frontiers | Frontiers in Marine Science

TYPE Review
PUBLISHED 21 January 2025
DOI 10.3389/fmars.2024.1538136

OPEN ACCESS

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RECEIVED 02 December 2024
ACCEPTED 27 December 2024
PUBLISHED 21 January 2025

CITATION
Pan C, Hassan SSu, Muhammad I and Jin H (2025) Marine fungi as a goldmine for novel antibiotics: a 2024 perspective.
Front. Mar. Sci. 11:1538136.
doi: 10.3389/fmars.2024.1538136

Marine fungi as a goldmine for novel antibiotics: a 2024 perspective

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The microbial diversity in oceans is considerable, widely distributed in seawater, marine sediments, and marine organisms. Compared with terrestrial resources in traditional natural product research, the living environments of marine microorganisms are starkly different. The drastic differences in survival conditions, such as high salinity, oligotrophic conditions, lack of light, and limited oxygen, determine that microorganisms exhibit distinctive characteristics in metabolism, survival modes, and adaptive mechanisms. These factors contribute to significant distinctions in secondary metabolic pathways and enzymatic reaction mechanisms between marine and terrestrial microorganisms. In this review, we summarized a total of 72 novel natural products with antibacterial activity, published in 2024, which are derived from marine-derived fungi. These products (polyketides, alkaloids, terpenoids, and peptides) are emphasized in terms of their structures and biological activities. This article aims to provide useful information for the research and development of novel antibiotics.

KEYWORDS

marine fungi, antibacterial activity, novel natural products, alkaloid, polyketide

1 Introduction

Since the late 1990s, with the increasing exploration of natural resources, discovering new biologically active natural products has become increasingly challenging (Atanasov et al., 2021). Traditional strategies for the isolation and identification of natural products have led to the repeated isolation of a large number of known compounds, slowing down the process of discovering structurally novel active compounds (Zhang et al., 2020; Pirintsos et al., 2022; Young et al., 2022). Meanwhile, the emergence of drug resistance in bacteria has made it urgent for humanity to seek new natural products with novel structures, unique biological activities, and mechanisms of action as lead compounds for new drug development (Schneider, 2021; Vaou et al., 2021).

Compared to terrestrial biological resources studied in traditional natural product research, the living environments of marine organisms are strikingly different. The drastic differences in survival conditions, such as high pressure, high salinity, oligotrophic conditions, lack of light, limited oxygen, and special habitats (submarine hydrothermal vents, deep-sea trenches), determine that marine organisms exhibit significant characteristics in metabolism, survival strategies, information transfer, and adaptive mechanisms (Hai et al., 2021; Lu et al., 2021; Srinivasan et al., 2021). These factors contribute to marine organisms having almost entirely distinct secondary metabolic pathways and enzymatic reaction mechanisms compared to terrestrial organisms. Notable drugs derived from marine sources include the antiviral drug vidarabine, the anticancer drugs cytosine arabinoside and eribulin, the analgesic conotoxin, the lipid-lowering drug ethyl ester of eicosapentaenoic acid (EPA), and the "warhead" of antibody-drug conjugates (ADCs), dolastatin (Alves et al., 2020). These drugs all possess unique chemical structures, and the exploration of lead molecules with significant pharmacological activities from marine organisms is gradually demonstrating significant research value and application potential.

Marine microorganisms, as an important group within marine organisms, have always been one of the research hotspots in marine natural products (Stincone and Brandelli, 2020; Crawford et al., 2021; Shams Ul Hassan et al., 2021; Gomez-Banderas, 2022; Hassan et al., 2022; Voser et al., 2022; Hassan et al., 2024). Thanks to the rapid development of high-throughput sequencing technology, more and more microbial genomes have been sequenced in recent years. Bioinformatics analysis has revealed that microbial genomes typically contain multiple secondary metabolite biosynthetic gene clusters. Limited by conventional laboratory cultivation conditions, the variety of compounds we have discovered so far is far less than the number of compounds that microorganisms are capable of producing, and a large number of potential secondary metabolites remain undiscovered (Scherlach and Hertweck, 2021; Albarano et al., 2020; Peng et al., 2021). Activating the expression of these silent gene clusters and seeking the active secondary metabolites they contain will become an important source for discovering novel drug precursors for anti-inflammatory, antibacterial, antitumor, antiviral, and enzyme inhibitor applications, opening up new avenues for fundamental research in drug discovery (Stuart et al., 2020; Zhu et al., 2022; El-Hawary et al., 2023; Tsipinana et al., 2023).

Based on data from Web of Science, PubMed, Elsevier, the American Chemical Society (ACS), and Google Scholar, this article selects studies that report novel compounds and provide minimum inhibitory concentration values (MICs), comprehensively summarizing the sources, structures, and biological activity progress of 56 newly isolated antibacterial natural products derived from marine fungi in 2024. Known compounds and compounds with other activities were not included in the statistics. According to their structural characteristics, these natural products are classified into four major categories, including polyketides (41.7%, 30/72), alkaloids (19.4%, 14/72), terpenoids (12.5%, 9/72), peptides (22.2%, 16/72), and miscellaneous (4.2%, 3/72) (Figure 1). Among these biological

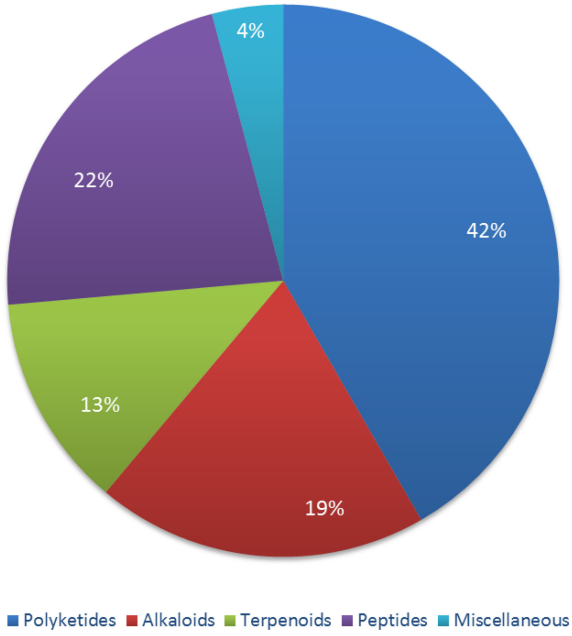

FIGURE 1
Antibacterial compounds derived from marine fungi according to structure types.

samples, 33.3% (8/24) originate from *Penicillium* fungi, indicating the great potential of *Penicillium* fungi secondary metabolites in the search for novel antibiotics. Meanwhile, the significance of *Aspergillus* fungi (29.2%, 7/24) in the exploration of novel antibiotics cannot be overlooked (Figure 2). Particularly noteworthy are the impressive discoveries by Professor Shu-Hua Qi from South China Sea Institute of Oceanology, whose 16-epiascomylactam B (**38**) exhibited strong antibacterial activity (Yao et al., 2024). Tables 1–5 list the names, isolation sources, categories, and activity levels (MIC) of the antibacterial active compounds.

