodic acid (32)     | Penicillium sp. SC50F60101 | Deep-sea sediment.             | -                                  | [46] |
|                     | Eurotium rubrum          | Inner tissue of semi-mangrove plant Hibiscus tilacens. | -                                  | [47] |
| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity | Ref. |
|----------|--------------------------|---------------------------------|-------------|-----|
| Macroporin (33) | Penicillium sp. | -Soft coral Sarcotheon tortuosum. | -Antibacterial activity. | [49] |
| | Altenaria sp. ZJ-2008003 | - | - | |
| | Stempheydium sp. 33231 | - | - | |
| | S. lycopersici | -Inner tissue of gorgonian soft coral Dictyotella gamnicosa. | - | [51] |
| | Phoma sp. L28 | -Mangrove plant Aspergillum bontiodes A. Gray. | -Anti-fungal activity. | [67] |
| | Phomopsis sp. PSU-MA214 | -Leaves of mangrove plant Rhizophora apiculata Grif. Ex T. Anderson. | - | |
| 1,7,8-Trihydroxy-3-methoxy-6-methylanthraquinone (34) | Penicillium sp. | -Soft coral Sarcotheon tortuosum. | - | [49] |
| 1-Hydroxy-3-methoxy-6-methylanthraquinone (35) | Penicillium sp. | -Soft coral Sarcotheon tortuosum. | - | [49] |
| | -Leaves of mangrove plant Rhizophora apiculata Grif. Ex T. Anderson. | - | - | [52] |
| Cannalitein (36) | Eurotium chevalieri MUT12316 | -Marine sponge Granatia compressa. | -Anti fouling and algicidal activities. | [55] |
| Acetylquestonil (37) | E. chevalieri KUFA0006 | -Inner twig of mangrove plant Rhizophora mucronata Polz. | -Reduction of biofilm formation. | [31] |
| | Nesoratiorus spinosus KUFA1047 | -Marine sponge Mycale sp. | - | [54] |
| Pachysbasin (38) | Trichoderma harzianum (XS-20090075) | -Inner tissue of a soft coral. | -Anti-acetylcholinesterase activity. | [55] |
| | Monodictys sp. | -Sea urchin Anthocidaris crassispina. | - | [60] |
| Phomarin (39) | T. harzianum (XS-20090075) | -Inner tissue of a soft coral. | - | [55] |
| 1-Hydroxy-3-hydroxy-7-methylanthraquinone (40) | T. harzianum (XS-20090075) | -Sea urchin Anthocidaris crassispina. | -Anti-acetylcholinesterase activity. | [49] |
| | -Inner tissue of a soft coral. | - | - | [55] |
| 1,3,6-Trihydroxy-8-methylanthraquinone (41) | Trichoderma sp. strain SCSIO41004 | -Marine sponge Calypsopora sp. | - | [56] |
| 1,4-Dihydroxy-2-methoxy-9,10-dimethoxy-7-methylanthraquinone-9,10-dione (43) | Halorosellia sp. (no. 1403) | -Estuarine. | - | [57] |
| 1,4-Dihydroxy-2-methoxy-9,10-dimethoxy-7-methylanthraquinone-9,10-dione (44) | Halorosellia sp. (no. 1403) | -Decayed Kandelia candel (L.) Druce. | - | [58] |
| 1,6-Dimethoxyaustroctortalin (45) | Halorosellia sp. (no. 1403) | -Decayed Kandelia candel (L.) Druce. | -Cytotoxic activity. | [58, 131] |
| Hydroxy-9,10-anthraquinone (46) | Halorosellia sp. (no. 1403) | -Decayed Kandelia candel (L.) Druce. | - | |
| Austroctortalin (47) | Altenaria sp. SK11 | -Root of mangrove tree Exocoetica agallocha. | - | |
| | Fusarium sp. PSU-F14 | -Gorgonian sea fan. | -Antibacterial and cytotoxic activities. | [59] |
| | Nigrospora sp. ZJ-2001006 | -Unidentified sea anemone. | - | [68] |
| | Nigrospora sp. ZJ-2010006 | -Inner tissue of the zoathid Palphea haddoni (GX-WZ-20100026). | -Antiviral activity. | [69] |
| | Halorosellia sp. (no. 1403) | -Decayed Kandelia candel (L.) Druce. | - | [58] |
| Monodictyquinone A (48) | Monodictys sp. | -Sea urchin Anthocidaris crassispina. | -Anti-acetylcholinesterase activity. | [60] |
| Rhoeomexdin (49) | Tamnium exscopatum KUFA027/ | -Marine sponge Mycale globulosa. | -Antibody activity. | [44] |
| Marcusporin (50) | Altenaria sp. 297-60 | -Mangrove tree Aegiceras corniculatus fruits. | - | |
| 6-Methylquinizarin (51) | Altenaria sp. SK11 | -Root of mangrove tree Exocoetica agallocha. | - | [61] |
| 6-O-Methylalaternin (52) | Altenaria tenuissima DFFSCS013 | -Marine sediment. | -Inhibition of human protein tyrosine phosphatases and inhibition of indoleamine 2,3-dioxygenase activity. | [63] |
| Lunatin (53) | Curvularia lunata | -Marine sponge Niphates olimda. | -Antibacterial activity. | [64] |
| | Gloeocladium catenulatum T31 | -Marine sediment. | -Anti-tumor activity. | [65] |
| 1,3,5-Trihydroxy-6-hydroxymethyl-7-methoxyanthraquinone (54) | Thermomyces lanuginosus Tsikl KMM 4681 | -Marine sediment. | - | [66] |
| 1,3,5-Trihydroxy-6-methyl-7-methoxyanthraquinone (55) | T. lanuginosus Tsikl KMM 4681 | -Marine sediment. | -Cytotoxic activity. | [66] |
| 7-Methoxyacrosporin (56) | Phomopsis sp. L28 | -Mangrove plant Aspergillum bontiodes A. Gray. | -Anti-fungal activity. | [67] |
| | Dimeethylalloxyacrosporin (57) | Phomopsis sp. L28 | -Mangrove plant M. bontiodes A. Gray. | -Anti-fungal activity. | [67] |
| | 3,5,8-Trihydroxy-7-methoxy-9,10-dimethoxy-7-methylanthraquinone (58) | Nigrospora sp. ZJ-2010006 | -Unidentified sea anemone. | -Antibacterial activity. | [68] |
| | Nigrospora sp. ZJ-2010006 | -Inner tissue of the zoathid Palphea haddoni (GX-WZ-20100026). | -Antiviral activity. | [69] |
| 1,6,8-Trihydroxy-4-benzoyloxyl-3-methylanthraquinone (59) | Eurotium sp. SCSIO F452 | -Marine sediment. | - | [70] |
