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REVIEW

Antibacterial properties of natural products from marine fungi reported between 2012 and 2023: a review

Ping Wang[1] · Xiaomei Huang[2] · Chenyuan Jiang[1] · Rushuang Yang[1] · Jialing Wu[1] · Yinghui Liu[1] · Shuangshuang Feng[1] · Tingting Wang[1]

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Abstract

The oceans are rich in diverse microorganisms, animals, and plants. This vast biological complexity is a major source of unique secondary metabolites. In particular, marine fungi are a promising source of compounds with unique structures and potent antibacterial properties. Over the last decade, substantial progress has been made to identify these valuable antibacterial agents. This review summarizes the chemical structures and antibacterial activities of 223 compounds identified between 2012 and 2023. These compounds, effective against various bacteria including drug-resistant strains such as methicillin-resistant *Staphylococcus aureus*, exhibit strong potential as antibacterial therapeutics. The review also highlights the relevant challenges in transitioning from drug discovery to product commercialization. Emerging technologies such as metagenomics and synthetic biology are proposed as viable solutions. This paper sets the stage for further research on antibacterial compounds derived from marine fungi and advocates a multidisciplinary approach to combat drug-resistant bacteria.

Keywords Marine natural products · Fungal metabolites · Antibacterial activity · Drug discovery

Introduction

Pathogenic bacteria are those capable of inducing harmful infections. They can cause illness via various pathways, such as by producing toxic metabolites that trigger a host's immune response and disrupting the function of healthy tissues. Common bacterial pathogens include *Salmonella* spp. (Guo et al. 2017), *Staphylococcus aureus* (Zafari et al. 2021), *Vibrio parahemolyticus* (Bhowmik et al. 2014), and *Listeria monocytogenes* (Jensen et al. 2016). *S. aureus* causes many diseases including the skin infection atopic dermatitis (Sasai-Takedatsu et al. 1997) and bacterial meningitis, which occurs when bacteria breach the barriers of the central nervous system (Smetana et al. 2013). If bacteria enter the cerebrospinal fluid, they can cause a pronounced inflammatory response leading to headache, fever, and neurological impairment. The occurrence of bacteremia in cases of pneumonia may reportedly be related to chromosomally encoded EDIN-B derived from *S. aureus* (Courjon et al. 2015). *Salmonella* spp. can cause enteric fever, acute enteritis, sepsis, and other diseases. Penicillins (Lopez et al. 2000) and cephalosporins (Cisneros-Farrar and Parsons 2007) are the main antibacterial clinical treatments for such diseases, but the widespread use of antibiotics has led to a gradual increase in drug resistance (Nichol et al. 2015). For example, some *S. aureus* strains such as methicillin-resistant *S. aureus* (MRSA), can produce enzymes that hydrolyze β-lactam rings, thereby conferring resistance to penicillin. The increasing drug resistance and the slow discovery of new antibacterial drugs pose a growing threat to public health (Hutchings et al. 2019).

As terrestrial resources dwindle, humankind is turning to the oceans that cover 71% of the planet. The oceans are vast and rich in resources, encompassing unique biological and abiotic environments. These environmental factors enable marine organisms, including bacteria, fungi, sponges, and ascidians, to produce unique secondary metabolites different from those of terrestrial creatures. These chemically and biologically diverse marine compounds have been shown to have insecticidal, antibacterial, anticoagulant, antifungal,

✉ Tingting Wang
wangtingting1@nbu.edu.cn

[1] Li Dak Sum Yip Yio Chin Kenneth Li Marine Biopharmaceutical Research Center, Health Science Center, Ningbo University, Ningbo 315211, Zhejiang, China

[2] Department of Marine Biology, Xiamen Ocean Vocational College, Xiamen 361100, Fujian, China

antimalarial, antiplatelet, antituberculous, and antiviral activities (Mayer and Hamann 2005). The common cephalosporin antibiotics were initially isolated from the marine fungus *Cephalosporium acremonium* by Giuseppe Brotzu in 1948 (Bo 2000). However, despite the large number of compounds isolated from marine sources, only 15 have been approved as drugs, and around 40 compounds are currently undergoing clinical drug trials (Mayer et al. 2019). Thus, marine natural products (MNPs) are under-represented among approved or clinically tested compounds, and a substantial number of MNPs have yet to be comprehensively screened for bioactivity.

Marine fungi are a significant group of microorganisms. Their secondary metabolites have become the focus of research in chemistry, biology, and pharmacy due to their diverse structures, rich biological activities, and high innovation index. These secondary metabolites can be categorized based on structure type, namely, terpenoids, sterols, alkaloids, glycosides, peptides, polysaccharides, macrolides, polyethers, and unsaturated fatty acids. From 2012 to 2023, among all such antibacterial metabolites, alkaloids are consistently the most commonly reported; they have the highest number of compounds and the highest frequency of discovery. Quinones come a close second, whereas steroids yield the lowest number of compounds (Fig. 1). Antibacterial metabolites are the most commonly reported to be active against *S. aureus* and are predominantly derived from *Aspergillus* spp. or *Penicillium* spp. (Figs. 2 and 3). At the genus level, the second and third most numerous metabolites target *Bacillus* spp. (*B. subtilis*, *B. thuringiensis*, *B. cereus*, and *B. amyloliquefaciens*) and *Escherichia coli* (Fig. 3). This review highlights and summarizes 223 marine fungal metabolites exhibiting antibacterial activity, as reported in 74 publications from 2012 to 2023 (Table 1).

Antibacterial compounds derived from marine *fungi*

Alkaloids

Nearly one-third of the marine fungal secondary metabolites exhibiting antibacterial activity listed in this review are alkaloids, as shown in Figs. 4, 5, 6, 7, 8.

Trichodin A (**1**), an uncommon pyridone, and pyridoxine (**2**) have been isolated from the marine fungus, *Trichoderma* sp. strain MF106. These compounds display antibiotic activity against the clinically relevant microorganism *S. epidermidis*, with IC_{50} of 24 and 4 μM, respectively (Wu et al. 2014). Cyclopiazonic acid (**3**) and brevianamide F (**4**) have been isolated from the marine-derived fungus *P. vinaceum* and exhibit different antibacterial activities: **4** is active against *S. aureus*, whereas **3** was only active against *E. coli* (Asiri et al. 2015). Nine diketopiperazines (**5**–**13**)

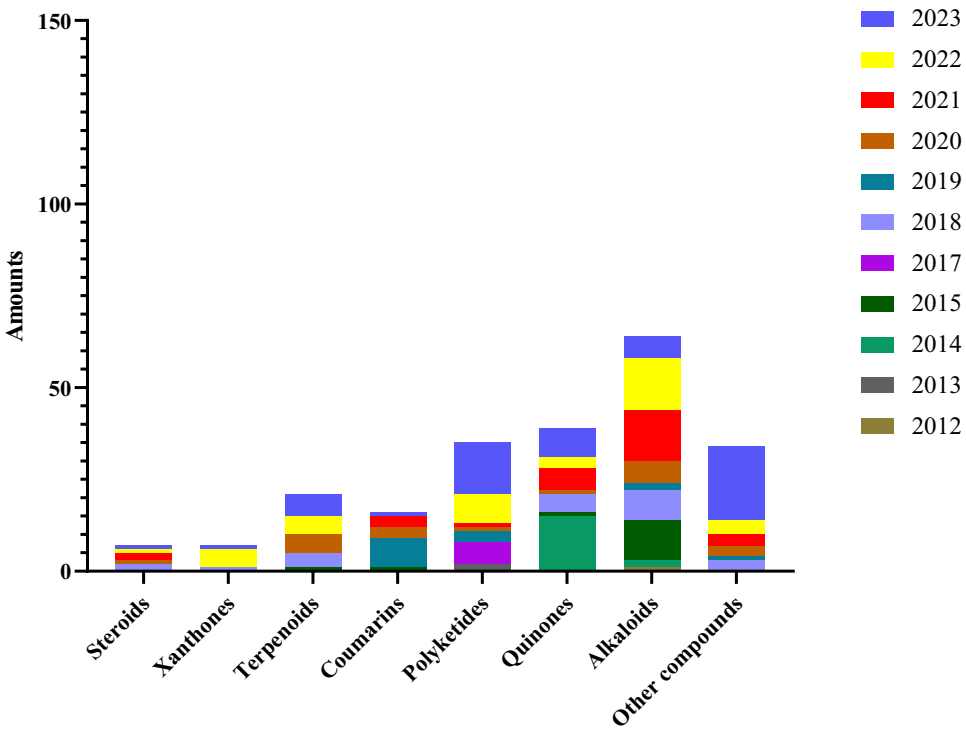


Fig. 1 Antibacterial compounds from marine fungi by class/year; $n = 223$

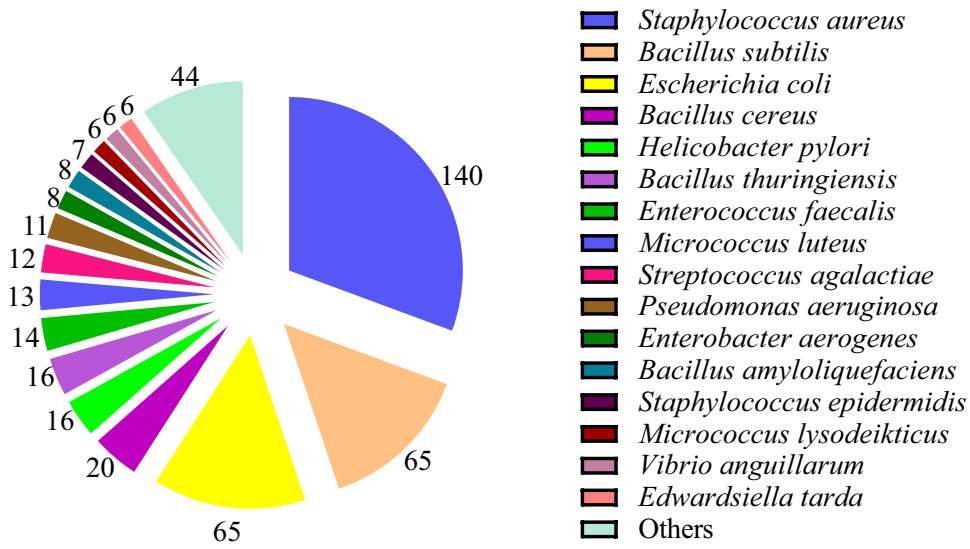


Fig. 2 Types of pathogenic bacteria studied and the amounts of antibacterial compounds targeting them

have been isolated from the marine fungus *A. fumigatus* and exhibit moderate to weak effects against Gram-positive bacteria (El-Gendy and Rateb 2015). Pyrrospirones C (**14**), F (**15**), and I (**16**) have been isolated from the marine-derived fungus *Penicillium* sp. ZZ380 and have antibacterial effects on MRSA and *E. coli*, having minimal inhibition concentration (MIC) of 2.0–5.0 mg/mL (Song et al. 2018). Three compounds, penicillatide B (**17**), cyclo(*R*-Pro–*S*-Phe) (**18**), and cyclo(*R*-Pro–*R*-Phe) (**19**) have been isolated from a marine-derived *Penicillium* sp.. These compounds exhibit significant activity against *V. anguillarum*, producing inhibition zones of 20, 24, and 25 mm, respectively. They also show moderate activity against *S. aureus*, with inhibition zones around 10 mm (Youssef and Alahdal 2018). Oxaline (**20**) and fumitremorgin B (**21**) have been isolated from the marine fungus *Aspergillus* sp. SCS-KFD66. Compound **20** shows inhibitory activity against *B. subtilis* ATCC 6633, with an MIC of 128 μg/mL, whereas **21** inhibits *S. aureus* ATCC 6538, having an MIC of 128 μg/mL (An et al. 2018). 16α-Methylaspochalasin J (**22**) and 16-hydroxymethylaspergillin PZ (**23**) have been isolated from the marine-derived fungus *W. dispera*. Both compounds show moderate antibacterial activity against *B. subtilis*, *Micrococcus luteus*, *S. enterica*, *Proteus vulgaris*, *E. coli*, and *Enterobacter*, with MICs in the range of 50–100 μg/mL (Xu et al. 2019). Asperteramide (**24**) has been isolated from marine-derived *A. terreus* BCC51799 and exhibits antibacterial activity against *B. cereus* and *Colletrichum acutatum*, with MICs of 25 and 50 mg/mL, respectively (Bunbamrung et al. 2020). Emethacin C (**25**) has been isolated from the marine-derived fungus *A. terreus* RA2905 and inhibits *Pseudomonas aeruginosa* (MIC 32 μg/mL; Wu et al. 2020a). Four alkaloids (**26**–**29**) have been isolated from the marine-derived fungus *A. fumigatus* MF071 and display weak antibacterial activity (Han et al. 2020). Cyclopiamide (**30**), speradines H (**31**), G (**32**), B (**33**), and C (**34**), and cyclopiazonic acid (**35**) have been isolated from the fungus *A. flavus* SCSIO F025 derived from deep-sea sediments of the South China Sea. These compounds exhibit weak antibacterial activity against *E. coli*, whereas compound **35** also inhibits *B. thuringiensis*, *M. lutea*, *S. aureus*, *B. subtilis*, and MRSA (Xiang et al. 2021). Paxilline (**36**), 7-hydroxyl-13-dehydroxypaxilline (**37**), 7-hydroxypaxilline-13-ene (**38**), 4a-demethylpaspaline-4a-carboxylic acid (**39**), PC-M6 (**40**), and emindole SB (**41**), with antibacterial activity against *S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633, have been isolated from the marine-derived fungus *Penicillium* sp. KFD28 (Dai et al. 2021). Two dimeric alkaloids—fusaripyridines A (**42**) and B (**43**)—have been isolated from marine-derived *Fusarium* sp. LY019. They selectively inhibit the growth of *C. albicans*, with MICs as low as 8.0 μM, and are moderately active against *S. aureus* and *E. coli* (MIC ≥ 32.0 μM; Shaala et al. 2021). Four diketopiperazine alkaloids (**44**–**47**) with moderate in vitro antibacterial activity against standard strains and drug-resistant clinical isolates of *Helicobacter pylori* have been isolated from the marine-derived fungus *Penicillium* sp. TW58-16 (Tian et al. 2022). Novobenzomalvin A (**48**) and hydroxy-4-(3-hydroxyphenyl)-2(1*H*)-quinolinone (**49**) have been isolated from the marine-derived fungus *Metarhizium* sp. P2100. Compound **48** shows antibacterial activity against *V. vulnificus* MCCC E1758 (MIC 6.25 μg/mL), whereas compound **49** inhibits the three aquatic pathogenic bacteria *V. vulnificus* MCCC E1758, *V. rotiferianus* MCCC E385, and *V. campbellii* MCCC E333, exhibiting MICs of 12.5, 12.5 and 6.25 μg/mL, respectively (Yao et al. 2022b). Pyrrospirones K (**50**), L (**51**), O (**52**), C (**53**), D (**54**), and F (**55**), along with FD7177CD6 (**56**) and GKK1032B (**57**), have been isolated from the marine-derived fungal strain *Penicillium* sp. SCSIO 41512. Compounds **52**, **54**, and **55** exhibit significant antibacterial activity against six