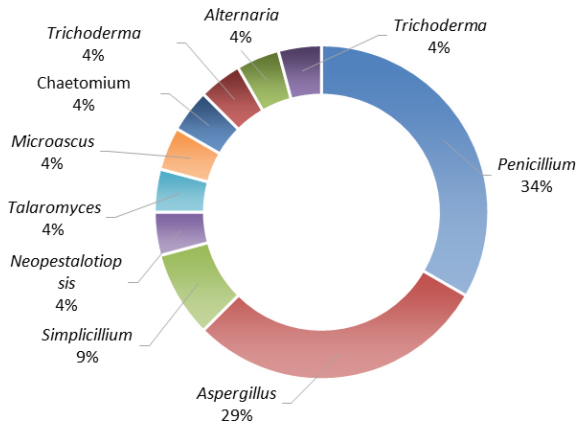

FIGURE 2
The different genus of marine fungi.

TABLE 1 Polyketides with antibacterial activity from marine fungi.

Metabolites	Sources	Species	Antibacterial Activities (MIC, μg/mL)	Ref
Harzianolide B **(1)**	China	*Trichoderma harzianum* ZN-4	*P. theae* 25	(Zhou et al., 2024)
Harzianolide C **(2)**			–	
Harzianolide D **(3)**			*P. theae* 100	
Harzianolide E **(4)**			*P. theae* 100	
Harzianolide F **(5)**			*P. theae* 100	
Harzianolide G **(6)**			*P. theae* 100	
Sumalarin D **(7)**	China	*Penicillium sumatrense* MA-325	*V. alginolyticus* 16; *V. harveyi* 8	(Wang YR. et al., 2024)
Sumalarin E **(8)**			*V. alginolyticus* 64; *V. harveyi* 64	
Butyrolactone J **(9)**	China	*Aspergillus terreus* BTBU20211037	*S. aureus* 12.5	(Zhang X. et al., 2024)
Penicisteckin G **(10)**	China	*Penicillium Steckii* SCISO41228	MRSA[a] 4.0; *M. luteus* 4.0	(Huang et al., 2024)
Penicisteckin H **(11)**			MRSA[a] 4.0; *M. luteus* 8.0	
Penicacid L **(12)**	China	*Penicillium* sp. HN-66	*E.coli* 50	(Mo et al., 2024)
Penicacid M **(13)**			*E.coli* 50	
Penicacid N **(14)**			*E.coli* 50	
Penirubenone A **(15)**	China	*Penicillium rubens* BTBU20213035	*C. albicans* 12.5	(Xu et al., 2024)
Penirubenone B **(16)**			*C. albicans* 50	
10-*epi*-Pestaphilone G **(17)**	China	*Neopestalotiopsis* sp. HN-1-6	–	(Feng et al., 2024)
12-*epi*-Pestaphilone H **(18)**			–	
Pestaphilone J **(19)**			*S. aureus* 64; *E.coli* 256	
9-Hydroxyl-versicoisochromane B **(20)**			*S. aureus* 256; *E.coli* 128	
Dicitrinol A **(21)**	China	*Penicillium citrinum* TW132-59	*C.albicans* 16; *F.oxysporum* 8	(Wei et al., 2024)
Dicitrinol B **(22)**			*C.albicans* 16; *F.oxysporum* 8	
Dicitrinol C **(23)**			*C.albicans* 8; *F.oxysporum* 4	
Slamysin **(24)**	China	*Simplicillium lamelliciola* HDN13430	*B. cereus* 50	(Wu Z. et al., 2024)
Carnemycin H **(25)**	China	*Aspergillus ustus*	*R. solanacearum* 25	(Xue et al., 2024)
Carnemycin I **(26)**			*R. solanacearum* 15	
Stromemycin B **(27)**			*R. solanacearum* 3	
Asperporonin A **(28)**	China	*Aspergillus terreus* SCSIO41202	*X. citri* 312.5	(Zhang J. et al., 2024)
Asperporonin B **(29)**			*X. citri* 312.5	
Asperbutenolide A **(30)**	China	*Aspergillus terreus*	*S.aureus* ATCC25923 4	(Jiang et al., 2024)

[a]MRSA, methicillin-resistant *Staphylococcus aureus*.

2 Polyketides

From the EtOAc extract of liquid fermentation cultures of *Trichoderma harzianum* ZN-4, sourced from sediments in the Zhoushan coastal region, five previously unreported γ-butyrolactone harzianolides named B-F (**1**-**5**), along with their precursor harzianolide G (**6**), were isolated and characterized (Figure 3) (Zhou et al., 2024). In biological testing, Compound **1** exhibited moderate inhibitory effects on the phytopathogenic fungus *P. theae*, with a minimum inhibitory concentration (MIC) of 25 μg/mL. Compounds **3**-**6** displayed weaker activity, each having an MIC of 100 μg/mL against the same fungus (Table 1). Additionally, two new curvularin derivatives, sumalarins D and E (**7**, **8**), were isolated and identified from the mangrove-associated fungus *Penicillium sumatrense* MA-325 (Figure 3) (Wang YR. et al., 2024). These compounds demonstrated activity against aquatic

TABLE 2 Alkaloids with antibacterial activity from marine fungi.