### Table 1. Cont.

| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity | Ref. |
|----------|--------------------------|-------------------------------|-------------|-----|
| 7-Acetyl-1,3,6-tetrahydroxyanthracene-9,10-dione (63) | Trichoderma sp. strain SCSIO41004 | -Marine sponge Callipogon sp. | - | [56] |
|  | Fusarium equiseti | -Intertidal marine plants. | -Antibacterial activity. | [73] |
| ZSU-H85 (64) | Trichoderma sp. strain SCSIO41004 | -Marine sponge Callipogon sp. | -Antiviral activity. | [56] |
| (11S)-13,6-Tetrahydroxy-7-[(1-hydroxyethyl)anthracene-9,10-dione (65) | F. equiseti | -Intertidal marine plants. | -Antibacterial activity. | [73] |
| 5-Acetoxyl-2-methoxy-1,4,6-trihydroxy-anthroquinone (66) | Fusarium sp. (no. b77) | -Coral environment. | - | [75] |
| 1-Acetoxyl-5-acetoxyl-2-methoxy-4,6-trihydroxy-anthroquinone (67) | Fusarium sp. (no. b77) | -Coral environment. | - | [75] |
| Isorhopointirimetrin (68) | Penicillium oxalicum 2HL-M-6 | -Sea mud. | - | [36] |
|  | Penicillium sp. SCSGAP0023 | -Gorgonian coral. | -Antifouling activity. | [39] |
|  | Gloeodictum sp. T31 | -Marine lichen. | - | [38] |
|  | G. catenulatum T31 | -Marine sediment. | - | [65] |
| (β-2,R1)-Hydroxyisorhopointirimetrin (69) | Penicillium sp. OUCMDZ-4736 | -Mangrove roots of Acanthus ilicifolius. | -Antiviral activity. | [76] |
| Isorhopointirimetrin-1-methyl ether (70) | Aspergillus versicolor | -Green alga Halimeda opuntia. | -Antibacterial activity. | [34] |
| (7S,2S,5R)-isorhopointirimetrin (71) | Trichoderma harzianum (XS-20090075) | -Inner tissue of a soft coral. | -Antibacterial, cytotoxic and anti-acetylcholinesterase activities. | [55] |
| Nalgiovenin (72) | A. alliaceus | - | - | [72] |
| 1-Methylthiethyl nalgiovenin (73) | Emericella sp. SCSIO 05240 | -Marine sediment. | -Antibacterial activity. | [78] |
| Penicillin A (74) | Neurospora sp. KUFA 1047 | -Marine sponge Mycale sp. | -Anti-tirosinase activity. | [52] |
| Acetylnaprin (75) | N. sp. sp. strain KUFA 1047 | -Marine sponge Mycale sp. | - | [59] |
| 1,3,6-Tetrahydroxy-7(1H)-dihydroxypiperyl)anthraquinone (76) | Thermomycetes lanuginosus Tsikl KMM 4681 | -Marine sediment. | - | [66] |
| 6',8'-Dimethoxy-1-methyl-2-(3-oxobutytl)-anthraquinone (77) | Fusarium sp. ZZH60 | -Marine mangrove plant. | -Cytotoxic activity. | [79] |
| Norgorinol acid (78) | A. nidulans MA-143 | -Leaves of mangrove plant Rhizophora stylosa. | - | [80] |
| 8-O-Methyl versiconol (79) | A. penicicu SCSIO z021 | -Deep-sea sediment. | -Inhibition of human protein tyrosine phosphatases. | [81] |
| 2',3'-Dihydroxy versiconol (80) | A. penicicu SCSIO z021 | -Deep-sea sediment. | - | [81] |
| Methyl averantin (81) | A. penicicu SCSIO z021 | -Deep-sea sediment. | -Inhibition of human protein tyrosine phosphatases. | [81] |
|  | A. versicolor | -Marine sponge Petrosia sp. | -Antibacterial and cytotoxic activities. | [84] |
|  | A. versicolor INF 16-17 | -Inner tissue of an unidentified marine clam. | - | [88] |
|  | Aspergillus sp. SCSIO F063 | -Deep-sea sediment. | -Cytotoxic activity. | [91] |
|  | A. versicolor SCSIO-41502 | -Deep-sea sediment. | - | [92] |
| Versiconol (82) | A. penicicu SCSIO z021 | -Deep-sea sediment. | -Inhibition of human protein tyrosine phosphatases. | [81] |
|  | A. versicolor | -Marine sponge Petrosia sp. | -Cytotoxic activity. | [84] |
|  | A. versicolor SCSIO-41502 | -Deep-sea sediment. | - | [93] |
|  | Aspergillus sp. F40 | -Marine sponge Petrosia sp. | -Antibacterial activity. | [83] |
|  | Penicillium flavidum SHK1-27 | -Mangrove Acanthus ilicifolius Linn. | -Anti-proliferative activity. | [85] |
|  | Strain ZSUH-36 | - | - | [83] |
| 6,8'-Dir-O-methylaversatrin (83) | A. versicolor EN-7 | -Brown algae Saragassum thunbergii. | -Antimicrobial activity. | [82] |
| 6,8'-Dir-O-methylversiconol (84) | A. versicolor EN-7 | -Brown algae Saragassum thunbergii. | -Antimicrobial activity. | [82] |
|  | Strain ZSUH-36 | -Mangrove Acanthus ilicifolius Linn. | - | [83] |
| Averantin (85) | A. versicolor | -Marine sponge Petrosia sp. | -Antibacterial and cytotoxic activities. | [84] |
|  | A. versicolor INF 16-17 | -Inner tissue of an unidentified marine clam. | - | [88] |
|  | A. versicolor A-21-2-7 | -Deep-sea sediment. | -Cytotoxic activity. | [91] |
|  | Aspergillus sp. SCSIO F063 | - | - | [85] |
|  | Penicillium flavidum SHK1-27 | - | - | [83] |
| 6,8',1-Tri-O-methylaversatrin (86) | Aspergillus sp. SF-6796 | - | -Anti-neuroinflammatory activity. | [87] |
|  | Strain ZSUH-36 | -Mangrove Acanthus ilicifolius Linn. | - | [86] |
| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity | Ref. |
|----------|--------------------------|---------------------------------|-------------|-----|
| Averufanin (87) | A. versicolor INF-16-17 | Inner tissue of an unidentified marine clam. | - | [89] |
| | A. versicolor A-21-2-7 | Deep-sea sediment. | - | [89] |
| Aspergillus sp. 16-5C | Leaves of *Spongia testudinaria*. | - | [89] |
| Aspergillus sp. SCSIO F063 | Deep-sea sediment. | - | [89] |
| (1S)-3,4,5-Trisubstituted dimethylaverufin (88) | Aspergillus sp. SCSIO F063 | Deep-sea sediment. | - | [91] |
| (S)-3-Averufanin (89) | Aspergillus sp. SCSIO F063 | Deep-sea sediment. | - | [91] |
| 6-O-Methylaverufin (90) | Aspergillus sp. SCSIO F063 | Deep-sea sediment. | - | [91] |
| Averatrin (101) | A. niger SCSIO-41202 | Deep-sea sediment. | - | [91] |
| | A. versicolor SCF-41502 | Deep-sea sediment. | - | [92] |
| Coccoisporon A (94) | Aspergillus sp. F40 | Marine sponge *Callipogon sp*. | - | [92] |
| Versicol B (95) | A. niger WZXY-SX-4-1 | Marine sponge *Zostera marina*. | - | [21] |
| (-)-Variecolorquinone A (96) | A. flavus WZXY-SX-4-1 | Marine sponge *Zostera marina*. | - | [21] |
| | A. glaucus HB-18 | - | - | [22] |
| | Eurotium cristatum EN-220 | Marine brown alga *Sargassum thunbergii*. | - | [93] |
| 6-O-Methylaverufin (98) | A. nidulans MCC 3A/00050 | Deep-sea sediment. | - | [96] |
| | A. versicolor EN27 | - | - | [96] |