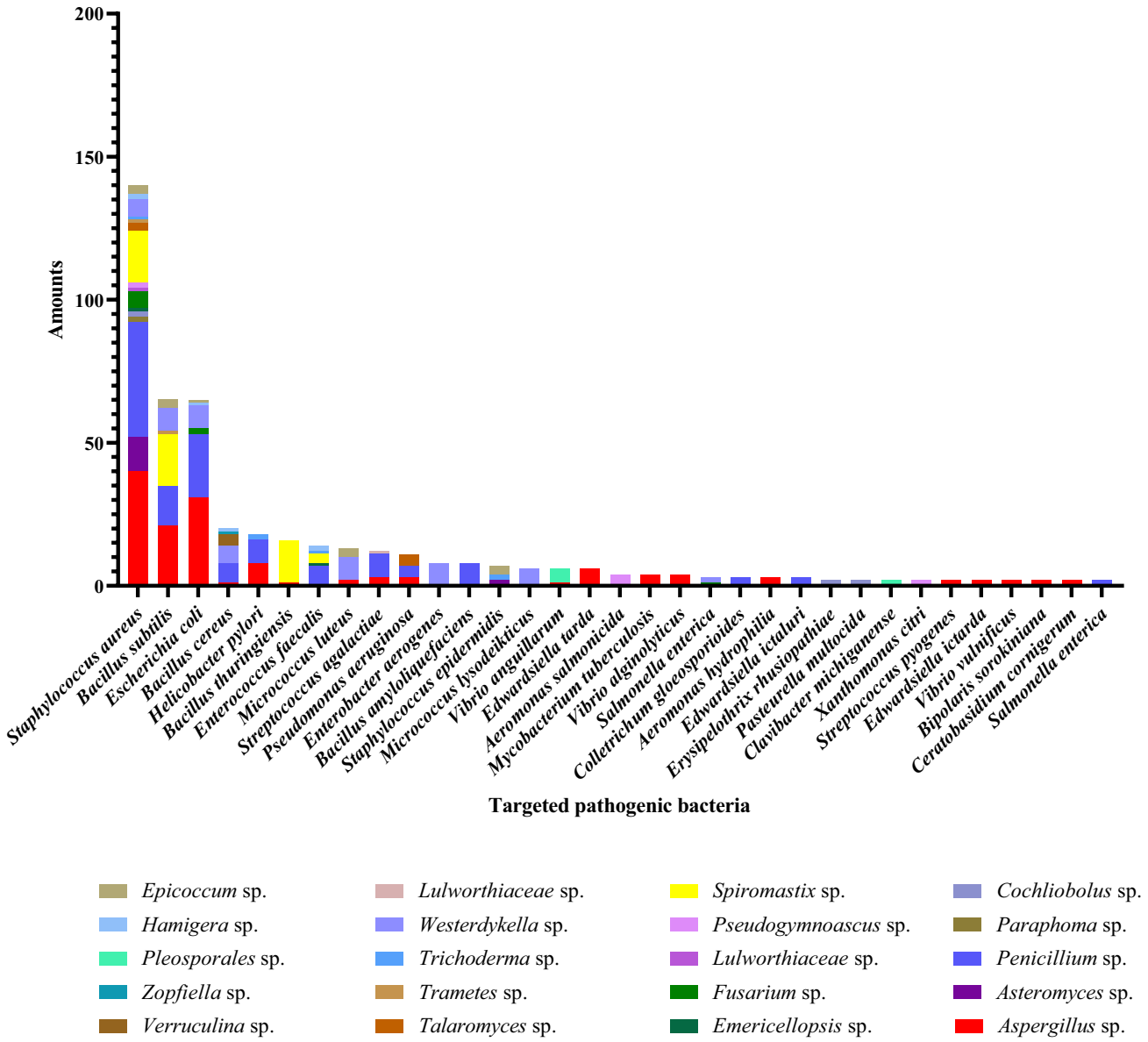


Fig. 3 Antibacterial compounds by producing fungi/targeted pathogenic bacteria

pathogens (*B. amyloliquefaciens*, *B. subtilis*, *E. coli*, *S. aureus*, MRSA, and *Streptococcus agalactiae*), with MICs in the range of 5.0–20 μg/mL, whereas the other five compounds displayed medium activity (MICs 20 − 50 μg/mL; Yao et al. 2022a). An antibiotic compound (3,1′-didehydro-3[2″(3″,3‴-dimethyl-prop-2-enyl)-3″-indolylmethylene]-6-methyl pipera-zine-2,5-dione) (**58**) containing an indole and a diketopiperazine moiety has been isolated from the marine-derived fungus *P. chrysogenum* MTCC 5108. Its antibacterial activity is comparable to the standard antibiotic streptomycin and it is selectively active against the human pathogen *V. cholerae* MCM B-322, producing an inhibition zone of 14–16 mm (Devi et al. 2012). One 2,5-diketopiperazine derivative (**59**) has been isolated from the marine fungus *Penicillium* sp. ZJUT-34 and exhibits antibacterial activity against *Enterococcus faecalis* FA2-2 (MIC = 96 μg/mL) comparable with that of the positive control gentamicin (MIC = 80 μg/mL) (Wang et al. 2023). One emestrin-type thiodiketopiperazine, 2″-desmethyl-MPC1001F (**60**), along with three analogs emestrin (**61**), dethiosecoemestrin (**62**), and emestrin H (**63**), have been isolated and identified from a culture extract of the marine fungus *A. nidulans* SD-531. Compounds **60**–**63** show antimicrobial activity against some of the tested strains (Lv et al. 2023). Gliovictin (**64**) has been isolated from the obligate marine fungus *Asteromyces cruciatus* KMM 4696, and it is less effective with an IC_{50} of 58.2 μM (Zhuravleva et al. 2023).

Table 1 Marine fungal-derived antibacterial compounds isolated from 2012 to 2022

Name	Species	Activities	MIC	References
Trichodin A (**1**) and pyridoxatin (**2**)	*Trichoderma* sp. strain MF106	*S. epidermidis*	IC_{50} of 24 µM and 4 µM	Wu et al. (2014)
Cyclopiazonic acid (**3**)	*P. vinaceum*	*E. coli*	Undetermined	Asiri et al. (2015)
Brevianamide F (**4**)	*P. vinaceum*	*S. aureus*	Undetermined	Asiri et al. (2015)
Diketopiperazines (**5**) and (**6**)	*A. fumigatus* MR2012	*S. aureus, B. subtilis* and *E. coli*	Weak to moderate	El-Gendy and Rateb (2015)
Diketopiperazines (**7–13**)	*A. fumigatus* MR2012	*S. aureus*	12.6–18.8 µg/mL	El-Gendy and Rateb (2015)
Diketopiperazines (**7–13**)	*A. fumigatus* MR2012	*B. subtilis*	8.7–18.2 µg/mL	El-Gendy and Rateb (2015)
Diketopiperazines (**7–13**)	*A. fumigatus* MR2012	*E. coli*	> 18.5 µg/mL	El-Gendy and Rateb (2015)
Pyrrospirones C (**14**), F (**15**) and I (**16**)	*Penicillium* sp. ZZ380	*S. aureus* and *E. coli*	2.0–5.0 mg/mL	Song et al. (2018)
Penicillatide B (**17**), cyclo(*R*-Pro–*S*-Phe) (**18**) and cyclo(*R*-Pro–*R*-Phe) (**19**)	*Penicillium* sp.	*S. aureus*	Inhibition zones between 10 and 19 mm	Youssef and Alahdal (2018)
Penicillatide B (**17**), cyclo(*R*-Pro–*S*-Phe) (**18**) and cyclo(*R*-Pro–*R*-Phe) (**19**)	*Penicillium* sp.	*V. anguillarum*	Inhibition zones of 20, 24, and 25 mm	Youssef and Alahdal (2018)
(*E*)-4-Oxonon-2- oxaline (**20**)	*Aspergillus* sp. SCS-KFD66	*B. subtilis* ATCC 6633	128 µg/mL	An et al. (2018)
Fumitremorgin B (**21**)	*Aspergillus* sp. SCS-KFD66	*S. aureus* ATCC 6538	128 µg/mL	An et al. (2018)
16α-Methylaspochalasin J (**22**) and 16-hydroxymethylaspergillin PZ (**23**)	*W. dispera*	*B. subtilis*, *M. luteus*, *S. enterica*, *Proteus vulgaris*, *E. coli*, and *E. aerogenes*	50 to 100 µg/mL	Xu et al. (2019)
Asperteramide (**24**)	*A. terreus* BCC51799	*B. cereus* and *C. acutatum*	25 and 50 mg/mL	Bunbamrung et al. 2020)
Emethacin C (**25**)	*A. terreus* RA2905	*P. aeruginosa*	32 µg/mL	Wu et al. (2020a)
13-Oxofumitremorgin B (**26**), fumitremorgin B (**27**)	*A. fumigatus* MF071	*S. aureu* and *E. coli*	100 µg/mL	Han et al. (2020)
fumiquinazoline J (**28**) and 9-deacetylfumigaclavine C (**29**)	*A. fumigatus* MF071	*S. aureu* and *E. coli*	100 µg/mL	Han et al. (2020)
Cyclopiamide (**30**), speradine H (**31**), speradine G (**32**), speradine B (**33**) and speradine C (**34**)	*A. flavus* SCSIO F025	*E. coli*	Undetermined	Xiang et al. (2021)
Cyclopiazonic acid (**35**)	*A. flavus* SCSIO F025	*B. thuringiensis*, *M. lutea*, *S. aureus*, *B. subtilis*, MRSA, and *E. coli*	Undetermined	Xiang et al. (2021)
Paxilline (**36**)	*Penicillium* sp. KFD28	*S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633	128 and 32 µg/mL	Dai et al. (2021)
7-Hydroxyl-13-dehydroxypaxilline (**37**)	*Penicillium* sp. KFD28	*S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633	64 and 16 µg/mL	Dai et al. (2021)
7-Hydroxypaxilline-13-ene (**38**)	*Penicillium* sp. KFD28	*S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633	64 and 64 µg/mL	Dai et al. (2021)
4a-Demethylpaspaline-4a-carboxylic acid (**39**)	*Penicillium* sp. KFD28	*S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633	64 and 128 µg/mL	Dai et al. (2021)
PC-M6 (**40**)	*Penicillium* sp. KFD28	*S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633	64 and 128 µg/mL	Dai et al. (2021)
Emindole SB (**41**)	*Penicillium* sp. KFD28	*S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633	32 and 128 µg/mL	Dai et al. (2021)
Fusaripyridines A (**42**) and B (**43**)	*Fusarium* sp. LY019	*S. Aureus* and *E. coli*	≥ 32.0 µM	Shaala et al. (2021)

Table 1 (continued)

Name	Species	Activities	MIC	References
Four diketopiperazine alkaloids (**44–47**)	*Penicillium* sp. TW58-16	*H. pylori*	Undetermined	Tian et al. (2022)
Novobenzomalvin A (**48**)	*Metarhizium* sp. P2100	*V. vulnificus* MCCC E1758	6.25 μg/mL	Yao et al. (2022b)
Hydroxy-4-(3-hydroxyphenyl)-2(1*H*)-quinolinone (**49**)	*Metarhizium* sp. P2100	*V. vulnificus* MCCC E1758, *V. rotiferianus* MCCC E385 and *V. campbellii* MCCC E333	12.5, 12.5 and 6.25 μg/mL	Yao et al. (2022b)
Pyrrospirone K (**50**), pyrrospirone L (**51**), pyrrospirone O (**52**), pyrrospirone D (**53**) and GKK1032B (**54**)	*Penicillium* sp. SCSIO 41512	*B. amyloliquefaciens*, *B. subtilis*, *E. coli*, *S. aureus*, MRSA, and *S. agalactiae*	20 to 50 μg/mL	Yao et al. (2022a)
Pyrrospirone C (**55**), pyrrospirone F (**56**) and FD7177CD6 (**57**)	*Penicillium* sp. SCSIO 41512	*B. amyloliquefaciens*, *B. subtilis*, *E. coli*, *S. aureus*, MRSA, and *S. agalactiae*	5.0 to 20 μg/mL	Yao et al. (2022a)
3,1′-Didehydro-3[2″(3‴,3‴-dimethyl-prop-2-enyl)-3″-indolylmethylene]-6-methyl pipera-zine-2,5-dione (**58**)	*P. chrysogenum* MTCC 5108	*V. cholerae* MCM B-322	Inhibition zone of 14–16 mm	Devi et al. (2012)
(−)-Isoroquefortine C (**59**)	*Penicillium sp.* ZJUT-34	*E. faecalis* FA2-2	96 μg/mL	Wang et al. (2023)
2″-Desmethyl-MPC1001F (**60**)	*A. nidulans* SD-531	*A. hydrophilia, E. tarda, P. aeruginosa,* and *V. alginolyticus*	0.5–32 μg/mL	Lv et al. (2023)
Emestrin (**61**)	*A. nidulans* SD-531	*A. hydrophilia, E. tarda, E. ictarda, E. coli, M. luteus, P. aeruginosa, V. alginolyticus, V. harveyi, V. parahaemolyticus, V. vulnificus, Bipolaris sorokiniana* and *Cerato-basidium*	0.5–16 μg/mL	Lv et al. (2023)
Dethiosecoemestrin (**62**)	*A. nidulans* SD-531	*A. hydrophilia, E. tarda, E. ictarda, E. coli, P. aeruginosa* and *V. algi-nolyticus*	4–16 μg/mL	Lv et al. (2023)
Emestrin H (**63**)	*A. nidulans* SD-531	*A. hydrophilia, E. tarda, E. ictarda, E. coli, P. aeruginosa, V. algino-lyticus, V. harveyi* and *V. parahaemolyticus*	4–16 μg/mL	Lv et al. (2023)
Gliovictin (**64**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} of 58.2 μM	Zhuravleva et al. (2023)
Pleosporallin E (**65**)	*Pleosporales* sp.	*C. michiganense* subsp. *Sepedonicus*	7.44 μg/mL	Chen et al. (2015)
Questin (**66**)	*A. fumigatus* MF071	*S. aureu* and *E. coli*	100 μg/mL	Han et al. (2020)
Aspergiloxathene A (**67**)	*Aspergillus* sp. IMCASMF180035	*E. coli*, *E. faecium, P. aeruginosa* and *H. pylori*	Undetermined	Song et al. (2021)
Aspergiloxathene A (**67**)	*Aspergillus* sp. IMCASMF180035	*S. aureus* and MRSA	5.60 and 22.40 μM	Song et al. (2021)
6,8-Di-*O*-methylversicol-orin A (**68**), 6,8,1'-tri-*O*-methylaverantin (**69**) and 6,8-di-*O*-methylaver-antin (**70**)	*Aspergillus* sp. WHUF05236	*H. pylori*	20.00– 43.47 μM	Lv et al. (2022)
(+)-Scleroderolide (**71**)	*Penicillium* sp. ZZ901	MRSA and *E. coli*	7.0 and 9.0 mg/mL	Li et al. (2018))

Table 1 (continued)

Name	Species	Activities	MIC	References
(+)-Sclerodione (**72**)	*Penicillium* sp. ZZ901	MRSA and *E. coli*	23.0 and 35.0 mg/mL	Li et al. (2018))
Three peniciphenalenins (73–75), coniosclerodione (**76**) and (-)-sclerodinol (**77**)	*Pleosporales* sp. HDN1811400	MRSA	6.25–50 μM	Han et al. (2021)
Asperphenone A (**78**) and B (**79**)	*Aspergillus* sp. YHZ-1	*S. aureus, B. subtilis, S. pyogenes* and *M. luteus*	32–64 μM	Guo et al. (2018)
Depsidone-based analogues (**80–94**)	*Spiromastix* sp.	*S. aureus, B. thuringiensis* and *B. subtilis*	0.125–8.0 μg/mL	Niu et al. (2012)
Bisvertinolone (**95**)	*A. protuberus* MUT 3638	*S. aureus*	30 μg/mL	Corral et al. (2018)
1,6-Dihydroxy-3-methoxy-8-methyl-9H-xanthen-9-one (**96**)	*P. arabicum* ZH3-9	*S. aureus*	50 μg/mL	Yang et al. (2023a)
Norlichexanthone (**97**)	*P. arabicum* ZH3-9	*S. aureus*	12.5 μg/mL	Yang et al. (2023a)
Acruciquinone C (**98**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} near 100 μM	Zhuravleva et al. (2023)
Rubrumol (**99**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} of 35.4 μm	Zhuravleva et al. (2023)
ω-Hydroxypachybasin (**100**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} of 45.3 μM	Zhuravleva et al. (2023)
Aspergillusidone C (**101**)	*P. oxalicum* M893	*E. faecalis, S. aureus, B. cereus* and *S. enterica*	2, 2, 2, and 2 μg/mL	Nguyen et al. (2023)
Nidulin (**102**)	*P. oxalicum* M893	*E. faecalis, S. aureus, B. cereus, E. coli* and *P. aeruginosa*	2–16 μg/mL	Nguyen et al. (2023)
Emeguisin B (**103**)	*P. oxalicum* M893	*E. faecalis, S. aureus* and *B. cereus*	16–32 μg/mL	Nguyen et al. (2023)
Penicitrinol J (**104**) and penicitrinol K (**105**)	*Penicillium* sp. ML226	*S. aureus*	Inhibition zones of 10 and 9 mm	Wang et al. (2013)
(12*R*,13*R*)-Dihydroxylanomycinol (**106**), (12*S*,13*S*)-dihydroxylanomycinol (**107**), (12*R*,13*S*)-dihydroxylanomycinol (**108**), (12*S*,13*R*)-dihydroxylanomycinol (**109**), (12*S*,13*R*)-*N*-acetyl-dihydroxylanomycin (**110**) and (12*S*,13*S*)-*N*-acetyl-dihydroxylanomycin (**111**)	*W. dispersa*	*M. lysodeikticus, B. subtilis, B. cereus, M. luteus, S. aureus, B. megaterium, B. anthraci, B. paratyphosum B, P. vulgaris, S. typhi, P. aeruginosa, E. coli, E. aerogenes*	100 μg/mL	Xu et al. (2017)
Pleosporalone G (**112**)	*Pleosporales* sp. CF09-1	*V. anguillarum* and *V. parahemolyticus*	13 and 6.3 μg/mL	Cao et al. (2019)
Pleosporalone H (**113**)	*Pleosporales* sp. CF09-1	*V. anguillarum* and *V. parahemolyticus*	6.3 and 25 μg/mL	Cao et al. (2019)
Karimunone B (**114**)	*Fusarium* sp. KJMT.FP.4.3	*Salmonella enterica ser.* Typhi	125 μg/mL	Sibero et al. (2019)
Enalin A (**115**)	*V. enalia* BCC 22226	*E. faecium* and *B. cereus*	50 and 25 μg/mL	Bunyapaiboonsri et al. (2020)
Pseudophenone A (**116**)	*Pseudogymnoascus* sp. HSX2#-11	*X. citri pv. malvacearum, S. aureus, P. fulva, A. salmonicida* and *X. citri*	35.64 ± 3.78–47.44 ± 7.21 μM	Shi et al. (b)
Polyketide **117**	*Trichoderma* sp. JWM29-10-1	*H. pylori, S. aureus,* MRSA, vancomycin-resistant *E. faecium* and *E. faecalis*	2–16 μg/mL	Lai et al. (2022)

Table 1 (continued)