Metabolites	Sources	Species	Antibacterial Activities (MIC, μg/mL)	Ref
Talarohydrazone A **(31)**	China	*Talaromyces amestolkiae*	*B. cereus* >150; *S. aureus* 32	(Wu J. et al., 2024)
Talarohydrazone B **(32)**		HDN21-0307	*B. cereus* >150; *S. aureus* 64	
Talarohydrazone C **(33)**			*B. cereus* 128; *S. aureus* 128	
Talarohydrazone D **(34)**			*B. cereus* 128; *S. aureus* 128	
Microascone A **(35)**	China	*Microascus* sp. SCSIO41821	*S. aureus* >100; *E. coli* 100; *B. subtilis* 100	(Yao et al., 2024)
Microascone B **(36)**			*S. aureus* >100; *E. coli* 100; *B. subtilis* 100	
2,3-Epoxyphomapyrrolidone C **(37)**			*S. aureus* 13; *E. coli* 100; *B. subtilis* 100	
16-Epiascomylactam B **(38)**			*S. aureus* 0.80; *E. coli* 0.20; *B. subtilis* 0.20	
24-Hydroxyphomapyrrolidone A **(39)**			*S. aureus* >100	
Microascone C **(40)**			*S. aureus* >100; *E. coli* 100; *B. subtilis* 100	
Microascone D **(41)**			*S. aureus* >100; *E. coli* 100; *B. subtilis* 100	
Microascone E **(42)**			*S. aureus* >100; *E. coli* >100; *B. subtilis* 100	
Methyl 3-((1-((2-carbamoylphenyl)amino)-1-oxopropan-2-yl) amino)-3-oxopropanoate **(43)**	Vietnam	*Penicillium chrysogenum* VH17	*E. faecalis* 32; *B.cereus* 128; *C. albicans* 64	(Anh et al., 2024)
O-dihydroxycyclopenol **(44)**		*Penicillium* sp. ZJUT-34	*C. violaceum ATCC12472* (20.65%) at 6.25 μg/mL	(Wang C. et al., 2024)

pathogenic bacteria, *V. alginolyticus* and *V. harveyi*, with MIC values spanning from 8 to 64 μg/mL, respectively (Table 1).

A novel compound, designated as butyrolactone J (**9**), has been extracted from the secondary metabolites produced by the marine-derived fungal strain *Aspergillus terreus* BTBU20211037 (Zhang X. et al., 2024). This compound displayed inhibitory activity against *Staphylococcus aureus* ATCC 25923, with a minimal inhibitory concentration (MIC) of 12.5 μg/mL (Table 1). Meanwhile, a pair of uncharacterized atropo-diastereomeric dimers, named penicisteckins G (**10**) and H (**11**), were isolated from the marine coral-associated fungus *Penicillium steckii* SCISO41228 (Figure 3) (Huang et al., 2024). Both compounds exhibited moderate antibacterial activity against a range of pathogenic strains tested, particularly against methicillin-resistant *Staphylococcus aureus* (MRSA) and *Micrococcus luteus*, with MIC values of 4.0 μg/mL (Table 1).

Three newly discovered mycophenolic acid derivatives, penicacids L-N (**12**-**14**), were obtained from a fungal isolate, *Penicillium* sp. HN-66, sourced from marine sediments in the

TABLE 3 Terpenoids with antibacterial activity from marine fungi.

Metabolites	Sources	Species	Antibacterial Activities (MIC, μg/mL)	Ref
Sesterchaetin A **(45)**	China	*Chaetomium globosum* SD-347	*E. coli* 32; *E. tarda* 16; *V. harveyi* 8.0	(Li XD. et al., 2024)
Sesterchaetin B **(46)**			*E. coli* 32; *V. harveyi* 16	
Chaetoketoics A **(47)** and B **(48)**			*E. coli* 4.0; *E. tarda* 4.0; *V. harveyi* 8.0	
Trichoderene A **(49)**	China	*Trichoderma effusum*	*A. tumefactions* 3.1	(Liu et al., 2024)
Trichoderene B **(50)**			*A. tumefactions* 12.5	
Trichoderene C **(51)**			*A. tumefactions* 12.5	
Trichoderene D **(52)**			–	
Millmerranones G **(53)**	China	*Aspergillus* sp. GXIMD 03004	*V. harveyi* 11.6 μM	(Cao et al., 2024)

TABLE 4 Peptides with antibacterial activity from marine fungi.

Metabolites	Sources	Species	Antibacterial Activities (MIC, μg/mL)	Ref
Cadophorin C **(54)**	China	*Penicillium* sp. GXIMD 03101	*V. harveyi* 3.12	(He et al., 2024)
Violaceotide B **(55)**	China	*Aspergillus insulicola*	–	(Li Q. et al., 2024)
Violaceotide C **(56)**		IMB18-072	*E. tarda* 128; *E. ictaluri* 128	
Violaceotide D **(57)**			*E. tarda* 128	
Violaceotide E **(58)**			–	
Simplicpeptaib A **(59)**	East Indian Ocean	*Simplicillium obclavatum* EIODSF 020	–	(Liang et al., 2024)
Simplicpeptaib B **(60)**			*R. solanacearum* 100	
Simplicpeptaib C **(61)**			*S. iniae* 100; *S. agalactiae* 100; *R. solanacearum* 50	
Simplicpeptaib D **(62)**			*S. agalactiae* 100; *R. solanacearum* 25	
Simplicpeptaib E **(63)**			*S. iniae* 25; *S. agalactiae* 50; *R. solanacearum* 100	
Simplicpeptaib F **(64)**			*S. iniae* 50; *S. agalactiae* 50; *R. solanacearum* 25	
Simplicpeptaib G **(65)**			*S. iniae* 12.5; *S. agalactiae* 25; *R. solanacearum* 100	
Simplicpeptaib H **(66)**			*S. iniae* 50; *S. agalactiae* 50; *R. solanacearum* 50	
Simplicpeptaib I **(67)**			*S. iniae* 12.5; *S. agalactiae* 50	
Simplicpeptaib J **(68)**			–	
Simplicpeptaib K **(69)**			*R. solanacearum* 100	

South China Sea (Figure 4) (Mo et al., 2024). Bioassay results indicated that these compounds exhibited weak inhibitory activity against *E. coli* ATCC25922, with minimum inhibitory concentrations (MICs) of 50 μg/mL (Table 1). Additionally, two novel polyketide derivatives, penirubenones A and B (**15** and **16**), were isolated from the marine-derived fungus *Penicillium rubens* BTBU20213035 (Xu et al., 2024). When combined with 0.0625 μg/mL rapamycin, compounds **15** and **16** demonstrated synergistic antifungal activity against *Candida albicans* at concentrations of 12.5 and 50 μg/mL, respectively (Table 1). Furthermore, four new compounds, three azaphilones (**17**-**19**) and one dihydroisocoumarin (**20**) were isolated from the sea-mud-derived fungus *Neopestalotiopsis* sp. HN-1-6, collected from the Beibu Gulf of China (Figure 4) (Feng et al., 2024). Among these, compounds **19** and **20** showed antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, with MICs ranging from 64 μg/mL to 256 μg/mL (Table 1).