| 6,8-Dihydroxyverufin (99) | A. nidulans MCC 3A/00050 | Deep-sea sediment. | - | [96] |
| | Aspergillus sp. SF-6796 | - | - | [96] |
| | A. versicolor EN-7 | Brown alga *Sargassum thunbergii*. | - | [82] |
| | Aspergillus sp. 16-5C | Leaves of *Spongia testudinaria*. | - | [90] |
| | P. floridum SHK1-27 | - | - | [89] |
| | Acrocomium vitulinum | Inner tissue of an unidentified marine red alga. | - | [85] |
| | Strain ZSUH 36 | - | - | [86] |
| Aversin (100) | A. nidulans MCC 3A/00050 | Deep-sea sediment. | - | [96] |
| | A. versicolor MF139 | Brown alga *Sargassum thunbergii*. | - | [97] |
| | Aspergillus sp. 16-5C | Leaves of *Spongia testudinaria*. | - | [90] |
| | P. floridum SHK1-27 | - | - | [89] |
| | Strain ZSUH 36 | - | - | [88] |
| | = A. versicolor | - | - | [89] |
| Isolarsiscolin C (101) | A. nidulans MCC 3A/00050 | Deep-sea sediment. | - | [96] |
| Versicol A (102) | A. nidulans MA-143 | - | - | [88] |
| | Strain ZSUH 36 | - | - | [88] |
| | Isolate 1850 | - | - | [88] |
| Averufin (104) | A. nidulans MA-143 | Leaves of mango grove plant *Rhizophora styloides*. | - | [96] |
| | Strain ZSUH 36 | - | - | [88] |
| | = A. versicolor | - | - | [88] |
| | Isolate 1850 | - | - | [88] |
| | = A. versicolor | - | - | [89] |
| Paeclisporon II (105) | A. nidulans MA-143 | Leaves of mango grove plant *Rhizophora styloides*. | - | [96] |
| Averufanin (106) | A. nidulans MA-143 | Leaves of mango grove plant *Rhizophora styloides*. | - | [86] |
| | Strain ZSUH 36 | - | - | [87] |
| | = A. versicolor | - | - | [100] |
| | Isolate 1850 | - | - | [86] |
| | = A. versicolor | - | - | [100] |
| Nidurufinin (107) | A. niger (MF-16) | Sea water. | - | [96] |
| | A. versicolor | Marine sponge *Petrosia sp.* | - | [88] |
| | A. versicolor | - | - | [96] |
| | A. versicolor MF139 | - | - | [100] |
| | Aspergillus sp. | - | - | [89] |
| | Aspergillus sp. | - | - | [89] |
| | P. floridum SHK1-27 | - | - | [86] |
| | Isolate 1850 | - | - | [100] |
| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity                                                                 | Ref. |
|----------|--------------------------|--------------------------------|----------------------------------------------------------------------------|------|
| 3′-Hydroxy-6-O-methylversicolorin B (180) | A. puniceus SCSIO z021       | -Deep-sea sediment.            | -Inhibition of protein tyrosine phosphatases                                  | [81] |
| Versicolorin B (109)                       | A. puniceus SCSIO z021       | -Deep-sea sediment.            | -Inhibition of protein tyrosine phosphatases and toxicity against Brine shrimps. | [81] |
|                                                   |                           | -Marine sediment.              | -Antibacterial activity.                                                       | [101]|
|                                                   |                           | -Aspergillus sp. F40           | -Marine sponge Calyptopogia sp.                                              | -    |
|                                                   |                           | -A. versicolor SCSIO 41016     | -Marine sponge.                                                               | -    |
|                                                   |                           | -A. versicolor A-21-2-7        | -Deep-sea sediment.                                                          | [102]|
|                                                   |                           | P. flavidum SH1-27             | -                                                                              |      |
| 8-O-Methylidarufin (110)                    | A. puniceus SCSIO z021       | -Deep-sea sediment.            | -Inhibition of protein tyrosine phosphatases                                  | [81] |
|                                                   |                           | Aspergillus sp.                | -Gorgonian Dichotella gemmacea.                                              | [103]|
| 2′-Hydroxyversicolorin B (111)              | A. versicolor SCSIO 41016    | -Marine sponge.                | -                                                                             | [102]|
| Noraerufanin (112)                          | Aspergillus versicolor SCSIO 41016 | -Marine sponge.                  | -Antiviral activity.                                                          | [102]|
| 6,8-Di-O-methylhidriasuran (113)            | A. versicolor EN-7           | -Brown alga Sargassum thunbergii. | -Antibacterial activity.                                                      | [82] |
|                                                   |                           | Aspergillus sp. 16-5C          | -Leaves of Sonneratia apetala.                                               | [90] |
|                                                   |                           | Acrenomonium vitellinum        | -Inner tissue of an unidentified marine red alga.                            | [104]|
| 6,8-Di-O-methylversicolorin A (114)         | A. versicolor EN-7           | -Brown alga Sargassum thunbergii. | -                                                                             | [82] |
|                                                   |                           | Aspergillus sp. 16-5C          | -Leaves of Sonneratia apetala.                                               | -    |
|                                                   |                           | Aspergillus sp.                | -Gorgonian D. gemmacea.                                                       | [105]|
| UCT102/2 (115)                              | A. versicolor A-21-2-7       | -Deep-sea sediment.            | -Antioxidant activity.                                                        | [89] |
| Aspergionone A (116)                         | Aspergillus sp. 16-5C        | -Leaves of Sonneratia apetala. | -Antioxidant activity.                                                         | [90] |