Name	Species	Activities	MIC	References
Polyketide **118**	*Trichoderma* sp. JWM29-10-1	*H. pylori* G27, *H. pylori* 159, *H. pylori* JIGC360 and *H. pylori* 511	2–8 μg/mL	Lai et al. (2022)
Acrucipentyn A (**119**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} of 12.5 μM	Zhuravleva et al. (2022)
Acrucipentyn C (**120**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} of 100 μM	Zhuravleva et al. (2022)
Acrucipentyn B (**121**), Acrucipentyn D (**122**) and Acrucipentyn E (**123**)	*A. cruciatus* KMM 4696	*S. aureus*	$IC_{50} > 100$ μM	Zhuravleva et al. (2022)
Acrucipentyn F (**124**)	*A. cruciatus* KMM 4696	*S. aureus*	100 μM	Zhuravleva et al. (2022)
5-Sulfonic acid (**125**)	*H. avellanea*	*E. faecalis, S. aureus, B. cereus* and *E. coli*	64–128 μg/mL	Minh et al. (2023)
Monomethylsulochrin (**126**)	*H. avellanea*	*E. faecalis* and *S. aeureus*	16 and 16 μg/mL	Minh et al. (2023)
Fusarisolin H (**127**)	*F. solani* 8388	MRSA NCTC 10442	6 μg/mL	Lin et al. (2023b)
Fusarisolin I (**128**)	*F. solani* 8388	MRSA n315	3 μg/mL	Lin et al. (2023a)
Fusarisolin J (**129**)	*F. solani* 8388	MRSA n315 and MRSA NCTC 10442	3 and 6 μg/mL	Lin et al. (2023a)
5-Deoxybostrycoidin (**130**)	*F. solani* 8388	MRSA n315	6 μg/mL	Lin et al. (2023a)
Bacillisporin A (**131**)	*T. pinophilus* KUFA 1767	*S. aureus* ATCC 29213 and MRSA	4 and 4 μg/mL	Machado et al. (2023)
Bacillisporin B (**132**)	*T. pinophilus* KUFA 1767	*S. aureus* ATCC 29213 and MRSA	8 and 16 μg/mL	Machado et al. (2023)
Isoquinocitrinin B (**133**)	*Penicillium* sp. TW131-64	*H. pylori, S. aureus, B. subtilis* and *E. faecium*	1–16 μg/mL	Lai et al. (2023)
Isoquinocitrinin C (**134**)	*Penicillium* sp. TW131-64	*H. pylori*	4 μg/mL	Lai et al. (2023)
Isoquinocitrinin D (**135**)	*Penicillium* sp. TW131-64	*H. pylori*	8 μg/mL	Lai et al. (2023)
Penicyrones A and B (**136**)	*P. cyclopium*	*E. ictaluri*	16 μg/mL	Li et al. (2023a)
9-*O*-Methylpenicyrones A and B (**137**)	*P. cyclopium*	*E. coli, P. aeruginosa,* and *E. ictaluri*	4–16 μg/mL	Li et al. (2023c)
9-*O*-Ethylpenicyrones A and B (**138**)	*P. cyclopium*	*E. coli, P. aeruginosa,* and *E. ictaluri*	8–16 μg/mL	Li et al. (2023c)
Aspergillusene E (**139**)	*A. versicolor* XS-20090066	*S. epidermidis* and *S. aureus*	8–16 μg/mL	Wu et al. (2020c)
(*Z*)-12-Acetoxybisabol-1-one (**140**)	*T. asperellum* EN-764	*M. luteus, P. aeruginosa, V. alginolyticus* and *V. harveyi*	16, 32, 4, and 64 μg/mL	Li et al. (2023a)
Bisabolen-1,12-diol (**141**)	*T. asperellum* EN-764	*E. coli, M. luteus, V. alginolyticus* and *V. harveyi*	16, 32, 16, and 16 μg/mL	Li et al. (2023a)
12-Acetoxybisabolen-1-ol (**142**)	*T. asperellum* EN-764	*E. coli, M. luteus, P. aeruginosa, V. alginolyticus, V. harveyi* and *V. parahemolyticus*	4–64 μg/mL	Li et al. (2023a)
12-Nor-11-acetoxybisabolan-1-ol (**143**)	*T. asperellum* EN-764	*E. coli, M. luteus, P. aeruginosa, V. alginolyticus, M. luteus, P. aeruginosa, V. alginolyticus, V. harveyi* and *V. parahemolyticus*	8–64 μg/mL	Li et al. (2023a)
(7*S*,11*S*)-(+)-12-Hydroxysydonic acid (**144**)	*A. sydowii* LW09	*P. syringae*	32 μg/mL	Yang et al. (2023a)
Oxaliterpenoid (**145**)	*P. oxalicum* M893	*S. aureus, B. cereus* and *E. coli*	32, 32, and 32 μg/mL	Nguyen et al. (2023)
Dendryphiellin I (**146**)	*C. lunatus* SCSIO4	*S. aureus, E. rhusiopathiae* and *P. multocida*	1.5, 13, and 13 μg/mL	Fang et al. (2018)

Table 1 (continued)

Name	Species	Activities	MIC	References
Pleosporallin D (**147**)	*Pleosporales* sp.	*Clavibacter michiganense* subsp. *Sepedonicus*	9.48 μg/mL	Chen et al. (2015)
Purpuride E (**148**)	*P. minioluteum* ZZ1657	*S. aureus* and *E. coli*	6–12 μg/mL	Ma et al. (2020)
Purpuride F (**149**)	*P. minioluteum* ZZ1657	*S. aureus* and *E. coli*	3–6 μg/mL	Ma et al. (2020)
Asperbrunneo acid (**150**)	*A. brunneoviolaceus* MF180246	*S. aureus*	200 μg/mL	Xu et al. (2022)
16-*O*-Propionyl-16-*O*-deacetylhelvolic acid (**151**)	*A. fumigatus* HNMF0047	*S. agalactiae*	16 μg/mL	Kong et al. (2018)
6-*O*-Propionyl-6-*O*-deacetylhelvolic acid (**152**)	*A. fumigatus* HNMF0047	*S. agalactiae*	2 μg/mL	Kong et al. (2018)
Helvolic acid (**153**)	*A. fumigatus* HNMF0047	*S. agalactiae*	8 μg/mL	Kong et al. (2018)
Helvolinic acid (**154**)	*A. fumigatus* MF071	*S. aureu* and *E. coli*	6.25 and 6.25 μg/mL	Han et al. (2020)
Helvolic acid (**155**)	*A. fumigatus* MF071	*S. aureu* and *E. coli*	3.31and 3.13 μg/mL	Han et al. (2020)
Hemiacetalmeroterpenoid A (**156**), citreohybridone A (**157**) and andrastin B (**158**)	*Penicillium* sp. N-5	*Colletrichum gloeosporioides*	1.56–6.25 μg/mL	Chen et al. (2022)
Taladrimanin A (**159**)	*Talaromyces* sp. HM6-1-1	*S. aureus* 6538P	15.2 μg/mL	Hong et al. (2022)
Asperpyranones A (**160**)	*A. terreus* RA2905	*P. aeruginosa*	32 μg/mL	Li et al. (2023a)
Citreoisocoumarin (**161**)	*Penicillium vinaceum*	*S. aureus*	Undetermined	Asiri et al. 2015)
(+)-Neocitreoviridin (**162**)	*Penicillium* sp. IMB17-046	*H. pylori* G27, and *H. pylori* 159	4 and 1 μg/mL	Li et al. (2019)
Naphtho-γ-pyrones, penicinaphones A–C (**163–165**)	*Penicillium* sp. HK1-22	*S. aureus* (ATCC 43300, 33591, 29213, and 25923)	12.5–50 μg/mL	Zheng et al. (2019)
Nipyrone A (**166**)	*A. niger*	*S. aureus*, *E. coli*, *B. subtilis,* MRSA, and *M. tuberculosis*	32–128 μg/mL	Ding et al. (2019)
Nipyrone B (**167**)	*A. niger*	*S. aureus*, *E. coli*, *B. subtilis,* MRSA, and *M. tuberculosis*	64–128 μg/mL	Ding et al. (2019)
Nipyrone C (**168**)	*A. niger*	*S. aureus*, *E. coli*, *B. subtilis,* MRSA, and *M. tuberculosis*	8–128 μg/mL	Ding et al. (2019)
Germicidin C (**169**)	*A. niger*	*S. aureus*, *E. coli*, *B. subtilis,* MRSA, and *M. tuberculosis*	32–128 μg/mL	Ding et al. (2019)
Enalin A (**170**)	*V. enalia* BCC 22226	*E. faecium* and *B. cereus*	50 and 25 μg/mL	Bunyapaiboonsri et al. (2020)
Aspergillactone (**171**)	*Aspergillus* sp. CSYZ-1	*H. pylori* and *S. aureus*	1–4 and 2–16 μg/mL	Cen et al. (2020)
7-Hydroxyoospolactone (**172**) and parapholactone (**173**)	*Paraphoma* sp. CUG-BMF180003	*S. aureus*	12.5 μg/mL	Xu et al. (2021)
Lulworthinone (**174**)	*Lulworthiaceae*	*S. aureus* and *S. agalactiae*	1.56–6.25 μg/mL	Jenssen et al. (2021)
Aspergimarin G (**175**)	*Aspergillus* sp. NBUF87	*S. aureus* and *S. enteritidis*	16–64 μg/mL	Lin et al. (2023b)
Purpureone (**176**)	*C. lunatus* SCSIO4	*E. rhusiopathiae, S. aureus* and *P. multocida*	25, 50, and 13 μg/mL	Fang et al. (2018)
Secalonic acid F1 (**177**)	*A. brunneoviolaceus* MF180246	*S. aureus*	25 mg/ml	Xu et al. (2022)
Secalonic acid H (**178**)	*A. brunneoviolaceus* MF180246	*S. aureus*	50 mg/ml	Xu et al. (2022)
Penicillixanthone A (**179**)	*A. brunneoviolaceus* MF180246	*S. aureus*	6.25 mg/ml	Xu et al. (2022)
Chrysoxanthone C (**180**)	*A. brunneoviolaceus* MF180246	*S. aureus*	50 mg/ml	Xu et al. (2022)

Table 1 (continued)

Name	Species	Activities	MIC	References
Asperdichrome (**181**)	*A. brunneoviolaceus* MF180246	*S. aureus*	25 mg/ml	Xu et al. (2022)
Homodimeric tetrahydroxanthone secalonic acid D (**182**)	*A. aculeatinus* WHUF0198	*H. pylori* G27, *H. pylori* 26,695, *H. pylori* 129, *H. pylori* 159, *S. aureus* USA300, and *B. subtilis* 168	1.0–2.0 μg/mL	Wu et al. (2023)
Ergosta-5,7,22-triene-3β-ol (**183**)	*Aspergillus* sp. SCS-KFD66	*B. subtilis* ATCC 6633	128 μg/mL	An et al. (2018)
Volemolide (**184**)	*Aspergillus* sp. SCS-KFD66	*B. subtilis* ATCC 6633	128 μg/mL	An et al. (2018)
Aspergillsteroid A (**185**)	*Aspergillus* sp. LS116	*V. harveyi*	16 μg/mL	Xu et al. (2020)
Ganodermaside B (**186**)	*Pseudogymnoascus* sp. HSX2#-11	*A. salmonicida*	30 μM	Shi et al. (2021a)
Ganodermaside D (**187**)	*Pseudogymnoascus* sp. HSX2#-11	*A. salmonicida*	36 μM	Shi et al. (2021a)
4α-Hydroxy-17-methylincisterol (**188**)	*Trametes* sp. ZYX-Z-16	*S. aureus* ATCC 6538 and *B. subtilis* ATCC 6633	32 and 16 μg/mL	Ren et al. (2022)
3β-Hydroxy-5α,6β-methoxyergosta-7,22-dien-15-one (**189**)	*Aspergillus* sp.	*S. aureus*	64 μg/mL	Wen et al. (2023)
(*E*)-4-oxonon-2-enoic acid (**190**)	*Aspergillus* sp. SCS-KFD66	*B. subtilis* ATCC 6633 and *S. aureus* ATCC 6538	4 and 16 μg/mL	An et al. (2018)
Kipukasin K (**191**)	*A. versicolor* XS-20090066	*S. epidermidis* and *S. aureus*	8–16 μg/mL	Wu et al. (2020c)
Benzoic acid derivative (**192**)	*Pseudogymnoascus* sp. HSX2#-11	*X. citri pv. malvacearum, S. aureus, P. fulva* and *A. salmonicida*	29.86 ± 2.68–56.93 ± 6.69 μM	Shi et al. (2021a)
Verruculin (**193**)	*V. enalia* BCC 22226	*E. faecium* and *B. cereus*	50 and 25 μg/mL	Bunyapaiboonsri et al. (2020)
Emerimicin IV (**194**)	*E. minima*	*S. aureus* and vancomycin-resistant *E. faecalis*	100 and 12.5 μg/mL	Inostroza et al. (2018)
Salicylaldehyde derivative (**195**)	*Z. marina* BCC 18240 (or NBRC 30420)	*B. cereus*	12.5 μg/mL	Chokpaiboon et al. (2018)
Trypilepyrazinol (**196**)	*Penicillium* sp. IMB17-046	*H. pylori* G27 and *H. pylori* 159	4 and 16 μg/mL	Li et al. (2019)
Verruculinone (**197**)	*V. enalia* BCC 22226	*E. faecium* and *B. cereus*	50 and 25 μg/mL	Bunyapaiboonsri et al. (2020)
$\Delta^{2'}$-1'-Dehydropenicillide (**198**), and 1'-dehydropenicillide (**199**)	*Aspergillus* sp. IMCASMF180035	*S. aureus,* methicillin-resistant *S. aureus* (MRSA), *E. coli*, *E. faecium,* and *P. aeruginosa*	Undetermined	Song et al. (2021)
$\Delta^{2'}$-1'-Dehydropenicillide (**198**) and 1'-dehydropenicillide (**199**)	*Aspergillus* sp. IMCASMF180035	*H. pylori*	21.73 and 21.61 μM	Song et al. (2021)
Three diphenyl ethers (**200–202**)	*Spiromastix* sp. SCSIO F190	*S. aureus*, *E. faecalis* ATCC 29212, and *B. subtilis* BS01	0.25–32 μg/mL	Cai et al. (2022)
Peniprenylphenol A (**203**)	*P. chrysogenum* ZZ1151	MRSA, *E. coli*	6 and 13 μg/mL	Newaz et al. (2022)
Alternariol (**204**)	*P. arabicum* ZH3-9	*S. aureus*	50 μg/mL	Yang et al. (2023a,)
3-Ethylcyclopen-t-3-ene-1,2-diol (**205**)	*Trichoderma asperellum* EN-767	*P. aeruginosa* and *V. alginolyticus*	32, and 8 μg/mL	Li et al. (2023a)
3-(3-Hydroxypropyl) cyclopent-2-en-1-one (**206**)	*Trichoderma asperellum* EN-767	*E. coli* and *V. alginolyticus*	64, and 16 μg/mL	Li et al. (2023a)
Asperbutenolide A (**207**)	*A. terreus*	MRSA	4.0–8.0 μg/mL	Jiang et al. (2023)

Table 1 (continued)

Name	Species	Activities	MIC	References
Aspergetherin A (**208**)	*A. terreus* 164018	MRSA	128 µg/mL	Li et al. (2023b)
Aspergetherin C (**209**)	*A. terreus* 164018	MRSA	64 µg/mL	Li et al. (2023b)
Methyl 3,5-dichloroasterric acid (**210**)	*A. terreus* 164028	MRSA	1–16 µg/mL	Li et al. (2023b)
Methyl chloroasterrate (**211**)	*A. terreus* 164028	MRSA	64 µg/Ml	Li et al. (2023b)
Aspertide D (**212**)	*Aspergillus* sp.	*E. tarda, V. alginolyticus, V. anguillarum,* and *V. vulnificus*	8–32 µg/mL	Chi et al. (2023)
Aspertide E (**213**)	*Aspergillus* sp.	*E. tarda* and *S. aureus*	16 and 8 µg/mL	Chi et al. (2023)
Trans-3,4-dihydroxy-3,4-dihydroanofinic acid (**214**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} of 49.7 µM	Zhuravleva et al. (2023)
7-Hydroxymethyl-1,2-naphthalenediol (**215**)	*A. cruciatus* KMM 4696	*S. aureus*	IC_{50} of 52.1 µM	Zhuravleva et al. (2023)
Antaketide A (**216**)	*P. antarcticum* KMM 4670	*S. aureus*	IC_{50} near 100 µM	Yurchenko et al. (2023)
2-((2*R*,6*S*)-6-Methyltetrahydro-2*H*-pyran-2-yl) acetic acid (**217**)	*P. antarcticum* KMM 4670	*S. aureus* and *E. coli*	IC_{50} of 100 and 84.9 µM	Yurchenko et al. (2023)
Aspergillusether A (**218**)	*P. oxalicum* M893	*E. faecalis, S. aureus, B. cereus, E. coli* and *P. aeruginosa*	16–64 µg/mL	Nguyen et al. (2023)
Aspergillusether J (**219**)	*P. oxalicum* M893	*E. faecalis, S. aureus* and *B. cereus*	4–8 µg/mL	Nguyen et al. (2023)
Guisinol (**220**)	*P. oxalicum* M893	*E. faecalis, S. aureus, B. cereus,* and *S. enterica*	4, 4, 4, and 4 µg/mL	Nguyen et al. (2023)
3-Chloro-2,5-dihydroxybenzyl acetate (**221**)	*E. sorghinum*	MRSE, *S. epidermidis, S. aureus, M. luteus* and *B. subtilis*	7.81–31.25 µg/mL	Xing et al. (2023)
3-Chlorogentisyl alcohol (**222**)	*E. sorghinum*	MRSE, *S. epidermidis, S. aureus, Actinomyces viscosus, M. luteus, B. subtilis* and *E. coli*	7.81–31.25 µg/mL	Xing et al. (2023)
2-Chloro-6-(methoxymethyl) benzene-1,4-diol (**223**)	*E. sorghinum*	MRSE, *S. epidermidis, S. aureus, M. luteus* and *B. subtilis*	7.81–31.25 µg/mL	Xing et al. (2023)

Quinones

Fifteen compounds were reported in 2012, all of which are quinones exhibiting strong inhibitory effects against Gram-positive bacteria. Figures 9 and 10 illustrate the structures of quinones and ketones.