Three novel and unusual citrinin derivatives, featuring a distinctive 6/5/7/5 core structure, named dicitrinols A-C (**21**-**23**), were isolated through the fermentation process of the hydrothermal vent-associated fungus *Penicillium citrinum* TW132-59 (Figure 5) (Wei et al., 2024). These compounds exhibited moderate antifungal activity against *Candida albicans* and *Fusarium oxysporum*, with MIC values ranging from 4 to 16 μg/mL (Table 1). Additionally, a new compound called slamysin (**24**) (Figure 5) was discovered from a cryptic cytochalasin-like gene cluster (*sla*) within the antarctic-derived *Simplicillium lamelliciola* HDN13430. This compound is characterized by an *N*-acylated amino acid structure and demonstrated weak anti-*Bacillus cereus* activity with an MIC of 50 μg/mL (Wu Z. et al., 2024).

Through biological activity-guided screening, three previously undescribed compounds, carnemycins H-I (**25**, **26**) and stromemycin B (**27**) were isolated from the secondary metabolites of a marine-derived *Aspergillus ustus* (Figure 5) (Xue et al., 2024). Among them, compound **27** exhibited excellent inhibitory activity against *R. solanacearum*, with an MIC value of 3 μg/mL (Table 1). Furthermore, asperporonin A (**28**) and asperporonin B (**29**) were identified as novel compounds possessing a highly unusual structural skeleton from a bioassay-guided isolation of the deep-sea fungus *Aspergillus terreus* SCSIO41202 (Zhang J. et al., 2024). These compounds showed weak activity against *Xanthomonas citri*

TABLE 5 Other natural products with antibacterial activity from marine fungi.

Metabolites	Sources	Species	Antibacterial Activities (MIC, μg/mL)	Ref
Terrein **(70)**	China	*Aspergillus terreus* HT5	membrane bactericidal ratios (*E. coli* 98.0%, *S. aureus* 94.9%)	(Zhang L. et al., 2024)
3b-Hydroxy-5a,6b-methoxyergosta-7,22-dien-15-one **(71)**	China	*Aspergillus asclerogenus*	*S. aureus* 64	(Wen et al., 2024)
Ergosta-6,22-dien-3b,5a,8a-triol **(72)**			–	

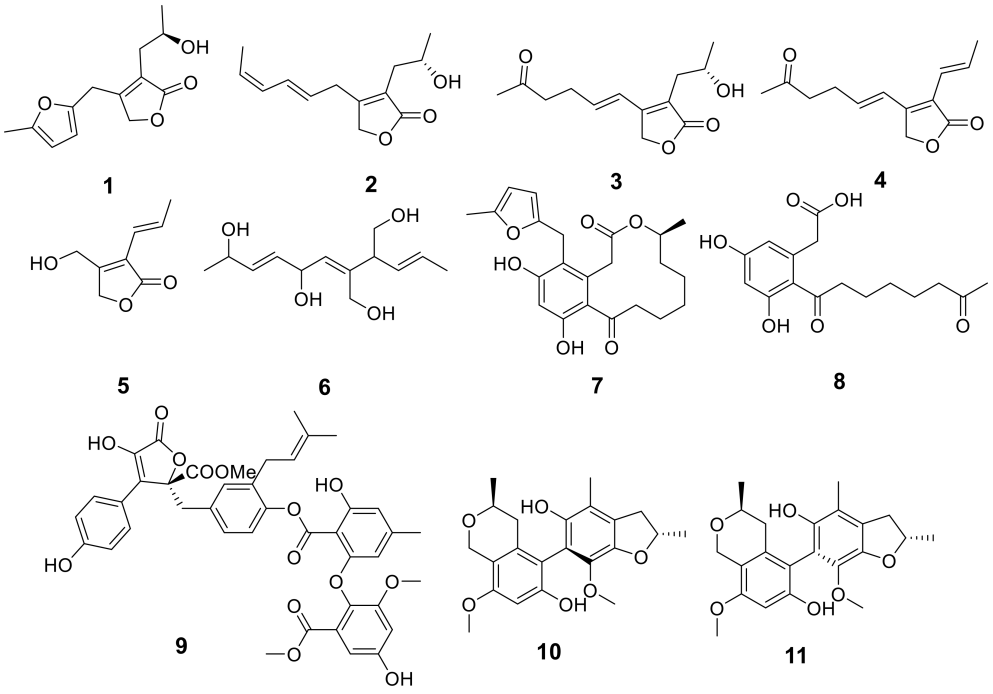

FIGURE 3
Chemical structures of compounds **1**-**11**.

at a concentration of 312.5 μg/mL (Table 1). An unusual aromatic butenolide, asperbutenolide A (**30**), with antimicrobial properties (*S. aureus* ATCC25923 4 μg/mL) from the marine fungus *Aspergillus terreus* SCAU011 (Jiang et al., 2024). Highlight the potential application valuation of asperbutenolide A as a new antibacterial agent.

3 Alkaloids

Using the one strain-many compounds (OSMAC) approach, four uncommon phenylhydrazone alkaloids, named talarohydrazones A-D (**31**-**34**), were isolated from the deep-sea cold seep-derived fungus *Talaromyces amestolkiae* HDN21-0307 (Figure 6) (Wu J. et al., 2024).