| 8-O-Methylidarufanin (117)                   | Aspergillus sp.              | -Gorgonian D. gemmacea.        | -Antibacterial activity.                                                      | [102]|
|                                                   |                           | P. flavidum SH1-27             | -                                                                              |      |
| Versicolorin A (119)                         | P. flavidum SHK1-27          | -                              | -Anti-proliferative activity.                                                 | [81] |
| 6,8-Di-O-methylhidiapolarin (120)            | A. vitellinum               | -Inner tissue of an unidentified marine red alga.                            | -Insecticidal activity.                                                       | [104]|
| 6,8-Di-O-methylaverutin (122)                | Strain ZSUH-36              | -Marine sponge.                | -                                                                             | [86] |
| Aspergicol (122)                             | A. versicolor SCSIO 41502    | -                               | -Antioxidant activity.                                                        | [92] |
| Aspergicol (122)                             | A. versicolor SCSIO 41502    | -Deep-sea sediment.            | -Antioxidant activity.                                                        | [92] |
| Aspergicol (122)                             | A. versicolor SCSIO 41502    | -Deep-sea sediment.            | -Antioxidant activity.                                                        | [92] |
| Aspergicol (115)                             | A. versicolor SCSIO 41502    | -Deep-sea sediment.            | -Antioxidant activity.                                                        | [92] |
| Penicillastatin (126)                        | Penicilium citrinum PSU-F51 | -Gorgonian Sea fan (Amella sp.) | -Antibacterial and cytotoxic activities.                                      | [37] |
| Penicillastatin B (127)                      | Penicilium sp. PSU-F51      | -Gorgonian Sea fan (Amella sp.) | -Antibacterial and cytotoxic activities.                                      | [37] |
| Emocadime A (128)                            | Penicilium sp. SCSIOsof101   | -                               | -Anti-inflammatory activity.                                                  | [46] |
| Emocadimide A (129)                          | Penicilium sp. SCSIOsof101   | -                               | -Anti-inflammatory activity.                                                  | [46] |
| Emocadimide D (130)                          | Penicilium sp. SCSIOsof101   | -                               | -Anti-inflammatory activity.                                                  | [46] |
| Emocadimide H (132)                          | Penicilium sp. SCSIOsof101   | -                               | -Anti-inflammatory activity.                                                  | [46] |
| Anthrinonone B (133)                         | Alternaria tenuissima DFFSCS013 | -                               | -Inhibition of human protein tyrosine phosphatases and inhibition of indoleamine 2,3-dioxygenase activity | [63] |
| Anthrinonone C (134)                         | Alternaria tenuissima DFFSCS013 | -                               | -Inhibition of human protein tyrosine phosphatases and inhibition of indoleamine 2,3-dioxygenase activity | [63] |
| 7-Chloroemodin (135)                         | Penicilium ochrochiron       | -Sea sand.                      | -                                                                             | [11] |
| 2-Chloro-1,3,8-trihydroxy-6-(hydroxy- methyl) anthraacene-9,10-dione (136) | Penicilium sp. SCSIOsof101 | -Marine sediment.                | -                                                                             | [46] |
| 2′-Acetoxy-2′-chlorocibroreosin (137)         | P. citrinum HL-5126         | -                               | -Antibacterial activity.                                                      | [41] |
| 7-Chloro-1′-hydroxysorbothiptetinmetrin (138) | Penicilium sp. SCSIO sof101 | -Marine sediment.                | -                                                                             | [105]|
| (1′S)-7-Chloroaverantin (139)                | Aspergillus sp. SCSIO F063   | -                               | -Cytotoxic activity.                                                          | [91] |
| (1′S)-6-O-Methyl-7′-chloroveratrin (140)     | Aspergillus sp. SCSIO F063   | -                               | -Cytotoxic activity.                                                          | [91] |
| (1′S)-1′-O-Methyl-7′-chloroveratrin (141)     | Aspergillus sp. SCSIO F063   | -                               | -Cytotoxic activity.                                                          | [91] |
| (1′S)-6,1′-O,Di-Methyl-7′-chloroveratrin (142)| Aspergillus sp. SCSIO F063   | -                               | -Cytotoxic activity.                                                          | [91] |
| 7-Chloroveratrin (144)                       | Aspergillus sp. SCSIO F063   | -                               | -Cytotoxic activity.                                                          | [91] |

Table 1. Cont.
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| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity | Ref. |
|----------|---------------------------|--------------------------------|-------------|-----|
| 6-O-Methyl-5-chlonoaverrythin (145) | Aspergillus sp. SCSIO F063 | -Marine sediment. | -Cytotoxic activity. | [91] |
| Altenaria tenuissima (145) | A. tenuissima | -Marine algae. | - | [72] |
| 7-Chloro-versicolorin A (149) | A. punicus SCSIO z021 | -Deep-sea sediment. | -Inhibition of protein tyrosine phosphatases and toxicity against Brine shrimps. | [81] |