Pleosporallin E (**65**) has been isolated from a marine-derived fungus *Pleosporales* sp. and exhibits antibacterial activity with an MIC of 7.44 µg/mL against *Clavibacter michiganense* subsp. *Sepedonicus* (Chen et al. 2015). Compound **66** has been isolated from the marine-derived fungus *A. fumigatus* MF071 and displayed weak antibacterial activity (Han et al. 2020). Aspergiloxathene A (**67**) has been isolated from marine-derived *Aspergillus* sp. IMCASMF180035 and exhibits activity against *S. aureus*, MRSA, *E. coli*, *E. faecium*, *P. aeruginosa*, and *H. pylori* (Song et al. 2021). 6,8-Di-*O*-methylversicolorin A (**68**), 6,8,1'-tri-*O*-methylaverantin (**69**), and 6,8-di-*O*-methylaverantin (**70**) have been isolated from a fermentation extract of *Aspergillus* sp. WHUF05236 and display antibacterial activity against *H. pylori* with MICs ranging from 20.0 to 43.47 µM (Lv et al. 2022). (+)-Scleroderolide (**71**) and (+)-sclerodione (**72**) show antiproliferative activity against MRSA (MICs 7.0 and 23.0 mg/mL, respectively) and *E. coli* (MICs 9.0 and 35.0 mg/mL, respectively). They have been isolated from the marine-derived fungus *Penicillium* sp. ZZ901 (Li et al. 2018). Three peniciphenalenins (**73–75**) are phenalenone derivatives isolated from marine *Pleosporales* sp. HDN1811400, along with two related compounds, coniosclerodione (**76**) and (−)-sclerodinol (**77**). Compounds

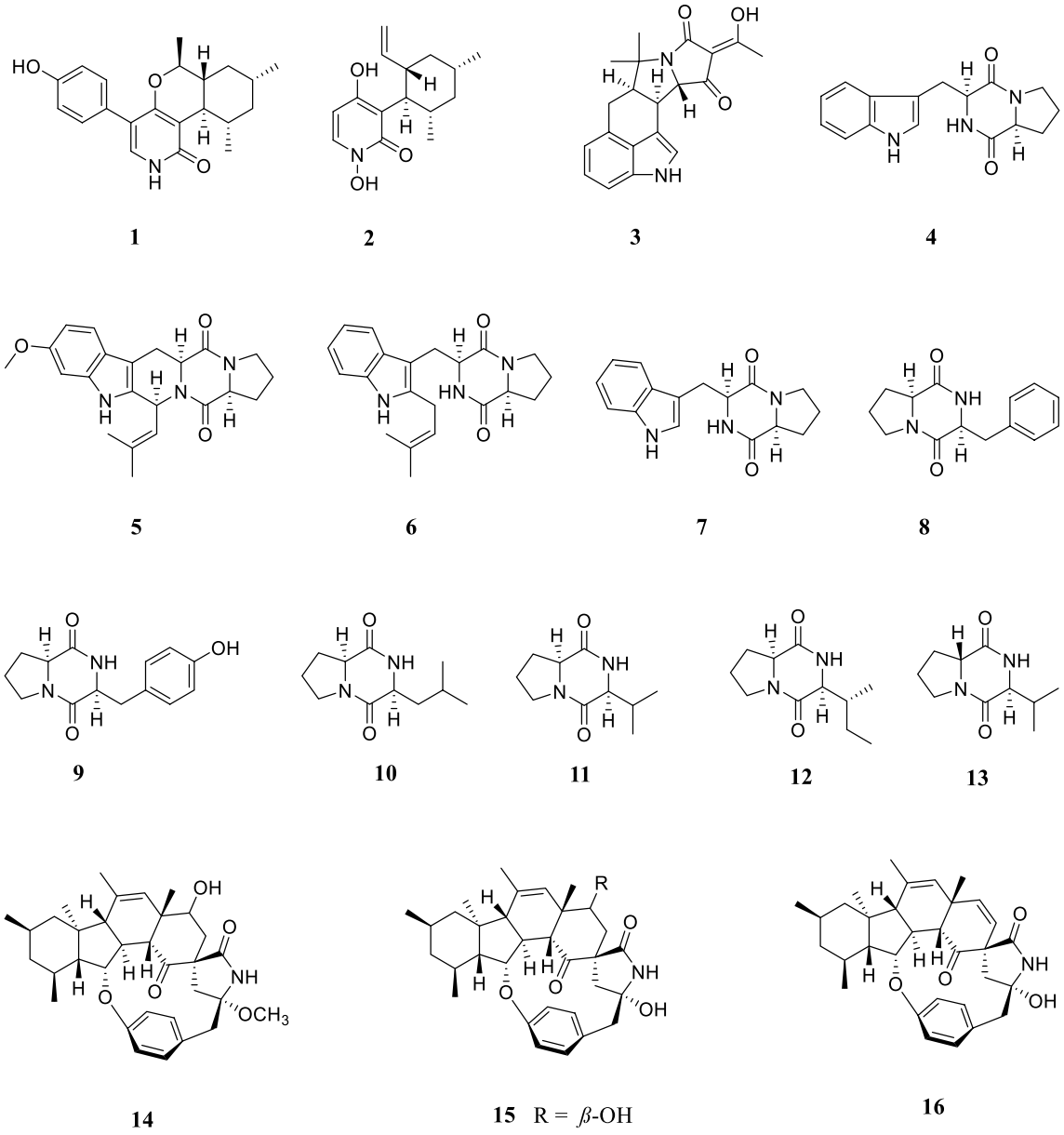


Fig. 4 Structures of compounds **1**–**16**

73, **74**, **76**, and **77** show broad antibacterial activity, the lowest MIC being 6.25 μM against MRSA (Han et al. 2021). Asperphenones A (**78**) and B (**79**) have been isolated from *Aspergillus* sp. YHZ-1, an endophytic fungus of mangrove plants on Hainan Island, China. They exhibit weak antibacterial activity against *S. aureus, B. subtilis, S. pyogenes*, and *M. luteus*, with MICs ranging from 32 to 64 μM (Guo et al. 2018). Fifteen depsidone-based analogs (**80**–**94**) have been isolated from a marine sediment-derived fungal *Spiromastix* sp. and all exhibit significant inhibition of Gram-positive bacteria, including *S. aureus*, *B. thuringiensis*, and *B. subtilis*, with MICs ranging from 0.125 to 8.0 μg/mL (Niu et al. 2014). Bisvertinolone (**95**), a member of the sorbicillonoid family, has been isolated from *A. protuberus* MUT 3638 and exhibits significant antibacterial activity against *S. aureus* (MIC 30 μg/mL; Corral et al. 2018). Compounds **96** and **97** have been isolated from a marine-derived fungus strain of *P. arabicum* ZH3-9. These compounds display antibiotic activity against *S. aureus* with MICs of 50 and 12.5 μg/mL (Yang et al. 2023a). One anthraquinone derivative acruciquinone C (**98**), together with rubrumol (**99**) and *ω*-hydroxypachybasin (**100**), have been isolated from the obligate marine fungus

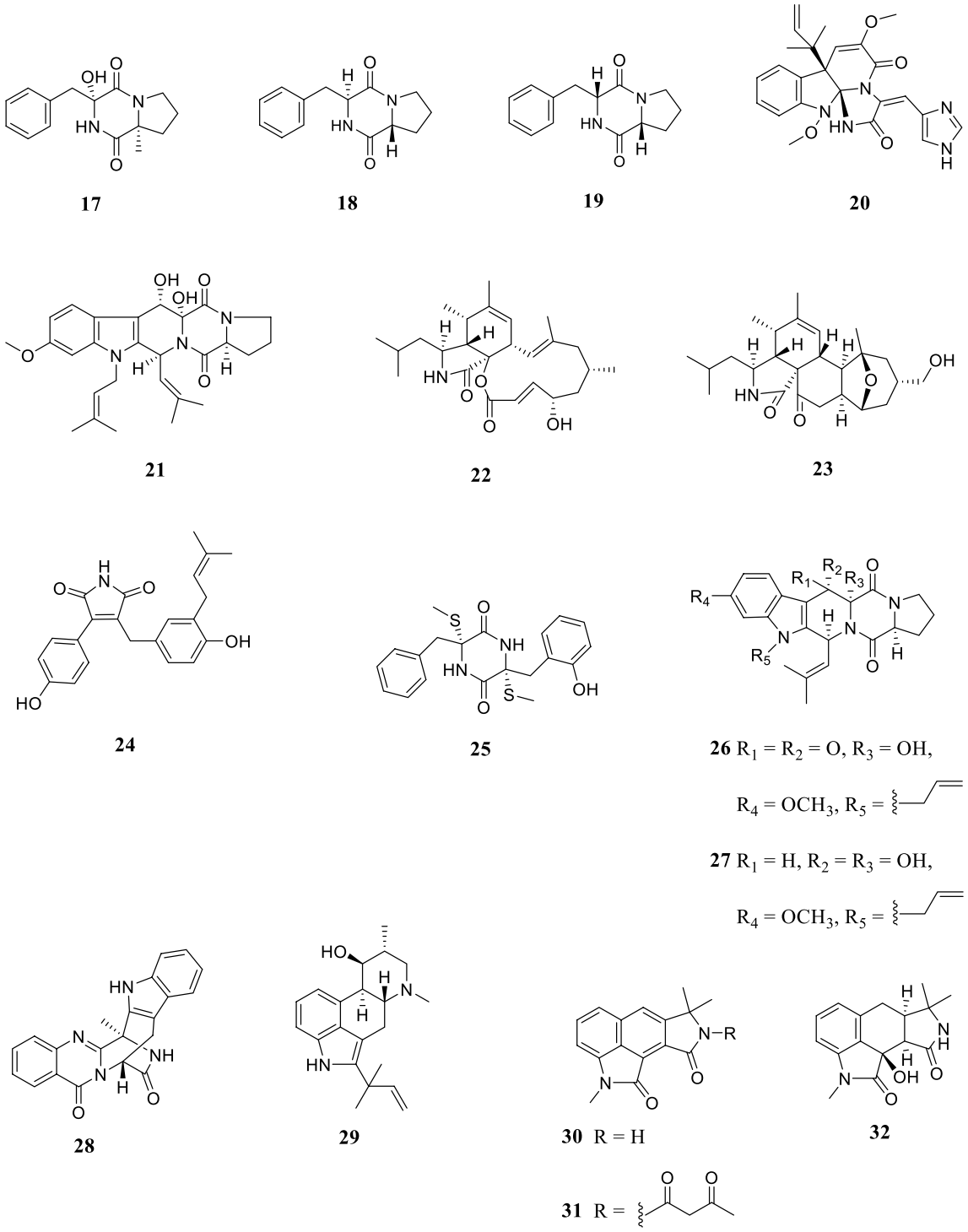


Fig. 5 Structures of compounds **17**–**32**

A. cruciatus KMM 4696. Compounds **99** and **100** show the best effect on *S. aureus* growth, with calculated IC_{50} of 35.4 and 45.3 µM, respectively. Acruciquinone C has an IC_{50} near 100 µM (Zhuravleva et al. 2023). Nidulin (**101**), emeguisin B (**102**), and aspergillusether A (**103**) have been isolated from the methanol extract of the culture broth of the marine fungus *P. oxalicum* M893. All compounds have potent antibacterial activities against Gram-positive bacteria, *E. faecalis* (ATCC299212), *S. aureus* (ATCC25923), and *B. cereus*

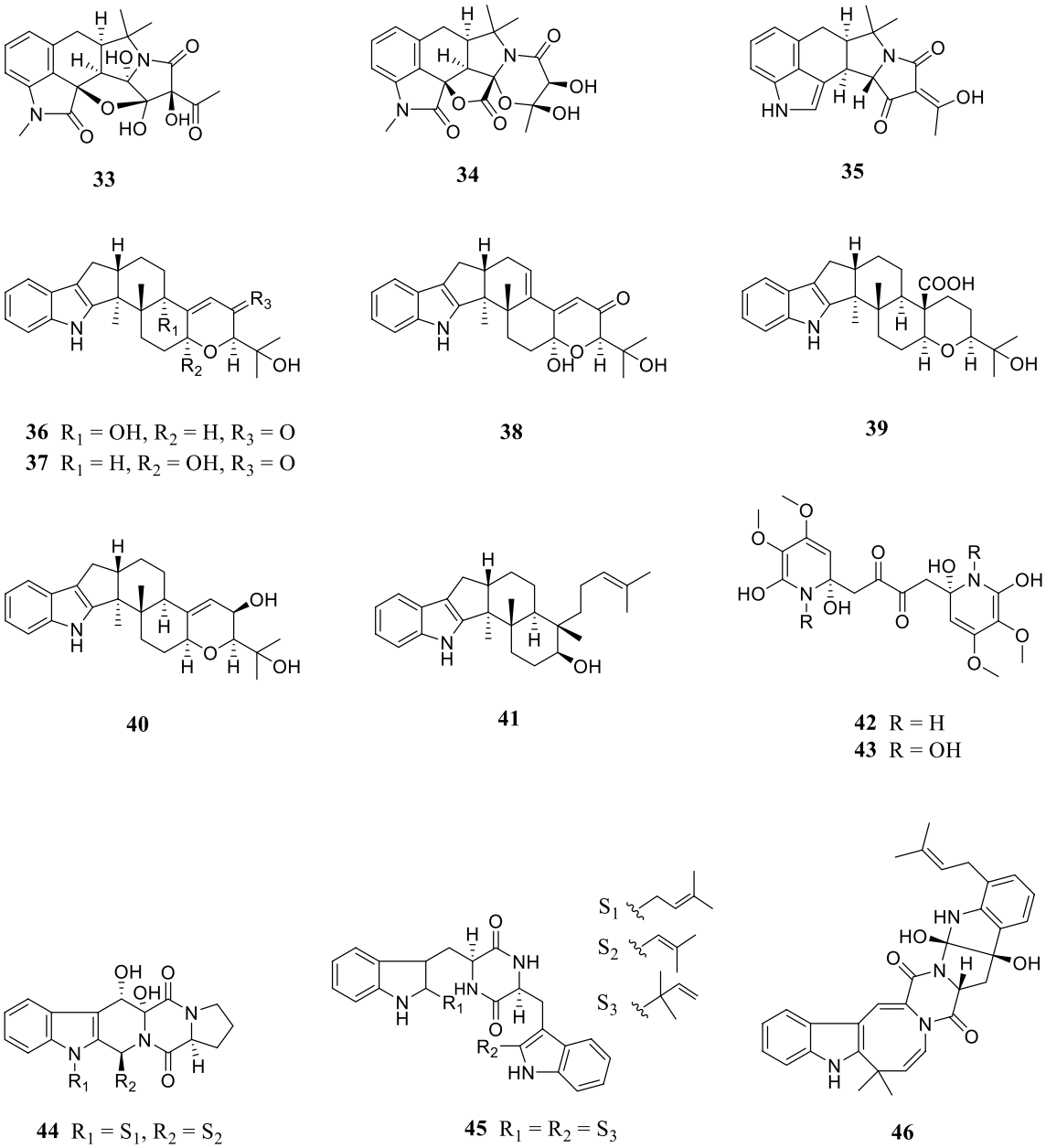


Fig. 6 Structures of compounds **33**–**46**

(ATCC14579), with MICs ranging from 2 μg/mL to 32 μg/mL (Nguyen et al. 2023).

Polyketides

Polyketides are derived from the polymerization of acetyl and propionyl groups, and their structure is illustrated in Figs. 11 and 12.

Two citrinin derivatives, penicitrinols J (**104**) and K (**105**), have been isolated from the marine-derived fungal strain *Penicillium* sp. ML226. They exhibit weak antibacterial activity against *S. aureus* (Wang et al. 2013). Six alkenylated tetrahydropyran derivatives, designated as (12*R*,13*R*)-dihydroxylanomycinol (**106**), (12*S*,13*S*)-dihydroxylanomycinol (**107**), (12*R*,13*S*)-dihydroxylanomycinol (**108**), (12*S*,13*R*)-dihydroxylanomycinol (**109**), (12*S*,13*R*)-*N*-acetyl-dihydroxylanomycin (**110**), and (12*S*,13*S*)-*N*-acetyl-dihydroxylanomycin (**111**) have been isolated from the marine sediment-derived fungus *Westerdykella dispersa* and found to have weak antibacterial activity (Xu et al. 2017). Pleosporalones G (**112**) and H (**113**) have been isolated from the marine-derived fungus *Pleosporales* sp. CF09-1 and display moderate anti-*Vibrio* activity against *V. anguillarum* and *V.*