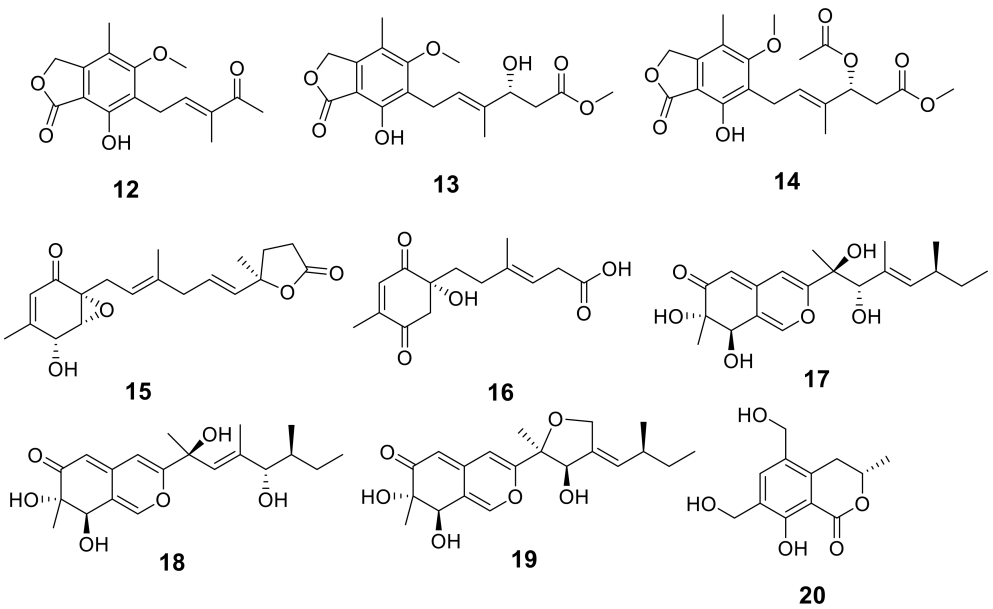

FIGURE 4
Chemical structures of compounds **12**-**20**.

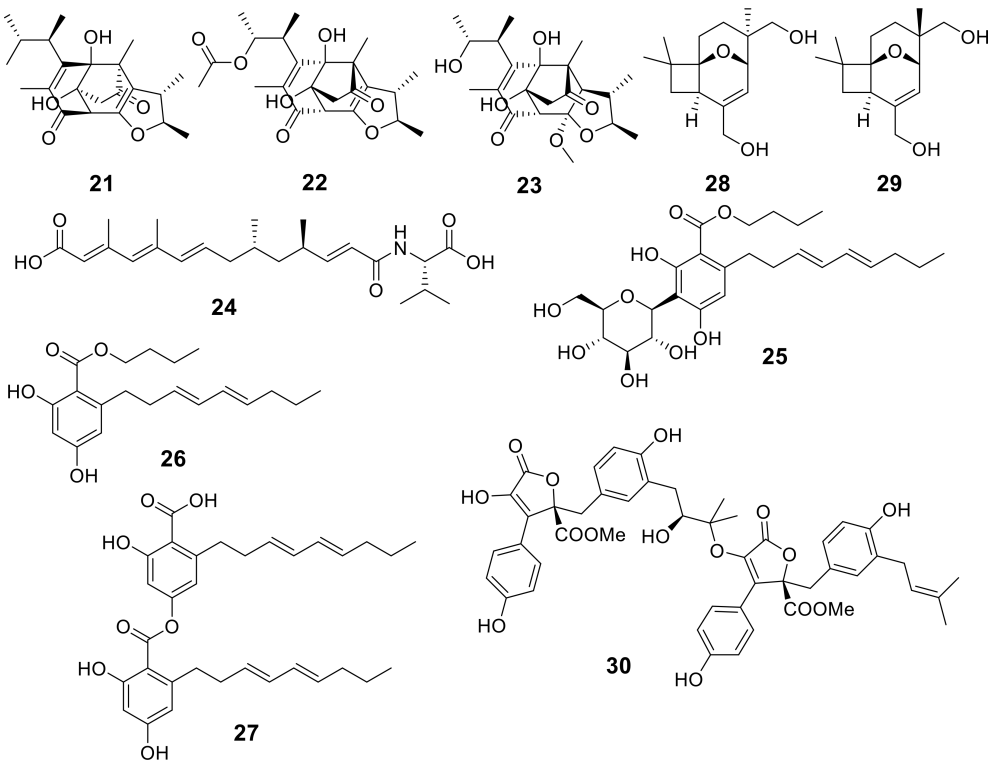

FIGURE 5
Chemical structures of compounds **21**-**30**.

These compounds exhibited weak antibacterial activity against *Staphylococcus aureus*, with MIC values falling between 32 and 128 μg/mL (Table 2). Additionally, eight novel decahydrofluorene-class alkaloids were isolated from the marine-derived fungus *Microascus* sp. SCSIO41821, including microascones A and B (**35** and **36**), 2,3-epoxyphomapyrrolidone C (**37**), 14,16-epiascomylactam B (**38**), 24-hydroxyphomapyrrolidone A (**39**), and microascones C-E (**40**-**42**) (Yao et al., 2024). Notably, compound **38** demonstrated potent antibacterial activity against various tested pathogens, with MIC values ranging from 0.20 to 0.80 μg/mL (Table 2). Furthermore, a new compound, methyl 3-((1-((2-carbamoylphenyl)amino)-1-oxopropan-2-yl)amino)-3-oxopropanoate (**43**), was isolated from the methanol extract of the marine-derived fungus *Penicillium chrysogenum* VH17 (Anh et al., 2024). Compound **43** showed antimicrobial activity against several reference microorganisms, with MIC values spanning from 32 to 128 μg/mL (Table 2). The marine fungus *Penicillium* sp. ZJUT-34, cultivated on a rice medium, yielded a novel alkaloid known as O-dihydroxycyclopenol (**44**). This compound exhibited a concentration-dependent inhibitory effect on the formation of violacein in *C. violaceum* ATCC12472 without affecting its growth. Specifically, at concentrations of 100, 50, 25, 12.5, and 6.25 μg/mL, compound **44** demonstrated inhibition rates of 42.03%, 39.77%, 34.69%, 29.41%, and 20.65%, respectively (Wang C. et al., 2024).