| Emodesamidame C (150) | Penicillium sp. SCSIOx0101 | -Marine sediment. | -Anti-inflammatory activity. | [46] |
| Emodesamidame F (151) | Penicillium sp. SCSIOx0101 | -Marine sediment. | - | [46] |
| Macrosporin 7-O-sulphate (153) | Staphylococcus sp. 32321 | -Mangrove tree Bruguiera sexangula var. rhynchopetala. | - | [50] |
| Emoindol 3-O-sulphate (154) | Penicillium F. oxalicum 2HIL-M-6 | -Sea mud. | - | [46] |
| Cetrerovin 3-O-sulphate (155) | P. oxalicum 2HIL-M-6 | -Sea mud. | - | [36] |
| 6-O-(α-D-ribofuranosyl)-questinol (156) | Eurotium rubrum | -Inner tissue of semi-mangrove plant Hibiscus tiliacis. | -DPPH radicals scavenging activity. | [106] |
| 6-O-(α-D-ribofuranosyl)-questin (156) | Eurotium rubrum | -Inner tissue of mangrove plant H. tiliacis. | -DPPH radicals scavenging activity. | [106] |
| 2-O-(6′-Acetyl)-α-D-glucoypuranoside (158) | A. wentii sp. EN-220 | -Marine brown alga Sargassum thunbergii. | -Antibacterial activity. | [95] |
| Macrosporin | S. lycopersici | -Inner tissue of gorgonian soft coral Dichtotella gammacae. | - | [51] |
| 2-O-(α-D-glucopyranoside) | Aspergillus wentii EN-48 | -Marine alga Sargassum sp. | - | [30] |
| Wentiquinone B (161) | A. wentii EN-48 | -Marine alga Sargassum sp. | - | [30] |
| 1,3-Dihydroxy-10-methoxy-3-methyldehydrobenzofuran (162) | A. wentii EN-48 | -Marine alga Sargassum sp. | - | [30] |
| Wentiquinone C (163) | A. wentii EN-48 | -Marine alga Sargassum sp. | - | [30] |
| 9-Dehydroxyeurotinone (164) | E. rubrum | -Inner tissue of semi-mangrove plant Hibiscus tiliacis. | -Cytotoxic activity. | [47] |
| 2-O-Methyl-9-dehydroxyeurotinone (165) | Eurotium sp. SCSIO F452 | -Marine sediment. | - | [47] |
| 2-O-Methyl-9-dehydroxyeurotinone (166) | E. rubrum | -Inner tissue of semi-mangrove plant H. tiliacis. | -DPPH radicals scavenging activity. | [106] |
| 2-O-Methyl-4-(α-D-ribofuranosyl)-9-dehydroxyeurotinone (167) | Eurotium rubrum | -Inner tissue of semi-mangrove plant H. tiliacis. | -DPPH radicals scavenging activity. | [106] |
| Asperitetrone B (168) | A. tritici SPP-8-1 | -Soft coral Galaxea fascicularis. | -Antibacterial and cytotoxic activities. | [28] |
| (3E)-Deoxyaustracortilutein (169) | Altenticaria tenuissina DFFS5013 | -Marine sediment. | - | [63] |
| Altersaponin B (for dactylarin, 170) | Altenticaria tenuissina DFFS5013 | -Marine sediment. | - | [63] |
| Altersaponin A (79) | Altenticaria tenuissina DFFS5013 | -Fruits of a mangrove tree Aegiceras corniculatum. | - | [61] |
| Altersaponin Z | Stemphyllum sp. 33231 | -Marine brown alga Sargassum sp. | - | [49] |
| Altersaponin C (171) | Staphylococcus sp. 32321 | -Marine sediment. | - | [49] |
| Altersaponin A (172) | Staphylococcus sp. 32321 | -Marine brown alga Sargassum sp. | - | [49] |
| Altersaponin C (173) | Staphylococcus sp. 32321 | -Marine brown alga Sargassum sp. | - | [49] |
| Auxarcthin C (173) | Xylaria sp. 2508 | -Marine brown alga Sargassum sp. | - | [49] |
| 2-O-Acetylaltersapone B (174) | Stemphyllum sp. 33231 | -Marine brown alga Sargassum sp. | - | [49] |
Table 1. Cont.

| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity | Ref. |
|----------|---------------------------|-------------------------------|-------------|-----|
| Lentisone (175) | Trichoderma sp. (H1) | Sea cucumber. | -Antibacterial and antiangiogenic activities. | [43] |
| S2-68SC (known as 1408C, 176) | Haloruecia sp. (no. 1403) | Mangrove plant. | -Anti-proliferative activity. | [108] |
| | - | - | - | |
| | Phomopsis sp. PSU-MA214 | Leaves of a mangrove tree Rhizophora apiculata Griff. Ex. T. Anderson. | -Antibacterial and cytotoxic activities. | [52] |
| Auxarthrol D (178) | Spondonema casei HDN16-802 | Marine sediment. | -Antibacterial and cytotoxic activities. | [109] |
| Auxarthrol C (179) | S. casei HDN16-802 | Marine sediment. | -Antibacterial and anticoagulant activities. | [109] |
| 4-Dehydroalsterosanol A (180) | S. casei HDN16-802 | Marine sediment. | - | [109] |
| Aspergitoine A (181) | Aspergillus tritici sp. SCSIO F452 -Marine sediment. -Cytotoxic activity. | | | [116] |
| Botrycin (182) | Aspergillus sp. strain 05F16 | Unidentified marine alga. - | - | [110] |
| | Fusarium sp. PSU-F14 and PSU-F135 | - | - | |
| | Nigrospora sp. (strain no. 1403) | -Decayed wood of Kandelia candel (L.) Druce. -Decayed wood of Kandelia candel (L.) Druce. | -Antibacterial, antifungal, and cytotoxic activities. | [112] |
| Nigrospora sp. ZJ-2010006 | -Unidentified marine alga. | - | - | |
| Xylaria sp. 2508 | -Mangrove plant. | - | - | |
| | Strain no. 1403 | - | - | |
| | - | - | - | |
| | - | - | - | |
| Nigrospora A (183) | Fusarium sp. PSU-F14 and PSU-F135 | Gorgonian sea fan (Annella sp.). | - | [59] |
| Nigrospora B (184) | Fusarium sp. PSU-F14 and PSU-F135 | -Gorgonian sea fan (Annella sp.) | -Antimarial and anti-Mycobacterium tuberculosis, and cytotoxic activities. | [59, 130] |
| Nigrospora sp. ZJ-2010006 | -Unidentified marine alga. | - | - | |
| Fusarinaphthoquinone C (185) | Fusarium sp. PSU-F14 and PSU-F135 | - | - | |
| 4-Deoxybotrycin (186) | Nigrospora sp. (strain no. 1403) | -Decayed wood of Kandelia candel (L.) Druce. | -Antibacterial, antifungal, and cytotoxic activities. | [112] |
| | - | - | - | |
| | - | - | - | |
| | - | - | - | |
| | - | - | - | |
| | Nigrospora sp. ZJ-2010006 | -Unidentified marine alga. | -Anti-tumor activity. | [134] |
| Xylaria sp. 2508 | -Mangrove plant. | - | - | |
| 10-Deoxybotrycin (187) | Nigrospora sp. ZJ-2010006 | -Unidentified marine alga. | -Anti-mycobacterial activities. | [119] |
| Nigrospora sp. ZJ-2010006 | Inner tissue of the zoanthid Polychaeta hadoni (G-XWZ-20100326). | - | - | |
| Hydroxybotrycin (188) | Alteneria sp. (SK11) | Root of mangrove tree Exoccoccus agallocha. | - | [62] |
| 1403F-3 (189) | Heterorhizinia sp. (no. 1403) | Mangrove plant. | -Apoptosis in cancer cells. | [113] |
| Aspergiolide A (190) | A. glauca HB1-19 | Marine sediment. | - | [114] |
| Aspergiolide B (191) | A. glauca HB1-19 | Marine sediment. | -Cytotoxic activity. | [115] |