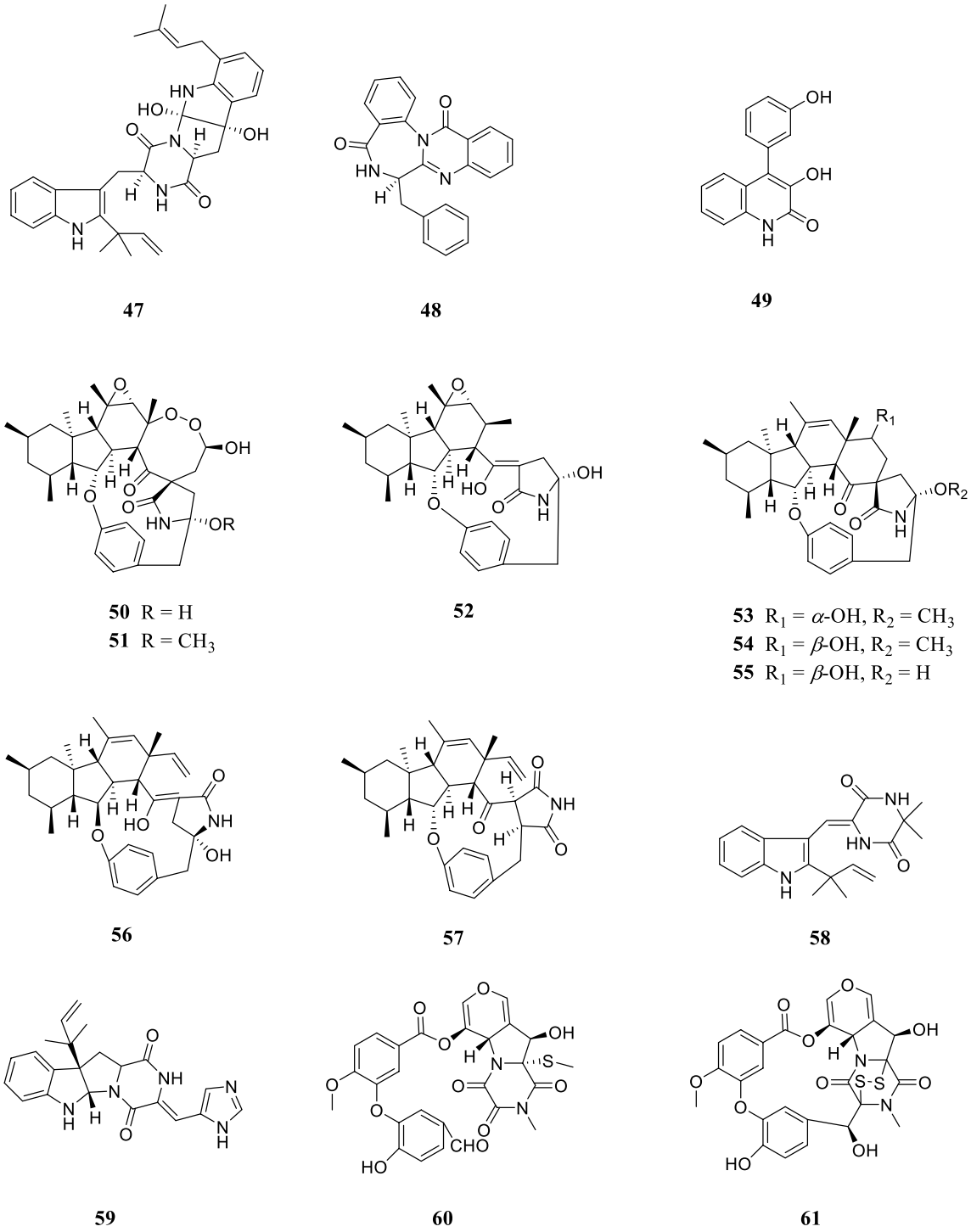
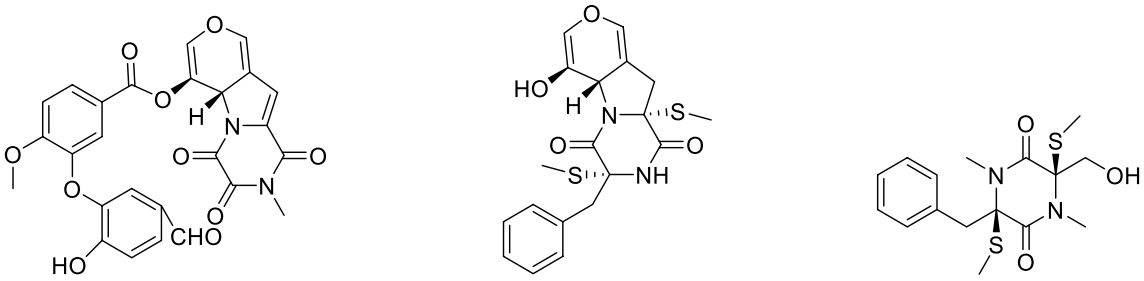


Fig. 7 Structures of compounds **47**–**61**

parahemolyticus, with MICs of 13 and 6.3 µg/mL (**112**), and 6.3 and 25 µg/mL (**113**), respectively (Cao et al. 2019). An aromatic polyketide named karimunone B (**114**) has been isolated from the marine-derived fungus *Fusarium* sp. KJMT.FP.4.3. It displays antibacterial activity against multidrug-resistant *S. enterica* ser. Typhi, having an MIC of 125 µg/mL (Sibero et al. 2019). Nine compounds have been isolated from the marine fungus *V. enalia* (Kohlm.) Kohlm. & Volkm-Kohlm. BCC 22226, one of which, (-)-cercosporamide (**115**), exhibits weak antituberculous and antibacterial activities, with MICs of 25–50 mg/mL (Bunyapaiboonsri et al. 2020).



62 63 64

Fig. 8 Structures of compounds **62**–**64**

A polyketide, pseudophenone A (**116**), has been isolated from marine-derived *Pseudogymnoascus* sp. HSX2#-11 and displays antibacterial activity against a panel of bacteria (Shi et al. 2021b). Two polyketides, **117** and **118**, have been obtained from the culture of the marine-derived fungus *Trichoderma* sp. JWM29-10-1. They display antibacterial activity against *H. pylori* standard strains and clinical isolates, including three multidrug-resistant strains, with MICs ranging from 2 to 8 μg/mL. Interestingly, compound **117** also exhibits significant inhibition of the growth of Gram-positive pathogens, including *S. aureus,* MRSA, vancomycin-resistant *E. faecium* (VRE), and *E. faecalis*, with MICs of 2 to 16 μg/mL (Lai et al. 2022). Six polyketides, acrucipentyns A–F (**118**–**124**), have been isolated from the algae-derived fungus *A. cruciatus* KMM 4696 and exhibit pronounced antibacterial effects against Gram-positive *S. aureus*. Compound **120** almost completely inhibits the growth of *S. aureus* at a concentration of 100 μM, whereas 100 μM compound **119** reduces growth by 60%. Dropping the concentration to 12.5 μM reduces antibacterial activity by up to 50%. Compound **121** at 100 μM inhibits *S. aureus* growth by 50%, but **120**, **122**, and **123** did not achieve 50% inhibition, even at 100 μM (Zhuravleva et al. 2022). 5-Sulfonic acid (**125**) and monomethylsulochrin (**126**), have been isolated from the marine sponge-associated fungus *Hamigera avellanea.* Compound **125** selectively inhibits *E. faecalis, S. aureus, B. cereus*, and *E. coli* with MICs ranging within 32–256 μg/mL, compound **126** displays moderate antibacterial activity against *E. faecalis* and *S. aureus*, with MICs of 16 and 16 μg/mL, respectively (Minh et al. 2023). Three polyketides named fusarisolins H–J (**127**–**129**) and 5-deoxybostrycoidin (**130**) have been isolated from the marine-derived fungus *F. solani* 8388. In the bioassays, fusarisolins I (**127**) and J (**129**), and 5-deoxybostrycoidin (**130**) exhibit obvious antibacterial activities against MRSA n315, with MICs of 3, 3, and 6 μg/mL, respectively. Fusarisolins H (**127**) and J (**129**) show inhibitory effects against MRSA NCTC 10442 with the same MIC of 6 μg/mL (Lin et al. 2023a). Bacillisporins A (**131**) and B (**132**) have been isolated from the ethyl acetate extract of the culture of a marine sponge-derived fungus, *Talaromyces pinophilus* KUFA 1767, and exhibited significant antibacterial activity against *S. aureus* ATCC 29213 and MRSA (Machado et al. 2023). Three citrinin derivatives (**133**–**135**), are acquired from *Penicillium* sp. TW131-64, a marine-derived fungus strain. Citrinin derivatives **133**–**135** and their corresponding enantiomers (**133a**, **134a**, **135a**, **133b**, **134b**, and **135b**) exhibit potent antimicrobial activities toward *H. pylori* standard strains and multidrug-resistant strains (MICs ranging within 0.25–8 μg/mL), which are comparable with or even better than those of metronidazole (Lai et al. 2023). Three pairs of C-9 epimeric verrucosidin derivatives, namely, the known compounds penicyrones A and B (**136a/136b**) and 9-*O*-methylpenicyrones A and B (**137a/137b**) and the compounds 9-*O*-ethylpenicyrones A and B (**138a/138b**), have been isolated and identified from the culture extract of *P. cyclopium* SD-413. They exhibit growth inhibition against some pathogenic bacteria (Li et al. 2023c).

Terpenoids

Among the 223 antibacterial compounds listed in this review, 21 are terpenoids. Most of them are sesquiterpenes and tetracyclic triterpenes (Figs. 13 and 14).

Aspergillusene E (**139**) has been isolated from the marine-derived fungus *A. versicolor* XS-20090066. It exhibits its antibacterial activity against *S. epidermidis* and *S. aureus* (MICs 8–16 μg/mL; Wu et al. 2020c). Four bisabolane sesquiterpenes (**140**–**143**), have been isolated from the culture of the endophytic fungus *T. asperellum* EN-764. They exhibit inhibitory activity against some aquatic pathogens with MICs ranging within 4–64 μg/mL (Li et al. 2023a). One sulfoxide-containing bisabolane sesquiterpenoid analogs (**144**) has been isolated from the marine-derived *A. sydowii* LW09 and shows inhibitory activity against *P. syringae*, with a MIC of 32 μg/mL (Yang et al. 2023b). One sesterterpenoid,

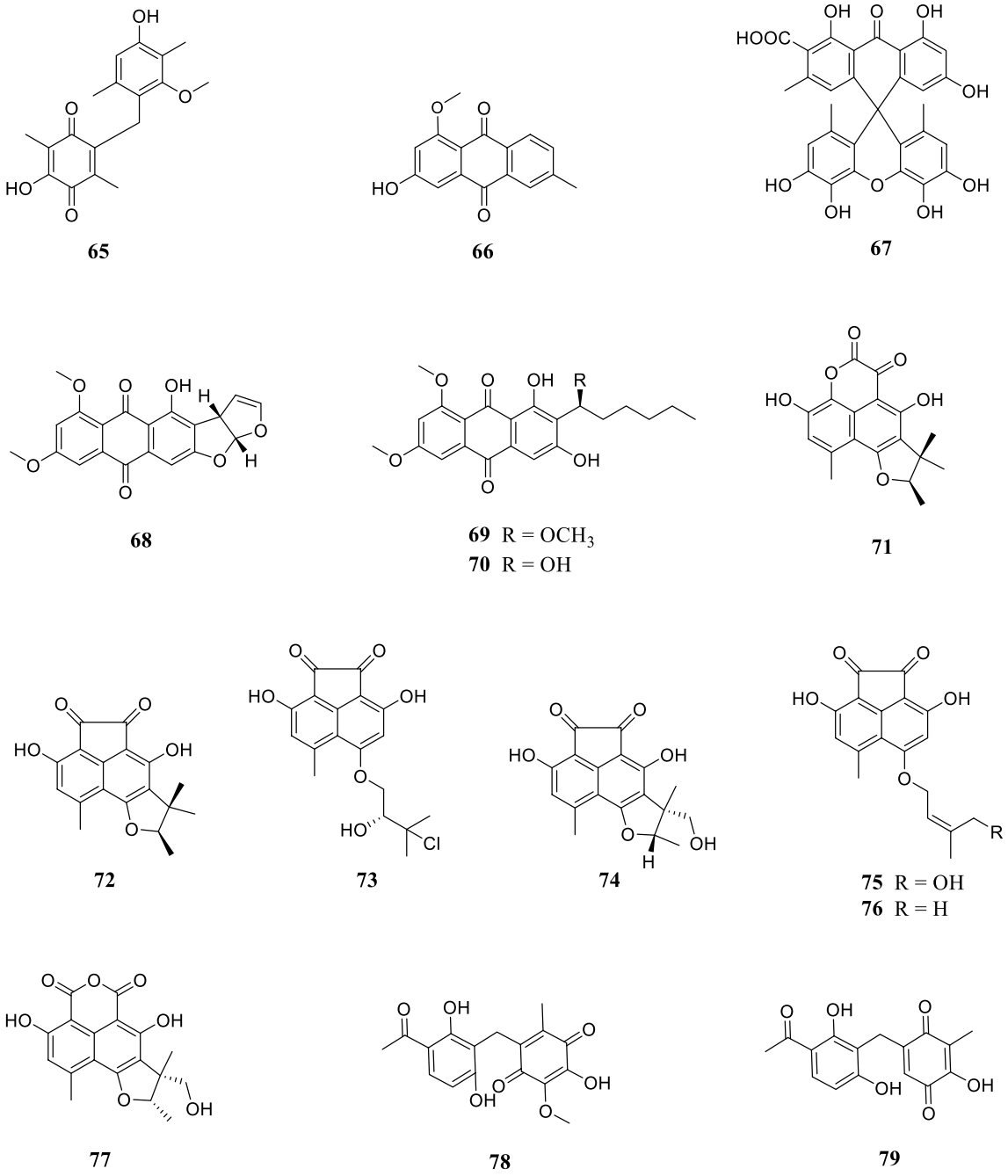
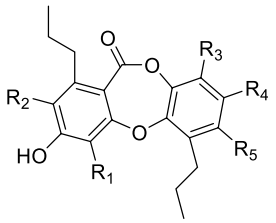
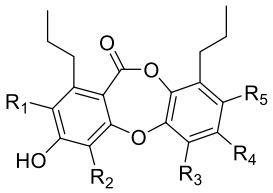
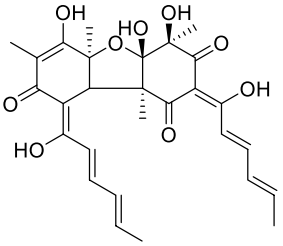


Fig. 9 Structures of compounds **65**–**79**

oxaliterpenoid (**145**) has been isolated from the methanol extract of the culture broth of the marine fungus *P. oxalicum* M893. It shows potent antibacterial activities against Gram-positive bacteria, *E. faecalis* (ATCC299212), *S. aureus* (ATCC25923), and *B. cereus* (ATCC14579), with MICs of 32, 32, and 32 µg/mL, respectively (Nguyen et al. 2023). Dendryphiellin I (**146**) has been isolated from the marine-derived fungus *Cochliobolus lunatus* SCSIO41401 and is active against *S. aureus*, with an MIC of 1.5 µg/mL. It is also active against two pathogenic bacteria of swine disease, *Erysipelothrix rhusiopathiae* and *Pasteurella multocida* (MICs 13 µg/mL; Fang et al. 2018). Pleosporallin D (**147**), has been isolated from a marine-derived fungus *Pleosporales* sp. and exhibits antibacterial activity against *C. michiganense* subsp. *Sepedonicus* (MIC 9.48 µg/mL; Chen et al. 2015). Two *N*-acetyl-L-valine-conjugated drimane sesquiterpenoids, named purpurides E (**148**) and F (**149**), have been isolated from the marine fungus *P. minioluteum* ZZ1657.



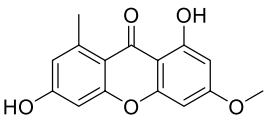




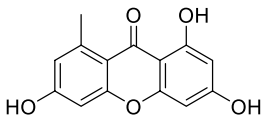
95

80 $R_1 = R_2 = R_3 = R_5 = H$, $R_4 = OH$
81 $R_2 = Cl$, $R_1 = R_3 = R_5 = H$, $R_4 = OH$
82 $R_1 = Cl$, $R_2 = R_3 = R_5 = H$, $R_4 = OH$
83 $R_2 = R_3 = H$, $R_1 = R_5 = Cl$, $R_4 = OH$
84 $R_3 = R_5 = H$, $R_1 = R_2 = Cl$, $R_4 = OH$
85 $R_1 = R_2 = R_5 = Cl$, $R_4 = OH$, $R_3 = H$
86 $R_1 = R_2 = R_5 = Cl$, $R_3 = H$, $R_4 = OMe$
87 $R_1 = R_2 = R_3 = Cl$, $R_5 = H$, $R_4 = OH$
88 $R_1 = R_2 = R_3 = R_5 = Cl$, $R_4 = H$
89 $R_1 = R_2 = R_3 = R_5 = Cl$, $R_4 = OMe$

90 $R_1 = R_2 = R_5 = Cl$, $R_3 = H$, $R_4 = OMe$
91 $R_1 = R_2 = R_3 = R_5 = Cl$, $R_4 = OMe$
92 $R_1 = R_2 = Cl$, $R_3 = R_5 = H$, $R_4 = OH$
93 $R_1 = R_2 = R_5 = Cl$, $R_3 = H$, $R_4 = OH$
94 $R_1 = R_2 = R_3 = R_5 = Cl$, $R_4 = OH$



96



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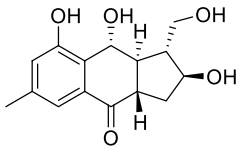

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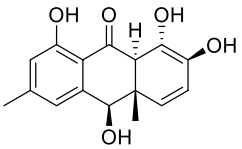

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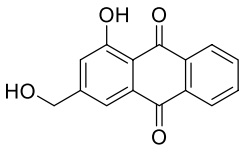

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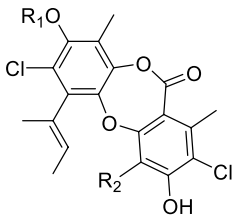
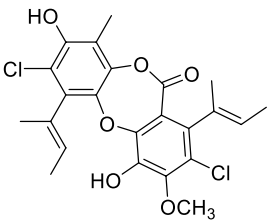


101 $R_1 = H$, $R_2 = H$
102 $R_1 = CH_3$, $R_2 = Cl$



103

Fig. 10 Structures of compounds **80–103**

Both exhibit antibacterial activity against MRSA and *E. coli*, with MICs of 6–12 and 3–6 μg/mL, respectively (Ma et al. 2020). One asperbrunneo acid (**150**) has been isolated from the marine-derived fungus *A. brunneoviolaceus* MF180246 and showed antibacterial activity against *S. aureus* (MIC 200 μg/mL; Xu et al. 2022). 16-*O*-propionyl-16-*O*-deacetylhelvolic acid (**151**), 6-*O*-propionyl-6-*O*-deacetylhelvolic acid (**152**), and helvolic acid (**153**) have been isolated from *A. fumigatus* HNMF0047. These compounds exhibit stronger antibacterial activity than a tobramycin control against *S.*