4 Terpenoids

Xiao-Dong Li et al. characterized two novel sesterterpenoids, named sesterchaetins A and B (**45** and **46**), as well as two new diepoxide polyketides, chaetoketoics A and B (**47** and **48**), from the culture extract of *Chaetomium globosum* SD-347, a fungal strain originating from deep-sea sediment (Li XD. et al., 2024). The sesterchaetins demonstrated significant inhibitory activity against the aquatic pathogen *Vibrio harveyi*, with MIC values of 8.0 and 16 μg/mL, respectively. The chaetoketoics exhibited notable antimicrobial activity against *E. coli* and *E. tarda*, both with an MIC value of 4.0 μg/mL (Table 3).

Furthermore, four new sesquiterpene derivatives, trichoderenes A-D (**49**-**52**), were isolated from the marine-derived fungus *Trichoderma effusum* (Liu et al., 2024). These compounds were tested for their antimicrobial activity against *A. tumefactions*, and compounds **49**-**51** showed inhibitory activity with MIC values of 3.1, 12.5, and 12.5 μg/mL, respectively (Table 3). Additionally, a new meroterpene derivative, millmerranones G (**53**), was identified from the mangrove-derived fungus *Aspergillus* sp. GXIMD 03004, which was isolated from the leaves of the mangrove plant *Acanthus ilicifolius* L. collected in Beibu Gulf, China (Cao et al., 2024). Compound **53** displayed weak activity against *Vibrio harveyi*, with an MIC value of 11.6 μM (Table 3; Figure 7).

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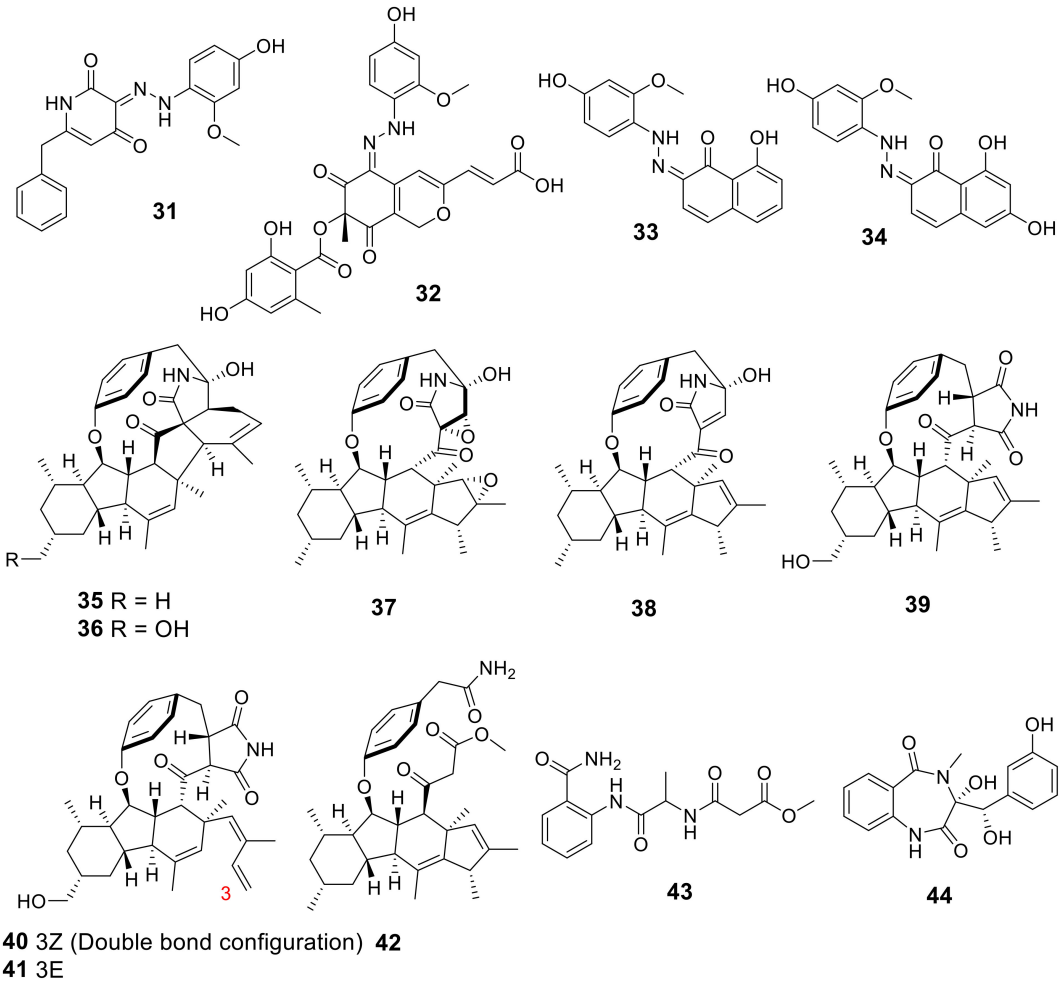

FIGURE 6
Chemical structures of compounds **31**-**44**.

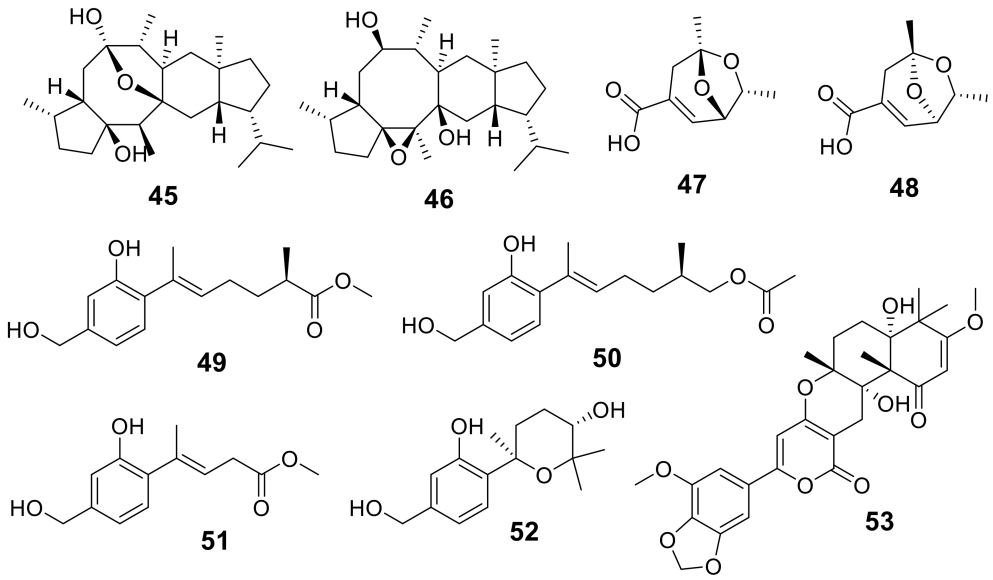

FIGURE 7
Chemical structures of compounds **45**-**53**.