| Aspergiolide C (192) | A. glauca HB1-19 | Marine sediment. | - | [115] |
| Aspergiolide D (193) | A. glauca HB1-19 | Marine sediment. | -Inhibition of receptor tyrosine kinases and anti-parasitic activities. | [115] |
| Variecolortin A (194) | Eurotium sp. SCSIO F452 | Marine sediment. | - | [116] |
| Variecolortin B (195) | Eurotium sp. SCSIO F452 | Marine sediment. | -Cytoxic activity. | [116] |
| | Variecolortin C (196) | Eurotium sp. SCSIO F452 | Marine sediment. | -Cytoxic activity. | [116] |
| Tetrahydrobotrycin (197) | Aspergillus sp. strain 05F16 | Unidentified marine alga. | - | [110] |
| | Alteraria sp. (SK11) | Root of mangrove tree Exoccoccus agallocha. | - | [62] |
| 1-Deoxytetrahydrobotrycin (198) | Aspergillus sp. strain 05F16 | Unidentified marine alga. | - | [110] |
| 8-Hydroxyconiothymin B (199) | Talaromyces islandicus EN-501 | Inner tissue of marine red alga Laurencia okamura. | -Antibacterial, DPPH*, and ABTS** radicals scavenging activities. | [117] |
| 4,8-Dihydroxyconiothymin B (200) | T. islandicus EN-501 | Inner tissue of marine red alga L. okamura. | -Antibacterial, cytotoxic, DPPH*, and ABTS** radicals scavenging activities. | [117] |
| | T. islandicus EN-501 | Inner tissue of marine red alga L. okamura. | -Antibacterial, DPPH*, and ABTS** radicals scavenging activities. | [117] |
| 4,8-Dihydroxyconiothymin B (201) | T. islandicus EN-501 | Inner tissue of marine red alga L. okamura. | -Antibacterial, DPPH*, and ABTS** radicals scavenging activities. | [117] |
| | T. islandicus EN-501 | Inner tissue of marine red alga L. okamura. | -Antibacterial, DPPH*, and ABTS** radicals scavenging activities. | [117] |
| 4,8-Dihydroxy-10-D-methylidendryl E (202) | T. islandicus EN-501 | Inner tissue of marine red alga L. okamura. | -Antibacterial, DPPH*, and ABTS** radicals scavenging activities. | [117] |
| Fusquinon A (204) | Fusarium sp. (no. ZH-210) | Mangrove sediment. | -Cytotoxic activity. | [118] |
| Fusquinon B (205) | Fusarium sp. (no. ZH-210) | Mangrove sediment. | -Cytotoxic activity. | [118] |
| Fusquinon C (206) | Fusarium sp. (no. ZH-210) | Mangrove sediment. | -Cytotoxic activity. | [118] |
Table 1. Cont.

| Compound | Fungus Species/Strain No. | Source of Marine-Derived Fungi | Bioactivity | Ref. |
|----------|--------------------------|--------------------------------|-------------|-----|
| Fusaransraquinone (207) | Fusarium sp. PSU-F14 and PSU-F135 | Gorgonian sea fan (Amella sp.) | - | [59] |
| 9a- | Hydroxydihydrodesoxybostry (208) | Altenaria sp. (SK11) | Root of mangrove tree Excoecaria agallocha. | - | [62] |
| 9a- | | Fusarium sp. PSU-F14 and PSU-F135 | - | [59] |
| 9a- | | Nigrospora sp. ZJ-2010006 | Unidentified sea anemone. | - | [66] |
| Nigrospora sp. ZJ-2010006 | Unidentified sea anemone. | - | [68] |
| 4a-epi-9a- | Methoxydihydrodesoxybostryc (210) | Nigrospora sp. ZJ-2010006 | Inner tissue of the zoathid Palyptha huddoni (GX-WZ-20100026). | - | [69] |
| Dihydroaltersolanol A (211) | Altenaria tenuissima DFFS013 | - | Marine sediment. | - | [63] |
|  | | Altenaria sp. ZJ-2080003 | - | [49] |
|  | | Stemphylium sp. 32321 | - | [50] |
| Altersolanol L (212) | A. tenuissima DFFS013 | - | Soft coral Sarcophyton sp. | - | [49] |
|  | | Altenaria sp. ZJ-2080003 | - | [49] |
|  | | Stemphylium sp. 32321 | - | [50] |
|  | | Phonm sp. L28 | - | [67] |
|  | | Phomopsis sp. PSU-MA214 | - | [52] |
| Aпольсanol (213) | Altenaria tenuissima DFFS013 | - | Marine sediment. | - | [63] |
|  | | Altenaria sp. ZJ-2080003 | - | [49] |
|  | | Stemphylium sp. 32321 | - | [50] |
|  | | Phonm sp. L28 | - | [67] |
|  | | Phomopsis sp. PSU-MA214 | - | [52] |
| Tetrahydroaltersolanol B | Altenaria sp. ZJ-2080003 | - | Soft coral Sarcophyton sp. | - | [49] |
| (214) | | Stemphylium sp. 32321 | - | [50] |
|  | | Phonm sp. L28 | - | [67] |
| Halorsellina A (215) | Altenaria sp. (SK-11) | - | Root of mangrove tree Excoecaria agallocha. | - | [62] |
|  | | Halorsellina sp. (no. 1403) | - | Marine plant. | - | [58] |
| Tetrahydroaltersolanol C | Altenaria sp. ZJ-2080003 | - | Soft coral Sarcophyton sp. | - | [49] |
| (216) | | - | - | - | [58] |
|  | | - | - | - | [58] |
| Tetrahydroaltersolanol D | Altenaria sp. ZJ-2080003 | - | Soft coral Sarcophyton sp. | - | [49] |
| (217) | | - | - | - | [58] |
|  | | - | - | - | [58] |
| Tetrahydroaltersolanol E | Altenaria sp. ZJ-2080003 | - | Soft coral Sarcophyton sp. | - | [49] |
| (218) | | - | - | - | [58] |
|  | | - | - | - | [58] |
| Tetrahydroaltersolanol F | Altenaria sp. ZJ-2080003 | - | Soft coral Sarcophyton sp. | - | [49] |
| (219) | | - | - | - | [58] |
|  | | - | - | - | [58] |
| 2,6-Diacetaltersolanol L | Stemphylium sp. 32321 | - | Marine plant. | - | [63] |
| (220) | | Altenaria sp. ZJ-2080003 | - | [49] |
| Hariziamunnoe A (221) | T. harziaum (XS-20090075) | - | Soft coral. | - | [55] |
| Hariziamunnoe B (222) | T. hariziaum (XS-20090075) | - | Soft coral. | - | [55] |
| Coniothyriune A (223) | Trichoderma sp. (H-1) | - | Sea cucumber. | - | [55] |
| Xyloxythraquinone (224) | Xylaria sp. 2508 | - | Marine plant. | - | [43] |
| Axafrerol E (225) | Speroetania casei HDN16-802 | - | Marine sediment. | - | [109] |
| Axafrerol F (226) | S. casei HDN16-802 | - | Marine sediment. | - | [109] |
| Axafrerol E (227) | Speroetania casei HDN16-802 | - | Marine sediment. | - | [109] |
| Asperflavin (228) | A. glaucus HBI-19 | - | Marine sediment. | - | [22] |
|  | | Eurotium repens | - | [24] |
|  | | Exothem sp. | - | [24] |
|  | | Eurotium cristatum EN-220 | - | Marine brown alga Sargassum thunbergii. | - | [95] |
| Isoasperflavin (229) | A. glaucus HBI-19 | - | Marine sediment. | - | [22] |
| 3,4-Dihydro-3,5-dimethoxy-6,8-dimethoxy-3- methylanthracen-1(2H)-one (230) | A. wentii EN-48 | - | Marine sediment. | - | [30] |
| Exosulurin (231) | Eurotium rubrum | - | Inner tissue of mangrove plant H. tilacum. | - | [95] |
|  | | E. cristatum EN-220 | - | Marine brown alga Sargassum thunbergii. | - | [95] |
Table 1. Cont.