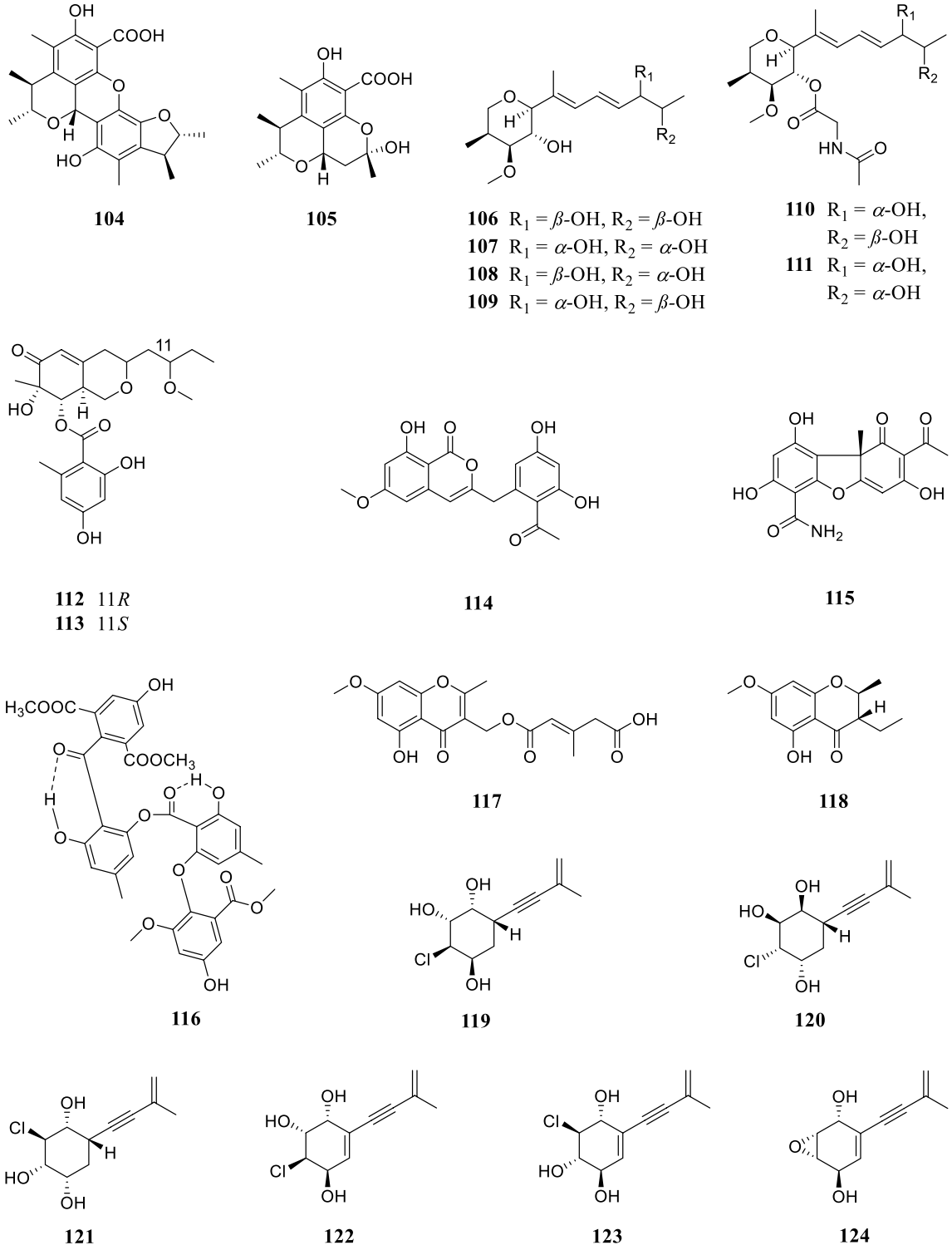


Fig. 11 Structures of compounds **104**–**124**

agalactiae, producing MICs of 16, 2, and 8 μg/mL, respectively (Kong et al. 2018). Compounds **154** and **155** have been isolated from the marine-derived fungus *A. fumigatus* MF071. They exhibit strong activity against *S. aureus* and *E. coli* (MIC 6.25 and 3.13 μg/mL, respectively, in both cases) (Han et al. 2020). An andrastin-type meroterpenoid, hemiacetalmeroterpenoid A (**156**), together with citreohybridone A (**157**) and andrastin B (**158**), have been isolated

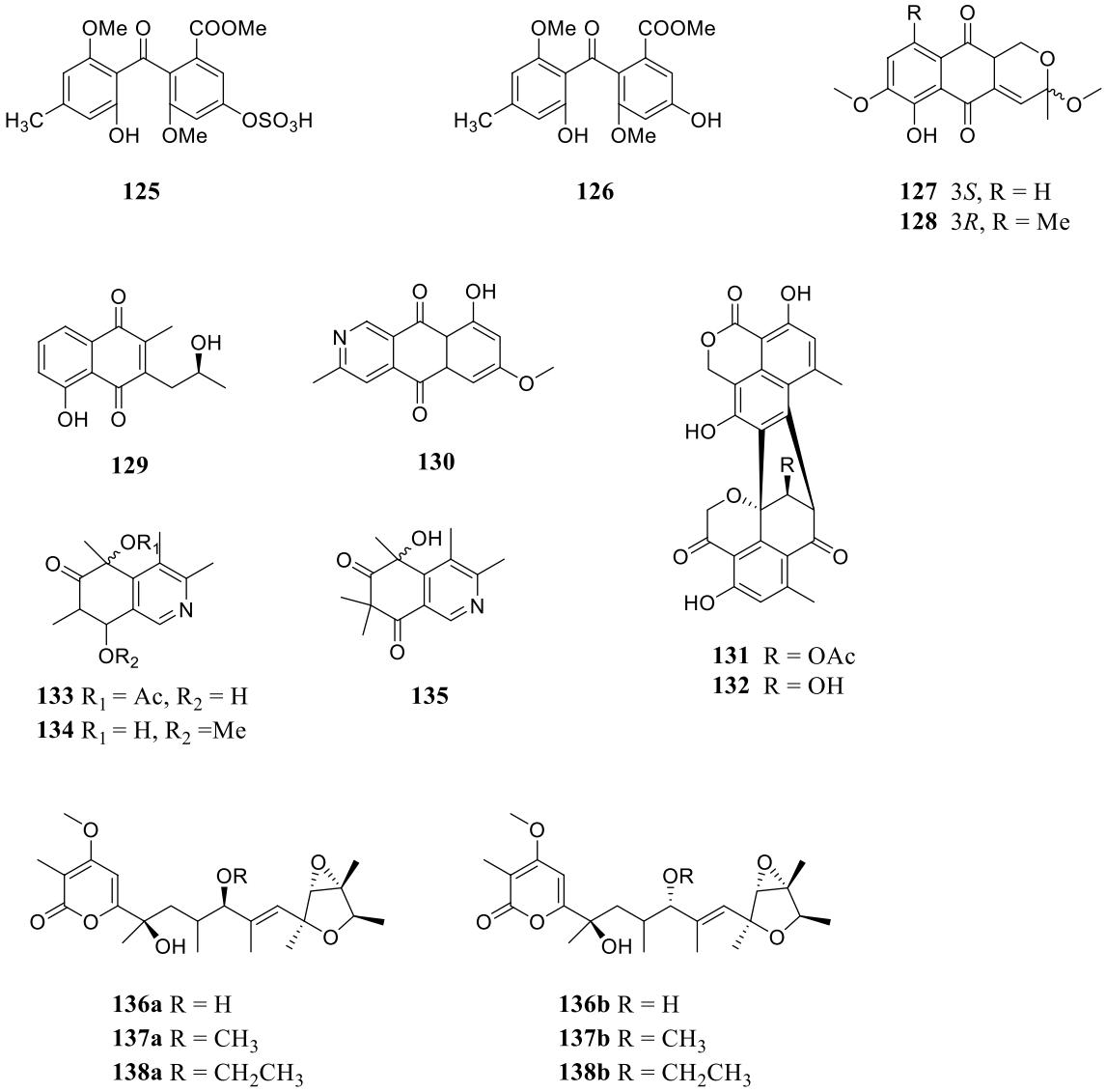


Fig. 12 Structures of compounds **125**–**138**

from the marine-derived fungus *Penicillium* sp. N-5. These compounds exhibit significant antibacterial activity against *P. italicum* and *C. gloeosporioides* (MICs 1.56–6.25 μg/mL; Chen et al. 2022). A meroterpenoid, taladrimanin A (**159**), has been isolated from the marine-derived fungus *Talaromyces* sp. HM6-1-1. It displays selective antibacterial activity against *S. aureus* 6538P and lower activity against strains of *V. parahaemolyticus* and *E. coli* (Hong et al. 2022).

Coumarins

Among the 16 coumarin analogs described below, 13 exhibit antibacterial activity against *S. aureus* (Fig. 15).

Asperpyranones A (**160**) has been isolated from the marine-derived fungus *A. terreus* RA2905 and displays activity against *P. aeruginosa* (MIC 32 μg/mL; Wu et al. 2020a). Citreoisocoumarin (**161**) has been isolated from the marine-derived fungus *P. vinaceum* and is active against *S. aureus* (Yamamura et al. 1991; Asiri et al. 2015). A *α*-pyrone polyketide, (+)-neocitreoviridin (**162**), has been isolated from the marine fungus *Penicillium* sp. IMB17-046 and exhibits antibacterial activity against the causative pathogens of various gastric diseases (Li et al. 2019). Three novel monomeric naphtho-*γ*-pyrones, peninaphones A–C (**163**–**165**), have been isolated from marine-derived *Penicillium* sp. HK1-22 and show antibacterial activity against *S. aureus* (ATCC 43300, 33591, 29213, and 25923) with MICs in the range of 12.5–50 μg/mL (Zheng et al. 2019). Four 4-hydroxy-*α*-pyrones, including three compounds named nipyrones A–C (**166**–**168**), together with the analog

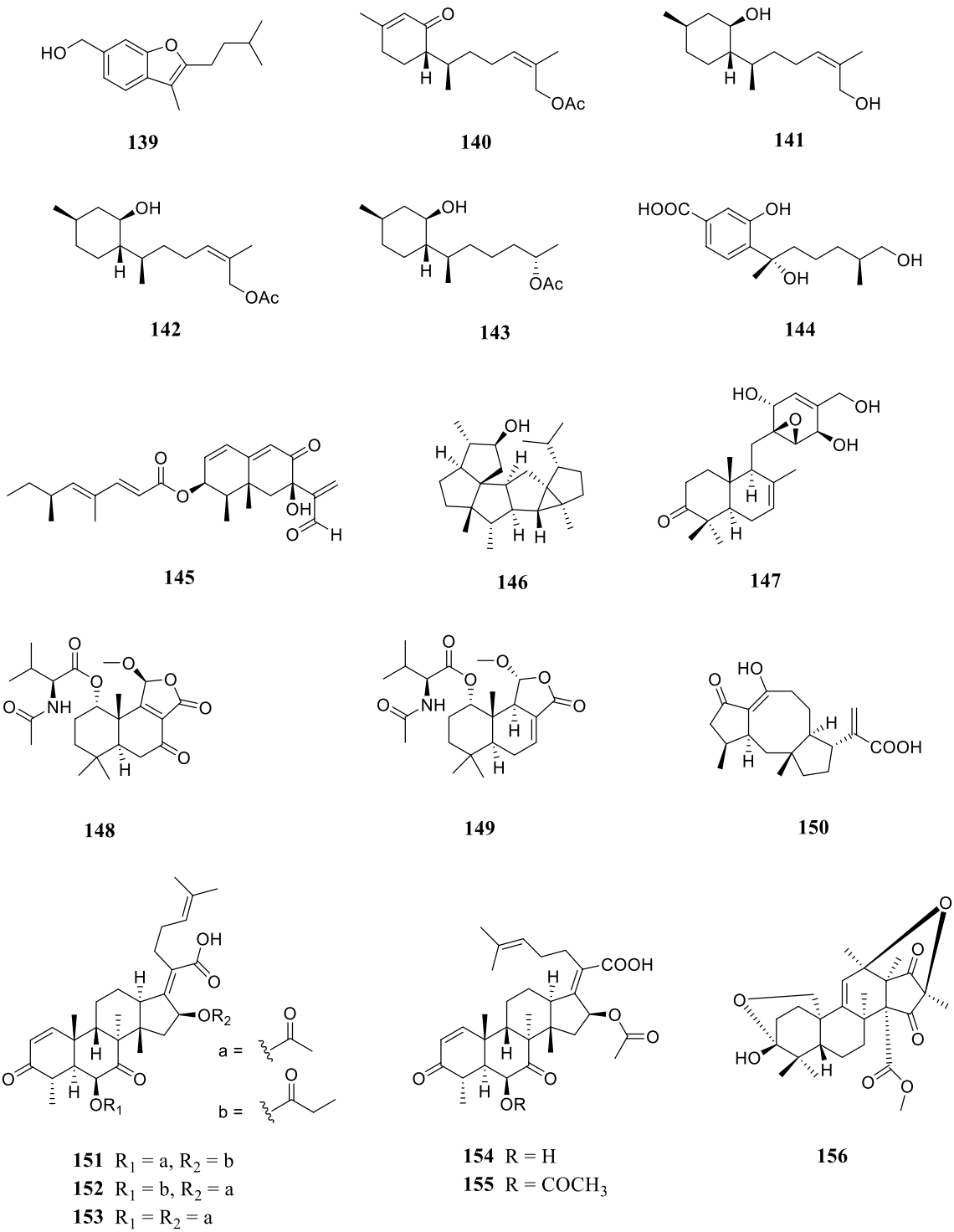
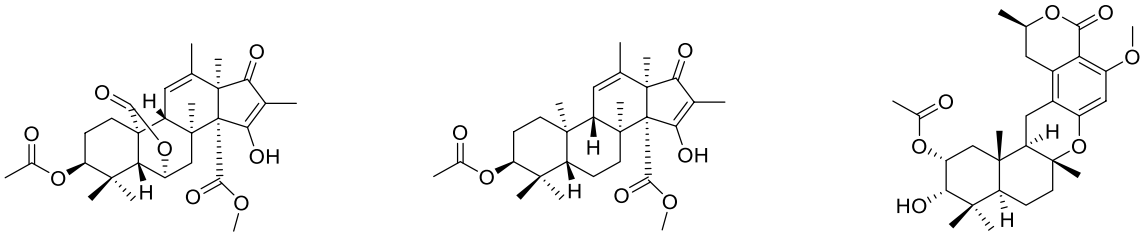


Fig. 13 Structures of compounds **139–156**

germicidin C (**169**), have been extracted from the marine-derived fungus *A. niger*. Compound **168** shows promising activity against *S. aureus* and *B. subtilis*, with MICs of 8 and 16 µg/mL, respectively, whereas **166**, **167**, and **168** exhibit moderate antibacterial effects against *S. aureus*, *E. coli*, and *B. subtilis*, having MICs in the range of 32–64 µg/mL. Compounds **167–169** also displayed weak antibiotic activity against MRSA (Ding et al. 2019). Nine compounds have been isolated from *Verruculina enalia* (Kohlm.) Kohlm. & Volkm-Kohlm. BCC 22226 included enalin A (**170**),



157 158 159

Fig. 14 Structures of compounds **157–159**

which has weak antituberculous and antibacterial properties (Bunyapaiboonsri et al. 2020). A 3,5-dimethylorsellinic acid-based meroterpenoid (**171**) with powerful antibacterial activity against *H. pylori* and *S. aureus* has been isolated from the marine fungus *Aspergillus* sp. CSYZ-1 (Cen et al.2020). 7-Hydroxyoospolactone (**172**) and parapholactone (**173**) have been isolated from the marine fungus *Paraphoma* sp. CUGBMF180003 and inhibit *S. aureus* (Xu et al. 2021). Lulworthinone (**174**), which has been isolated from the marine-derived fungus *Lulworthiaceae*, has antibacterial effects on reference strains of *S. aureus* and *S. agalactiae* and on several clinical MRSA isolates (MICs 1.56–6.25 µg/mL; Jenssen et al. 2021). A dihydroisocoumarin, aspergimarin G (**175**), has been isolated from the sponge-associated fungus *Aspergillus* sp. NBUF87. It shows moderate antibacterial activity toward *S. aureus* and *S. enteritidis*, with MICs ranging from 16 to 64 µg/mL (Lin et al. 2023b).

Xanthones

Only three reports of xanthones were identified by this review (Fig. 16).

Purpureone (**176**) has been isolated from the marine-derived fungus *C. lunatus* SCSIO41401 and displays antibacterial activity against two swine disease pathogenic bacteria, *S. aureus*, *E. rhusiopathiae*, and *P. multocida*, with MICs of 13 to 50 µg/mL (Fang et al. 2018). Five bistetrahydroxanthone analogs—secalonic acid F1 (**177**), secalonic acid H (**178**), penicillixanthone A (**179**), chrysoxanthone C (**180**), and asperdichrome (**181**)—have been isolated from the marine-derived fungus *A. brunneoviolaceus* MF180246. All display antibacterial activity against *S. aureus*, with MICs of 25, 50, 6.25, 50, and 25 µg/mL, respectively (Xu et al. 2022). Homodimeric tetrahydroxanthone secalonic acid D (**182**) has been isolated from the marine-derived fungus *A. aculeatinus* WHUF0198. Compound **182** is found to be active against *H. pylori* G27, *H. pylori* 26,695, *H. pylori* 129, *H. pylori* 159, *S. aureus* USA300, and *B. subtilis* 168, with MICs of 4.0, 4.0, 2.0, 2.0, 2.0, and 1.0 µg/mL, respectively (Wu et al. 2023).

Steroids

This review identified four publications reporting a total of six steroids (structures illustrated in Fig. 17).