5 Peptides

A novel cyclic heptapeptide, cadophorin C (**54**), was obtained from the mangrove-derived fungus *Penicillium* sp. GXIMD 03101, which was isolated from the mangrove species *Acanthus ilicifolius* L. (Figure 8) (He et al., 2024). Antibacterial testing revealed that compound **54** exhibited weak activity against the aquatic pathogen *Vibrio harveyi*, with an MIC value of 3.12 μg/mL (Table 4). Additionally, four new cyclic tetrapeptides, named violaceotides B-E (**55**-**58**), were discovered from the culture extract of the sponge-associated *Aspergillus insulicola* IMB18-072 after cocultivation with the marine-derived *Alternaria angustiovoidea* IMB20-805 (Figure 8) (Li Q. et al., 2024). Among these compounds, **56** and **57** demonstrated selective antimicrobial activity against the aquatic pathogenic bacteria *Edwardsiella tarda* and *E. ictaluri*, with MIC values of 128 μg/mL (Table 4).

To discover novel antibacterial agents, researchers employed a bioassay-guided method to explore the secondary metabolites of *Simplicillium obclavatum* EIODSF 020, a fungus sourced from the deep sea, which exhibits antibacterial properties against pathogens affecting plants and fish. This approach resulted in the identification of 11 novel peptaibiotics, named simplicpeptaibs A-K (**59**-**69**) (Figure 9) (Liang et al., 2024). Notably, compounds **62**, **64**, **65**, and **67** demonstrated potent activity against *Ralstonia solanacearum*, a tobacco pathogen, as well as *Streptococcus iniae* and *Streptococcus agalactiae*, pathogens that affect tilapia. The minimum inhibitory concentrations (MICs) of these compounds ranged from 12.5 to 100 μg/mL (Table 4).

Additionally, two novel cyclic depsipeptides, namely Rakicidin J and Rakicidin K, were extracted from the culture broth of the marine actinomycete *Micromonospora chalcea* FIM-R150103. Both compounds exhibited moderate antibacterial properties against ten strains of Gram-positive bacteria (Methicillin resistant *S. aureus*, *C. difficile*, etc.), with MIC values falling between 4 and over 32 μg/mL (Chen et al., 2024).

6 Miscellaneous

Terrein (**70**), a secondary metabolite initially sourced from the marine *Aspergillus terres* HT5 strain (Figure 10), demonstrated remarkable antibacterial properties. When integrated into a reverse osmosis membrane, it effectively eliminated 98.0% of *E. coli* and 94.9% of *S. aureus*, as shown in Table 5 (Zhang L. et al., 2024). Furthermore, two ergostane-type steroids containing oxygen, including a novel compound named 3b-hydroxy-5a,6b-methoxyergosta-7,22-dien-15-one (**71**), and a previously identified analogue, ergosta-6,22-dien-3b,5a,8a-triol (**72**), were extracted from crude samples of a marine sponge-associated fungus *Aspergillus* sp. (Figure 10) (Wen et al., 2024). Notably, compound **71** displayed antibacterial activity against *S. aureus* with a minimum inhibitory concentration of 64 μg/mL (Table 5).

7 Conclusions

The increasingly severe issue of global drug resistance has prompted vigorous efforts to search for new antibacterial agents. Marine natural products play a crucial role in drug discovery and serve as the premise for the early development of generic drugs (Hussain et al., 2021; Surendhiran et al., 2021). The marine medicinal organism resources are abundant, with good biodiversity and large variety reserves (Garcia-Perez et al., 2023;

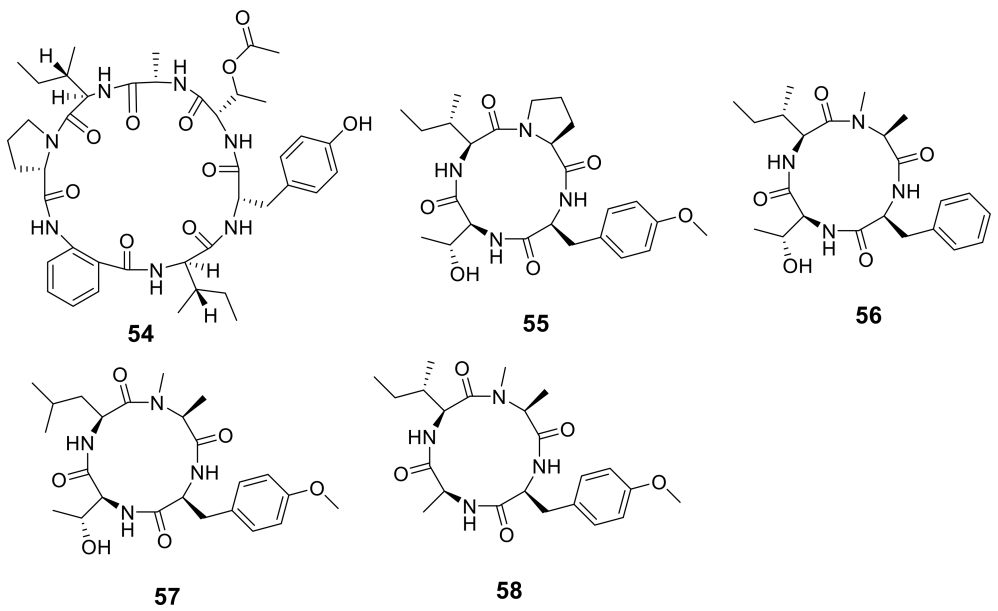

FIGURE 8
Chemical structures of compounds **54**-**58**.