| Compound                     | Fungus Speciess/Strain No. | Source of Marine-Derived Fungi | Bioactivity                                                                 | Ref.  |
|------------------------------|-----------------------------|--------------------------------|-------------------------------------------------------------------------------|-------|
| Anthrinonine A (233)         | Alternaea tenuissima DFFSC013 | Marine sediment.                | -Induction of intracellular calcium flux in HEK293 cells and inhibition of indoleamine 2,3-dioxygenase activity. | [63]  |
| Scorpine (234)               | Amoronia littoralis Biopora-like tropical fungus | Inertial sediment.              | -                                                                             |       |
| Brown alga                   | A. terreus (no. GX7-3B)     | Mangrove Bruguiera gymnolitiza (Linn.) Savigny. | -Anti-acetylcholinesterase activity.                                         | [122] |
| Biscortin (235)              | -                           | -                              | -                                                                             |       |
| 8-O-Methylbiscortin (236)    | A. terreus                  | Mangrove Bruguiera gymnolitiza (Linn.) Savigny. | -Anti-acetylcholinesterase activity.                                         | [122] |
| 6,6'-Oxybiprenyl-1,3,8-trihydroxy-2,(5)-l-methoxybenzeneanthracene-9,10-dione (237) | A. versicolor | The inner tissue of an unidentified marine clam. | -Anti-inflammatory activity.                                                 | [88]  |
| 6,6'-Oxybiprenyl-1,3,8-trihydroxy-2,(5)-l-hydroxybenzeneanthracene-9,10-dione (238) | A. versicolor | The inner tissue of an unidentified marine clam. | -Anti-bacterial activity.                                                   | [88]  |
| (-)-2,2'-(4-[(+)-a-methyl-1,4,5-trihydroxy-anthracene-9,10-dione] (239) | Talaromyces stipitatus KUFA0207 | Marine sponge Stylosa fabelilformis. | -                                                                             | [33]  |
| Alter Porriol K (240)         | Alternaea sp. ZJ9-6B         | Mangrove tree Aegiceras corniculatum fruits. | -Cytotoxic activity.                                                         | [61]  |
| Alter Porriol L (241)         | Alternaea sp. ZJ9-6B         | Mangrove tree A. corniculatum fruits. | -Cytotoxic activity.                                                         | [61], [63] |
| Alter Porriol M (242)         | Alternaea sp. ZJ9-6B         | Mangrove tree A. corniculatum fruits. | -                                                                             | [61]  |
| Alter Porriol S (243)         | Alternaea sp. (SK11)         | Root of mangrove tree Exocoria agallocha. | -Anti-Mycopatorium tuberculosis activity.                                    | [62]  |
| (-)-a5-Alter Porriol C (244)  | Alternaea sp. (SK11)         | Root of mangrove tree E. agallocha. | -Anti-Mycoporum tuberculosis activity.                                       | [62]  |
| Alter Porriol C (245)         | Alternaea sp. ZJ-2008003     | Soft coral reef Sarcophyton sp.  | -Antibacterial and cytotoxic activities.                                     | [49]  |
|                             | Stemphylium sp. 33231        | Mangrove tree Bruguiera sexangula var. rhynchoptera. | -Antibacterial activity.                                                   | [50]  |
| Alter Porriol N (246)         | Alternaea sp. ZJ-2008003     | Soft coral reef Sarcophyton sp.  | -                                                                             | [49]  |
|                             | Stemphylium sp. 33231        | Mangrove tree B. sexangula var. rhynchoptera. | -                                                                             | [50]  |
|                             | Stemphylium sp. FJ006        | Unidentified sponge.            | -                                                                             |       |
| Alter Porriol O (247)         | Alternaea sp. ZJ-2008003     | Soft coral reef Sarcophyton sp.  | -                                                                             | [49]  |
| Alter Porriol P (248)         | Alternaea sp. ZJ-2008003     | Soft coral reef Sarcophyton sp.  | -                                                                             | [49]  |
| Alter Porriol Q (249)         | Alternaea sp. ZJ-2008003     | Soft coral reef Sarcophyton sp.  | -                                                                             | [49]  |
| Alter Porriol R (250)         | Alternaea sp. ZJ-2008003     | Soft coral reef Sarcophyton sp.  | -                                                                             | [49]  |
| Alter Porriol W (260)         | Stemphylium sp. 33231        | Mangrove tree B. sexangula var. rhynchoptera. | -Antibacterial activity.                                                   | [50]  |
| Alter Porriol Y (261)         | Stemphylium sp. 33231        | Mangrove tree B. sexangula var. rhynchoptera. | -Antibacterial activity.                                                   | [50]  |
|                             | S. lycopersici               | Inner tissue of gorgonian soft coral Dichelota gammaca. | -                                                                             | [51]  |
| Alter Porriol T (262)         | Stemphylium sp. FJ006        | Marine sponge Niphates olemda. | -Antibacterial activity.                                                     | [64]  |
| Alter Porriol Z (263)         | Stemphylium sp. FJ006        | Unidentified sponge.            | -Anti-inflammatory activity.                                                | [124] |
| Alter Porriol Zc (264)        | Stemphylium sp. FJ006        | Unidentified sponge.            | -Anti-inflammatory activity.                                                | [124] |
| Alter Porriol Z (266)         | Stemphylium sp. FJ006        | Unidentified sponge.            | -Anti-inflammatory activity.                                                | [124] |
| Rubelin A (267)               | Strain F-F-3C                | Unidentified marine red alga.   | -Antibacterial activity.                                                    | [43]  |
| 14-Acetoxyrubelina A (268)    | Strain F-F-3C                | Unidentified marine red alga.   | -Antibacterial and antifungal activities.                                    | [44]  |
| 14-Acetoxyrubelina C (269)    | Strain F-F-3C                | Unidentified marine red alga.   | -Antibacterial activity.                                                    | [43]  |
| Physcion-10,10'-bienanthrone (270) | A. glauces HB1-19          | Deep-sea sediment.              | -                                                                             | [22]  |
|                             | A. ventii EN-48              | Brown alga Sargassum sp.        | -                                                                             | [30]  |
| trans-Emodin=physcion-10,10'-bienanthrone (271) | A. glauces HB1-19          | Deep-sea sediment.              | -Cytopathic activity.                                                       | [22]  |
| cis-Emodin=physcion-10,10'-bienanthrone (272) | A. glauces HB1-19          | Deep-sea sediment.              | -Cytopathic activity.                                                       | [22]  |
| Atropospor of 8,8'-dihydroxy-1,1',2,3'-tetramethoxy-6,6'-dimethyl-10,10'-bienanthrone (273) | A. ventii EN-48 | Brown alga Sargassum sp.        | -                                                                             | [30]  |