Ergosta-5,7,22-triene-3β-ol (**183**) and volemolide (**184**) have been isolated from the marine fungus *Aspergillus* sp. SCS-KFD66 and inhibit *B. subtilis* ATCC 6633, with MICs of 128 µg/mL. Compound **183** also inhibited *S. aureus* ATCC 6538 (MIC 128 µg/mL; An et al. 2018). Aspergillsteroid A (**185**) has been isolated from the marine fungus *Aspergillus* sp. LS116. It is a novel aquatic pathogen inhibitor displaying significant antibacterial activity against *V. harveyi* (MIC 16 µg/mL; Xu et al. 2020). Two steroids, ganodermasides B (**186**) and D (**187**) have been isolated from *Pseudogymnoascus* sp. HSX2#-11 and display antibacterial activity against the marine-fouling bacteria *Aeromonas salmonicida*, with MICs of 30 and 36 µM, respectively (Shi et al. 2021a). An ergostane steroid analog, 4α-hydroxy-17-methylincisterol (**188**), has been isolated from the marine-derived fungus *Trametes* sp. ZYX-Z-16. It displays antibacterial activity against *S. aureus* ATCC 6538 (MIC 32 µg/mL) and *B. subtilis* ATCC 6633 (MIC 16 µg/mL) (Ren et al. 2022). One oxygenated ergostane-type steroid, 3β-hydroxy-5α,6β-methoxyergosta-7,22-dien-15-one (**189**), has been isolated from the crude extract of the marine sponge-derived fungus *Aspergillus* sp.. They exhibit significant antibacterial activity against *S. aureus*, with a MIC of 64 µg/mL (Wen et al. 2023).

Other compounds

Benzoic acid derivatives, penicillin analogs, diphenyl ethers, glycosides, peptides, fatty acids, and other compounds account for a relatively small proportion of the secondary metabolites of marine fungi exhibiting antibacterial activity (Figs. 18, 19, 20).

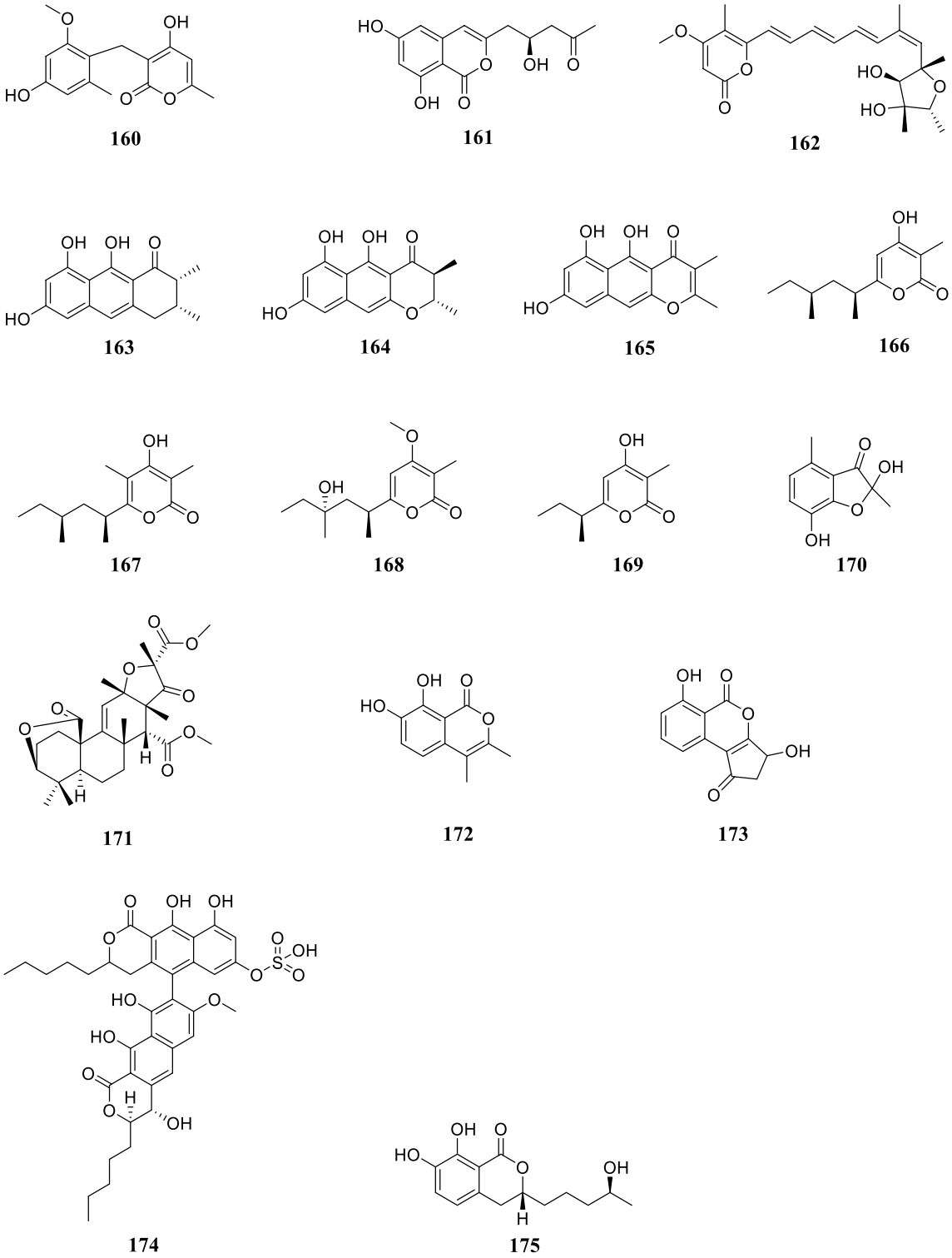


Fig. 15 Structures of compounds **160**–**175** (Absolute configurations of compounds **170**, **173** and **174** are undetermined)

(*E*)-4-Oxonon-2-enoic acid (**190**) has been isolated from the marine fungus *Aspergillus* sp. SCS-KFD66. It shows inhibitory activity against *B. subtilis* ATCC 6633 and *S. aureus* ATCC 6538, with MICs of 4 and 16 μg/mL, respectively (An et al. 2018). A nucleoside derivative, kipukasin K (**191**), exhibits antibacterial activity against *S. epidermidis* and *S. aureus* (MICs 8–16 μg/mL) after being isolated from the marine-derived fungus *A. versicolor*

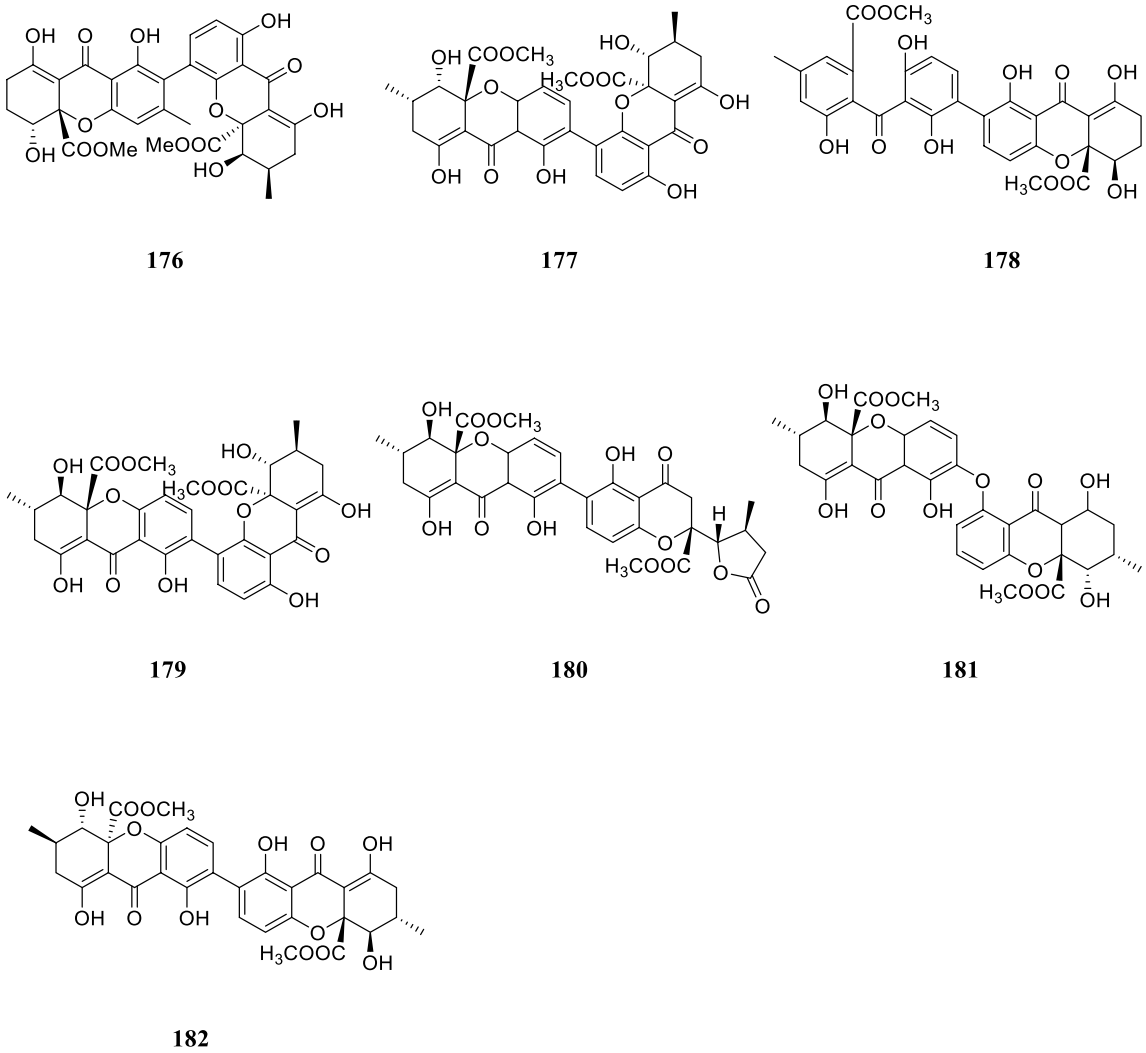


Fig. 16 Structures of compounds **176**–**182**

XS-20090066 (Wu et al. 2020c). A benzoic acid derivative (**192**) has been isolated from *Pseudogymnoascus* sp. HSX2#-11 and exhibits antibacterial activity against a panel of bacteria (Shi et al. 2021b). Among the nine compounds have been isolated from *V. enalia* (Kohlm.) Kohlm. & Volkm-Kohlm. BCC 22226, one is the cyclic lipodepsipeptide verruculin (**193**), which shows weak antituberculous and antibacterial activities (Bunyapaiboonsri et al. 2020). Emerimicin IV (**194**) has been isolated from the marine sediment-derived fungus *Emericellopsis minima.* It shows bacteriostatic activity against clinical isolates of MRSA and vancomycin-resistant *E. faecalis* (MICs 12.5–100 μg/mL; Inostroza et al. 2018). A salicylaldehyde derivative (**195**) has been isolated from the marine fungus *Zopfiella marina* BCC 18240 (or NBRC 30420) and exhibits antibacterial activity against *B. cereus* (MIC 12.5 μg/mL; Chokpaiboon et al. 2018). A pyrazine derivative, trypilepyrazinol (**196**), has been isolated from the marine fungus *Penicillium* sp. IMB17-046 and exhibits antibacterial activity against causative pathogens of various gastric diseases (Li et al. 2019). Among the nine compounds isolated from *V. enalia* (Kohlm.) Kohlm. & Volkm-Kohlm. BCC 22226, one is verruculinone (**197**), which shows weak antituberculous and antibacterial activities (Bunyapaiboonsri et al. 2020). Two penicillin analogs, $\Delta^{2'}$-1'-dehydropenicillide (**198**) and 1'-dehydropenicillide (**199**), have been isolated from marine-derived *Aspergillus* sp. IMCASMF180035. They are active against *S. aureus*, MRSA, *E. coli*, *E. faecium*, *P. aeruginosa*, and *H. pylori* (Song et al. 2021). Three diphenyl ethers (**200 – 202**) have been isolated from marine sediment-derived *Spiromastix* sp. SCSIO F190. All three, particularly compound **200**, exhibit strong activity against Gram-positive bacteria, including methicillin-resistant strains of *S. aureus*, *E. faecalis* ATCC 29212, and *B. subtilis* BS01 (MICs 0.5–4.0 μg/mL; Cai et al. 2022). A tetrasubstituted benzene derivative, peniprenylphenol A (**203**), has been isolated from the marine

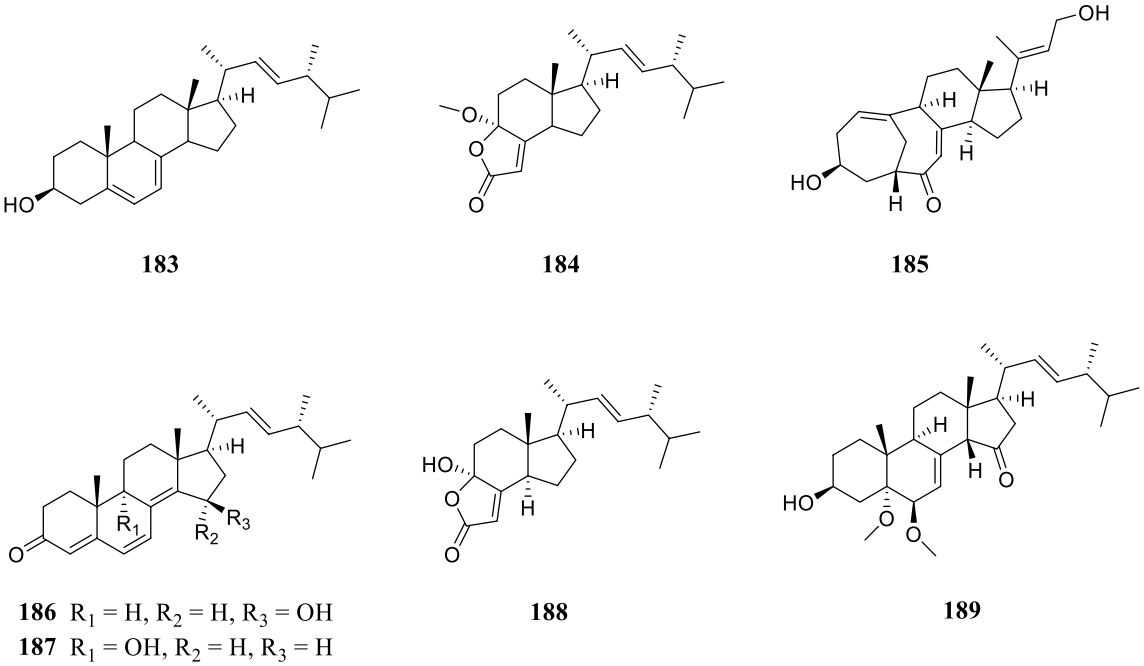


Fig. 17 Structures of compounds **183–189**

sediment-derived fungus *P. chrysogenum* ZZ1151 and exhibits activity against MRSA and *E. coli*, with MICs of 6 and 13 μg/mL, respectively (Newaz et al. 2022). Alternariol (**204**) has been isolated from a marine-derived fungus strain of *P. arabicum* ZH3-9. This compound displays antibiotic activity against *S. aureus*, with a MIC of 50 μg/mL (Yang et al. 2023a). A cyclopentene derivative (**205**), together with one naturally occurring cyclopentenone derivative (**206**), has been isolated from the culture of the endophytic fungus *T. asperellum* EN-764. They exhibit inhibitory activity against some aquatic pathogens, with MICs ranging within 4–64 μg/mL (Li et al. 2023a). Asperbutenolide A (**207**) has been isolated from the marine fungus *A. terreus*. It displays antibacterial activity against MRSA, with MICs of 4.0–8.0 μg/mL (Jiang et al. 2023). Aspergetherins A (**208**) and C (**209**), two chlorinated biphenyls, have been isolated from the rice fermentation of a marine sponge symbiotic fungus *A. terreus* 164018, along with two biphenyl derivatives (**210** and **211**). They show anti-MRSA activity with MICs of 1.0–128 μg/mL (Li et al. 2023b). Two pentadepsipeptides, aspertides D (**212**) and E (**213**), have been isolated from the marine fungus *Aspergillus* sp.. They exhibit antibacterial activities against aquatic-pathogenic bacteria, including *Edwardsiella tarda, V. alginolyticus, V. anguillarum, V. vulnificus,* and *S. aureus,* with MICs of 8 – 32 μg/mL. (Chi et al. 2023). *Trans*-3,4-dihydroxy-3,4-dihydroanofinic acid (**214**) and 7-hydroxymethyl-1,2-naphthalenediol (**215**) have been isolated from the obligate marine fungus *A. cruciatus* KMM 4696. Compound **214** shows the best effect on *S. aureus* growth, with a calculated IC_{50} of 49.7 μM, respectively. Compound **215** is less effective, with IC_{50} of 52.1 and 58.2 μM, respectively (Zhuravleva et al. 2023). From *P. antarcticum* KMM 4670, pentaketide derivative antaketide A (**216**) and 2-((2*R*,6*S*)-6-methyltetrahydro-2*H*-pyran-2-yl)acetic acid (**217**) have been isolated. Antaketide A (**216**) inhibits *S. aureus* growth by 48.5% at 100 μM and does not influence *S. aureus* growth at 12.5 μM. Compound **217** inhibits *S. aureus* growth by 46.5% at 100 μM and *E. coli* growth by 56.9% at 100 μM. IC_{50} is calculated as 84.9 μM (Yurchenko et al. 2023). Aspergillusethers A (**218**) and J (**219**), and guisinol (**220**) have been isolated from the methanol extract of the culture broth of the marine fungus *P. oxalicum* M893. All compounds show potent antibacterial activities against Gram-positive bacteria, *E. faecalis* (ATCC299212), *S. aureus* (ATCC25923), and *B. cereus* (ATCC14579), with MICs ranging within 4–64 μg/mL (Nguyen et al. 2023). 3-Chloro-2,5-dihydroxybenzyl acetate (**221**), 3-chlorogentisyl alcohol (**222**), and 2-chloro-6-(methoxymethyl)benzene-1,4-diol (**223**) have been isolated from the marine-derived fungus *Epicoccum sorghinum* GXIMD02001. They exhibit weak antibacterial activity, with MICs of 7.81–125 μg/mL (Xing et al. 2023).