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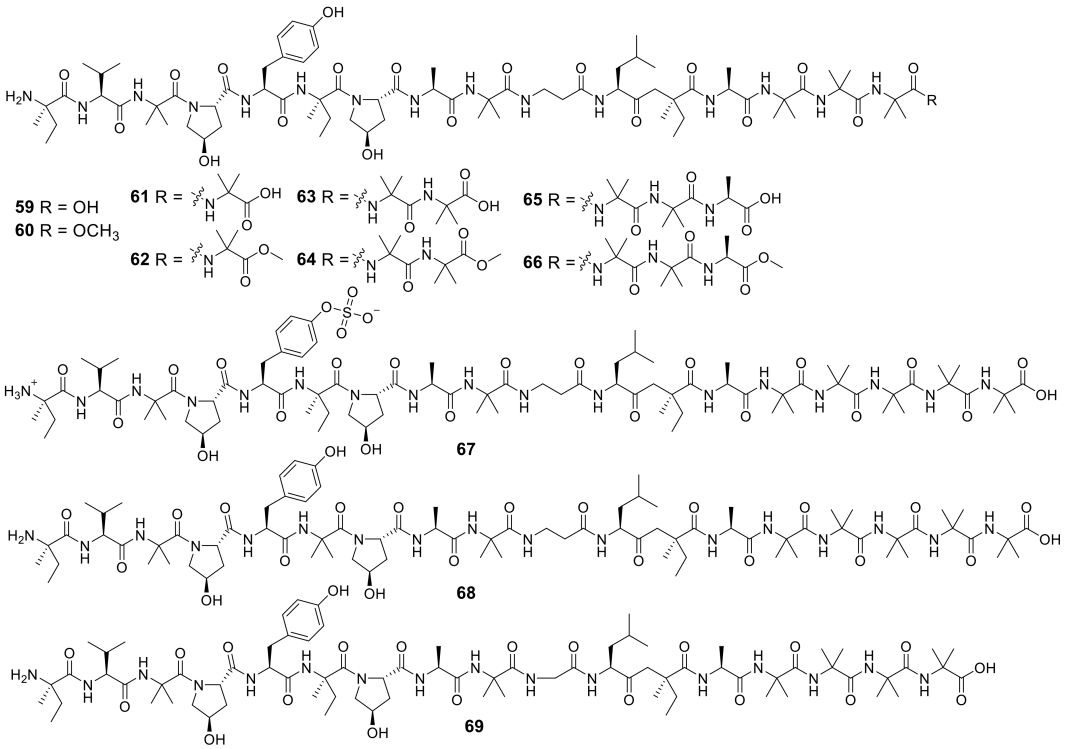

FIGURE 9
Chemical structures of compounds **59**-**69**.

Xu et al., 2023; Zhang Y. et al., 2024). Efficient development of these resources is the focus of marine drug development. Efforts should be made in multiple aspects simultaneously, including talent cultivation, scientific research, and industrialization research. While strengthening basic research, it is even more important to facilitate the entry of active compounds into clinical trials, achieve drug marketing and sales, drive economic development, and form a development model with a certain scale. Meanwhile, cooperation among enterprises, universities, and scientific research institutes should be strengthened to attract more government policy support and funding, thereby promoting the rapid development of the marine pharmaceutical economy and achieving greater leaps in marine drug development.

This review provides a detailed discussion of 72 compounds with antibacterial activity reported in 2024, originating from marine fungi, covering polyketides (Table 1), alkaloids (Table 2), terpenoids (Table 3), peptides (Table 4) and miscellaneous (Table 5). The article introduces the sources, chemical structures, biological activities of these compounds. In summary, the continuous emergence of drug-resistant pathogens poses a significant threat to human health. Currently, the effectiveness of most traditional antibiotics is waning, while secondary metabolites from marine microorganisms offer promising resources for exploring natural antimicrobials with unique structures, potent activities, and specific mechanisms of action. The marine environment serves as a valuable source of new natural products, potentially providing crucial leads for the discovery and development of novel antibiotics in the future. Natural products from marine fungi hold promise in inspiring medicinal chemists to search for antimicrobials superior to existing drugs. Furthermore, in recent years, novel structures and metabolic

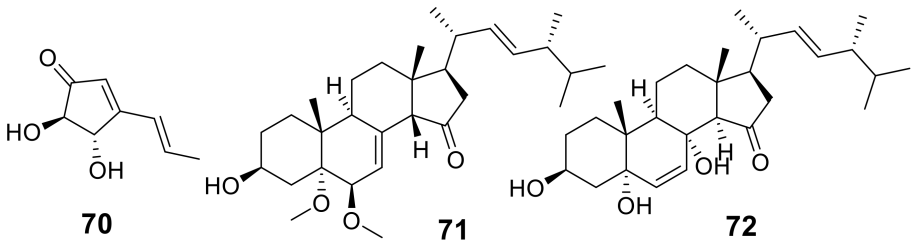

FIGURE 10
Chemical structures of compounds **70**-**72**.

(biosynthetic) pathways have attracted many researchers, and the bioactivities of these compounds have also sparked interest in the pharmaceutical development community. Overall, research on antibacterial natural drugs derived from marine fungi currently focuses mainly on isolation and structural elucidation, with a very limited number of subsequent pharmacological studies. More in-depth and thorough research efforts are needed to strengthen this promising field. Developing novel antibacterial agents from secondary metabolites of marine fungi and their synthetic derivatives deserves special attention.

Author contributions

CP: Data curation, Project administration, Resources, Visualization, Writing – review & editing. SH: Data curation, Methodology, Writing – original draft, Writing – review & editing. IM: Data curation, Formal Analysis, Methodology, Writing – review & editing. HJ: Data curation, Project administration, Supervision, Validation, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This work was supported by NSFC (No. 82404465), the Senior Talent Foundation of Jiangsu University (5501290012). The work was also supported by the Chugai foundation for innovative drug discovery science: C-FINDs (2025-CF-01). The work was supported by NSFC (81973191), project supported by the Modern Plateau Plant Medicine Research Project of Shanghai Jiao Tong University (SA1700208).

Conflict of interest

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

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