### Table 1. Cont.

| Compound                     | Fungus Species/Strain No.                                      | Source of Marine-Derived Fungi            | Bioactivity                                      | Ref. |
|------------------------------|----------------------------------------------------------------|------------------------------------------|-------------------------------------------------|------|
| Atropisomer of tetramethoxy-1,1',3,3'-8,8'-dihydroxy-6,6'-dime-      | A. wentii EN-48                                      | Brown algae Sargassum sp.                      | -                               | [30] |
| Allianthrone A (275)         | A. alliaceus                                                  | -Marine algae.                            | -Cytoprotective activity.                      | [77] |
| Allianthrone B (276)         | A. alliaceus                                                  | -Marine algae.                            | -Cytoprotective activity.                      | [77] |
| Allianthrone C (277)         | A. alliaceus                                                  | -Marine algae.                            | -Cytoprotective activity.                      | [77] |
| JBIR-97/98 (279)             | Engyodontium album                                           | -Marine sponge Cacospinga scalaris.       | -Antibacterial, antifungal, and cytotoxic       | [125]|
| JBIR-99 (280)                | E. album                                                     | -Marine sponge C. scalaris.               | -Antibacterial, antifungal, and cytotoxic       | [125]|
| Engyodontochone A (281)      | E. album                                                     | -Marine sponge C. scalaris.               | -Antibacterial, antifungal, and cytotoxic       | [125]|
| Engyodontochone B (282)      | E. album                                                     | -Marine sponge C. scalaris.               | -Antibacterial, antifungal, and cytotoxic       | [125]|
| Engyodontochone C (283)      | E. album                                                     | -Marine sponge C. scalaris.               | -Antibacterial and cytotoxic activity.          | [125]|
| Engyodontochone D (284)      | E. album                                                     | -Marine sponge C. scalaris.               | -Antibacterial activity.                        | [125]|
| Engyodontochone E (285)      | E. album                                                     | -Marine sponge C. scalaris.               | -Antibacterial activity.                        | [125]|
| Acremonidin A (287)          | Acremonium camptosporum                                      | -Marine sponge Aplysina fulva.            | -Antibacterial and cytotoxic activity.          | [126]|
| Acremonidin B (288)          | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonidin C (289)          | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonidin G (290)          | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonoxanthone A (291)     | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonoxanthone B (292)     | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonoxanthone D (293)     | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonoxanthone F (294)     | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonoxanthone G (295)     | A. camptosporum                                              | -Marine sponge A. fulva.                  | -Antibacterial and cytotoxic activities.        | [126]|
| Acremonoxanthone C (296)     | Unidentified fungus of the order Hypocreales (MSX 17022)     | -                                       | -20S proteasome inhibitory activity.            | [127]|

### 5. Concluding Remarks and Future Perspectives

This review shows that polyketides are the predominant metabolites reported from marine-derived fungi. Altogether, we have reported 296 specialized metabolites belonging to the anthraquinone class and their derivatives, which were isolated from 28 marine fungal strains, and less-studied fungal species highlighting the chemical diversity and their myriad biological/pharmacological properties. In general, these compounds exhibited a wide range of biological activities, including antibacterial and antifungal, antiviral, antiparasitic, anti-inflammatory, enzyme inhibitory, antioxidant, anticoagulant, anti-angiogenesis, anti-obesity, anti-fouling, algicidal, insecticide and cytotoxic activities. More specifically, members of the genus *Aspergillus*, *Penicillium*, *Eurotium*, and *Fusarium* are the most prolific sources of anthraquinones and their derivatives. Among the isolated anthraquinones, 112 were from *Aspergillus*, 37 from *Penicillium*, 36 from *Altenaria*, 26 from *Stemphylium*, 23 from *Eurotium*, 19 from *Fusarium*, 14 from *Trichoderma*, 13 from *Acremonium*, 11 from *Talaromyces*, 10 from *Nigrospora*, and the rest of anthraquinones are from other fungal resources (Figure 28). Members of the genera *Aspergillus* and *Penicillium* are found to be more versatile in terms of secondary metabolite biosynthesis, producing various types of anthraquinones viz. hydro-, alkylated, halogenated, seco-, furano and pyrano derivatives. Sulphated anthraquinoids and anthraquinones fused with xanthones and chromones have been also reported in species of *Penicillium*, while the glycosylated anthraquinones were reported from algicolous and mangrove endophytic fungi of the
genera *Fusarium* and *Stemphylium*, which have a close symbiotic relationship with the hosts, indicating that they can adjust the biosynthetic pathways to each other. Bianthraquinones are found predominantly in *Altenaria* and *Stemphylium* species, while the anthraquinone-xanthones are more preponderant in *Acremonium* and *Engyodontium* species, suggesting the species-specific metabolites. Another interesting observation is the elasticity of the biosynthetic capacity of fungi, for instance, cytoskyrin anthraquinone has been reported from the fungus *Curvularia* sp., which is associated with sponges. The influence of the fungal habitats, the organisms with which they are associated, the type of culture media and biotic and abiotic stressors can influence their capacity to biosynthesize a myriad of specialized metabolites with unique structural features, which ultimately can manifest different biological/pharmacological activities. The advantage of fungi in terms of secondary metabolite production over other organisms is their capacity to produce a large quantity of interesting compounds by fermentation. These compounds can be used as a scaffold for medicinal chemistry study. Given a versatility of the anthraquinoid scaffolds for their biological activities, it is legitimate to think that varying the side chains of the anthraquinoid scaffolds could render compounds with unique structures and efficient biological/pharmacological activities. Therefore, searching for marine-derived fungi from different niches, with different pressure, temperature and light intensity such as from thermal vent, deep-sea, polar habitats, and different animal hosts, can be promising to find structurally unique and biologically relevant compounds. Another perspective is the development of new culture media, which can allow for unculturable marine-derived fungi, which do not grow in normal media to thrive. In addition, taking advantage of the plasticity of the enzymology of the biosynthetic pathways of fungi, the addition of natural or synthetic amino acids to the culture media should be another challenging avenue to obtain compounds of unknown values.

**Figure 28.** The number of isolated anthraquinone metabolites and their derivatives from the marine-derived fungal resources.
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