Overview

A few reviews, akin to the forefront of antibacterial agents derived from marine fungi, can be accessed through databases. Wang et al. (2021) reviewed 272 compounds with

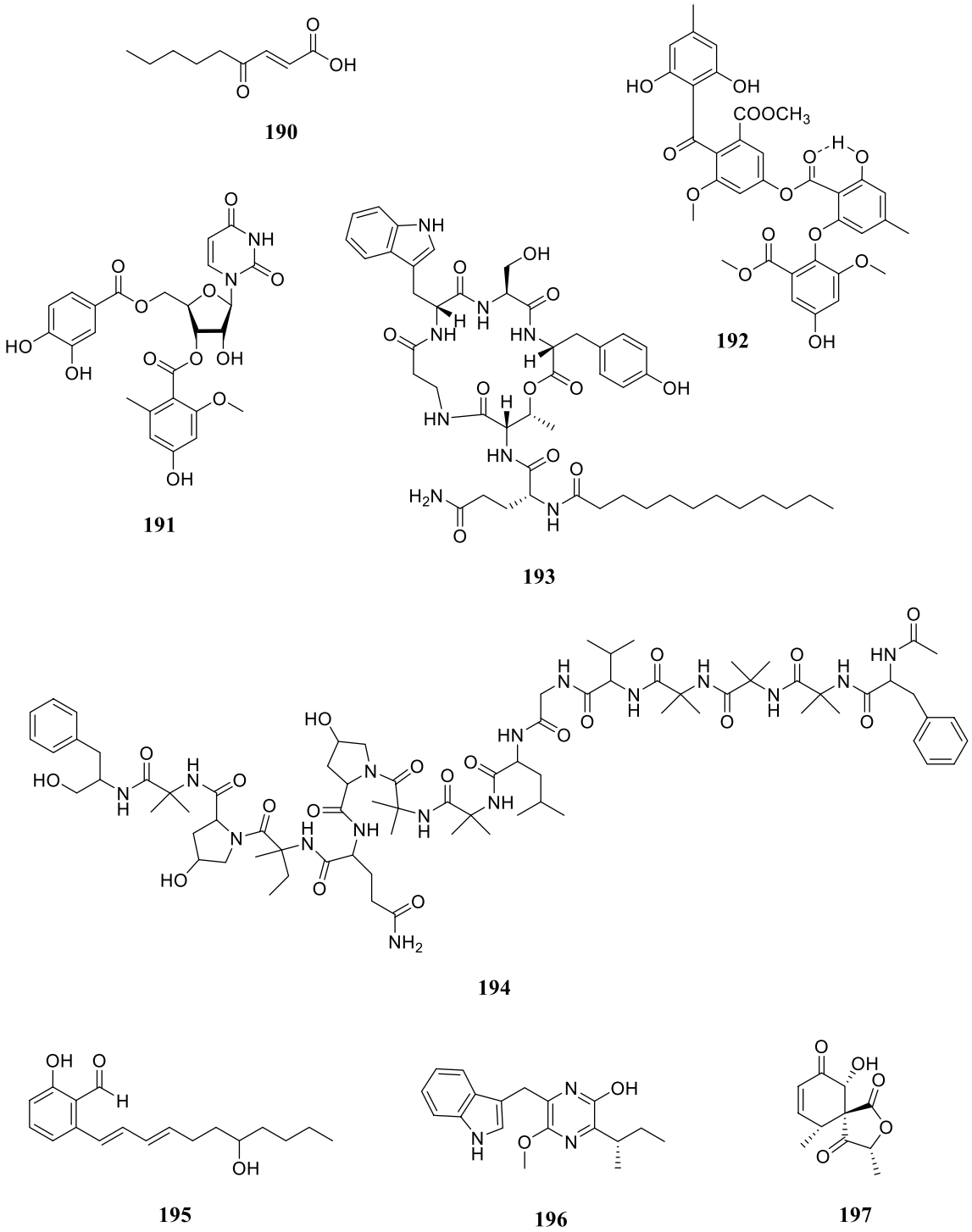


Fig. 18 Structures of compounds **190**–**197** (Absolute configurations of compounds **194**, and **195** are undetermined)

antimicrobial properties from marine fungi from 1998 to 2019. This review highlights the source of fungi, including *Penicillium* sp., *Aspergillus* sp., and other fungi, from animals, plants, sediments, and seawater. Herein, we conduct a comprehensive overview with varying time spans (2010 to 2023), encompassing all marine-derived fungi as producers of antimicrobial natural products. Wang et al. (2022) highlighted the natural bioactive compounds from marine fungi, ranging from 2017 to 2020. We focus on antibacterial compounds from marine fungi, placing particular emphasis on the types of pathogens investigated and quantifying the amounts of bioactive compounds toward

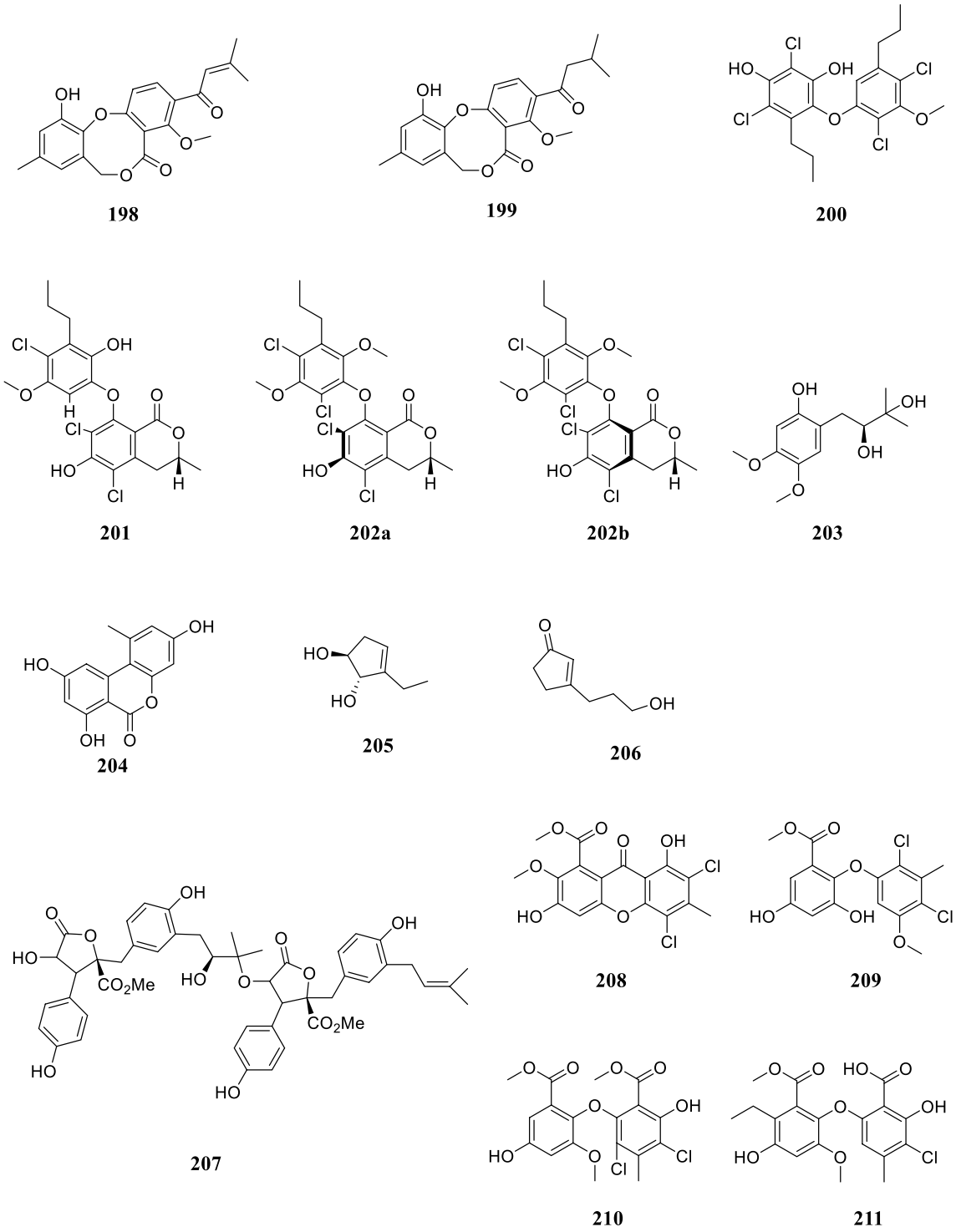


Fig. 19 Structures of compounds **198**–**211** (Absolute configuration of compound 207 is undetermined)

the targeted strains. Hasan et al. (2015) conducted a review of significant bioactive metabolites from marine fungi that were reported before 2015. Conversely, antibacterial products constitute a minor portion of the overall content. The present review updates these works and spans from 2012 to 2023, showcasing marine fungal metabolites exhibiting antibacterial activity. Their antibacterial efficacy, biological sources, and MICs are summarized (Table 1). Our findings enable readers to identify classes of fungal metabolites, the pathogenic bacteria they impact, and the fungal strains that

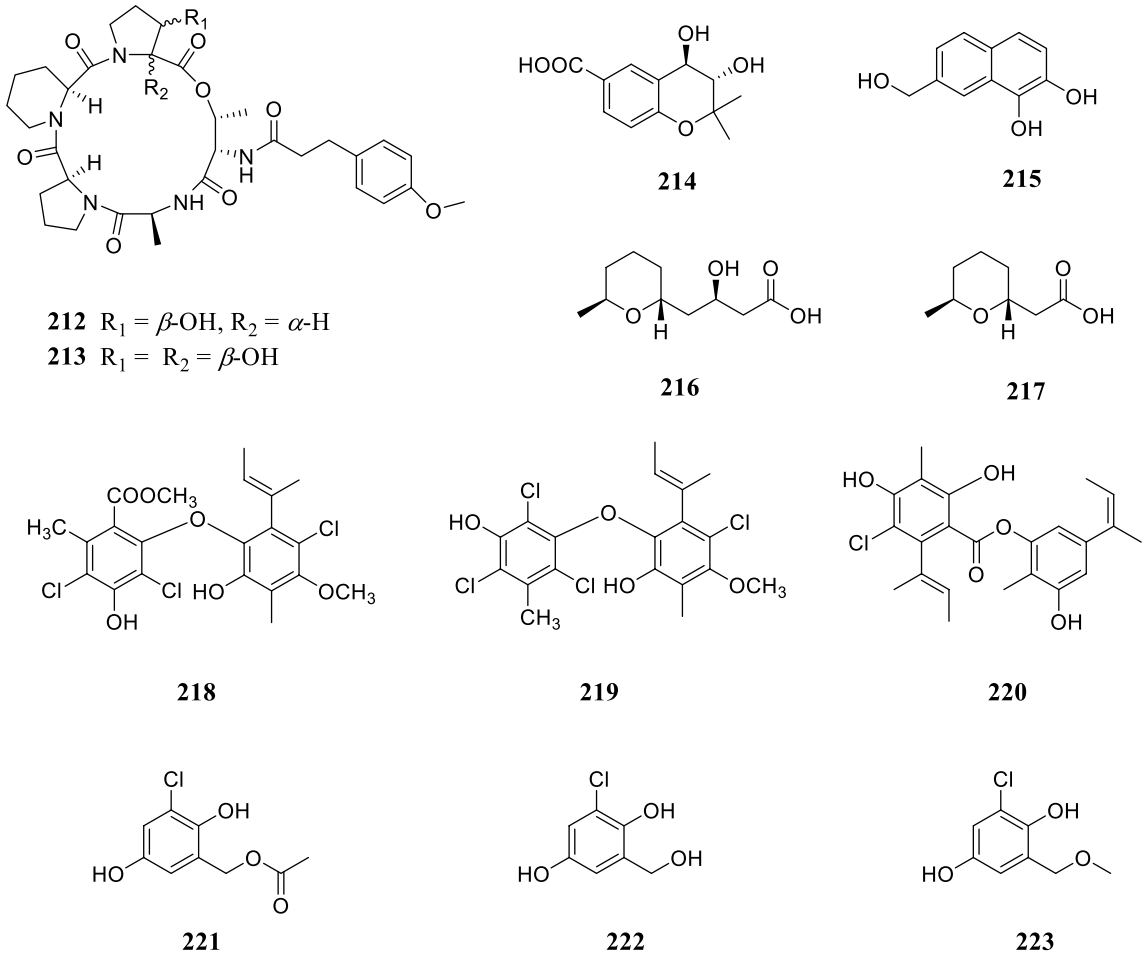


Fig. 20 Structures of compounds **212**–**223**

produce them (Figs. 1, 2, 3). The Simplified Molecular Input Line Entry System (SMILES) notation is used to search for specific compounds. This review provides useful guidance for screening compounds for desired antibacterial properties while highlighting the challenges faced from discovery to commercialization, particularly regarding structural synthesis. It also highlights emerging approaches such as metagenomics, semi-synthesis, and heterologous gene expression as potential strategies to overcome these challenges.

Conclusions and outlook

Infections caused by pathogenic bacteria can lead to inflammation and, in severe cases, sepsis, which can be fatal. The conventional treatment for bacterial infections involves antibiotics, but this strategy has been undermined by the rise in bacterial resistance due to the increased use of these diverse drugs. Thus, developing new antibacterial agents to combat resistant bacteria is urgent, and related research has recently accelerated the evaluation of marine fungi-derived compounds. This paper reviews 223 antibacterial compounds derived from marine fungi and reported between 2012 and 2023, highlighting their diverse sources and chemical structures. Antibacterial compounds account for over one-third of the compounds identified, which highlights the potential of this natural source in future drug discovery research. The majority of the reported antibacterial compounds primarily target 10 species of bacteria, namely, *S. aureus*, *B. subtilis*, *E. coli*, *B. cereus*, *H. pylori*, *B. thuringiensis*, *E. faecalis, M. Luteus*, *S. agalactiae*, and *P. aeruginosa*, among others (Fig. 2). Nearly half of the compounds inhibit *Staphylococci*, including 36 active molecules against MRSA. Some compounds such as *O*-propionyl-16-*O*-deacetylhelvolic acid and 6-*O*-propionyl-6-*O*-deacetylhelvolic acid, exhibit excellent activity that surpasses positive controls. These findings emphasize the potential of marine fungi as a valuable source of potent antibacterial agents. Many are capable of combating a range of bacteria, including drug-resistant strains.

Antibacterial metabolites from marine fungi are a potential source for the development of antibacterial drugs. Marine fungal secondary metabolites, with their remarkable chemical structural diversity and complexity, serve as

a bountiful reservoir for the discovery and design of novel antibacterial drugs. Their potent antibacterial activity, demonstrated by many of these metabolites, positions them as compelling candidates in the field of antibacterial drug development. Furthermore, the unique biosynthesis pathways used by marine fungi, which often diverge significantly from those of terrestrial fungi and other microorganisms, open up exciting prospects for identifying new targets in antibacterial drug discovery.

However, efforts to develop antibacterial agents from marine fungal secondary metabolites are fraught with their own set of challenges. Marine fungi predominantly reside in the deep sea or other inaccessible marine environments, making their collection a formidable task. These organisms' unique habitats demand specific conditions such as temperature, pressure, and nutrients, which complicate their cultivation in laboratory settings. Marine fungi also typically produce secondary metabolites in minute quantities, posing a significant challenge in obtaining sufficient amounts for drug development (Liang et al. 2019). Lastly, the intricate chemical structures of these secondary metabolites make their structural identification and functional research a daunting endeavor. Therefore, to overcome these challenges, innovating new collection methodologies, fine-tuning cultivation conditions, and enhancing product yields for functional studies are essential.

Current advancements in research on deep-sea submersibles, remote sensing, automated underwater samplers, and marine drilling technologies have made the collection of sediments, plankton samples, and seawater easier and safer. Deep-diving technology can also operate at depths of up to 100 m underwater. Metagenomics aims to elucidate the physiology and genetics of uncultured organisms by isolating organismal DNA directly from the environment and cloning it in microbial cultures. This technique enables the exploitation of the bioactive potential of the targeted fungi's genome (Handelsman 2004). The heterologous expression of biosynthetic gene clusters is another emerging approach to alleviating material-supply issues. It involves deleting, inserting, or replacing key genes or biosynthetic modules in genetically susceptible hosts to generate new biosynthetic pathways and analogs (Zhang et al. 2016). The successful heterologous expression of various compounds has been reported, including those of polyketides, non-ribosomal peptides, and isoprenoids (Zhang et al. 2011), thereby highlighting the potential of this approach for producing sufficient fungal metabolites for drug development. Semi-synthesis is also a solution to the limited supply of natural products. Pettit et al. (1982) reported the structure of a remarkable anticancer constituent of *Bugula neritina* designated bryostatin 1, which was found to prolong the lifespan of diseased mice (P388 lymphoblastic leukemia) in a bioactivity assay. The first total synthesis of this agent was described by Keck et al. (2011). Marshall et al. reported in (1998) the total synthesis of (+)-discodermolide, a polyketide marine natural product with potent immunosuppressive and potential antitumor activity. The above-described innovative strategies are essential for overcoming the supply shortages of marine fungal metabolites with desirable antibacterial properties.

The journey from discovering a natural active substance to bringing it to clinical trial, and ultimately to clinical application, is long. A multidisciplinary approach encompassing metabonomics, natural pharmaceutical chemistry, and pharmacology must be adopted. Such an integrated approach can lead to the discovery of more potent marine fungi-derived products with robust antibacterial activity. The untapped potential of marine fungi also offers an exciting avenue for future research in combating drug-resistant bacteria.

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Declarations

Conflicts of interest The authors declare that they have no conflict of interest.

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