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REVIEW

Antimicrobial compounds from marine actinomycetes

Cong Wang[1,2] · Yuanyu Lu[2] · Shugeng Cao[1]

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Abstract Marine actinomycetes were the main origin of marine natural products in the past 40 years. This review was to present the sources, structures and antimicrobial activities of 313 new natural products from marine actinomycetes reported from 1976 to 2019.

Keywords Marine actinomycetes · Marine natural products · Chemical structures · Antimicrobial bioactivities

Introduction

Marine actinomycetes were the major resource of marine natural products owing to their chemical structures and diverse bioactivities. According to a statistic analysis of marine microbial natural products from 2010 to 2013, marine-derived actinomycetes accounted for 28% (= 253/895) of new marine natural products isolated from microbial origin (Zhao et al. 2013). This review covered the sources, structures and antimicrobial activities of 313 compounds derived from marine actinomycetes reported from 1976 to 2019. These new antimicrobial compounds have diverse chemical structures including polyketides, nitrogen-containing compounds, sterols and terpenoids. Majority of these compounds were antibacterial natural products, which consisted of 87% of the new marine natural products from marine-derived actinomycetes.

✉ Shugeng Cao
scao@hawaii.edu

[1] Department of Pharmaceutical Sciences, Daniel K. Inouye College of Pharmacy, University of Hawai'i at Hilo, 200 W. Kawili St., Hilo, HI 96720, USA

[2] Guangxi Key Laboratory of Chemistry and Engineering of Forest Products, School of Chemistry and Chemical Engineering, Guangxi University for Nationalities, Nanning 530006, China

Antimicrobial compounds from *Streptomyces* species

Antimicrobial compounds from *Streptomyces* sp. associated with sponges

Urauchimycins A and B (**1** and **2**) (Fig. 1) were isolated from *Streptomyces* sp. Ni-80. Compounds **1** and **2** exhibited antifungal activity against *Candida albicans* at 10 μg/mL (Imamura et al. 1993). Eight new antibacterial streptophenazines A–H (**3–10**) were obtained from *Streptomyces* sp. HB202 (Mitova et al. 2008). These compounds showed broad spectrum of inibitory activity against bacterial strains with MIC values ranging from 15.6 to 62.5 μg/mL (Mitova et al. 2008). Mayamycin (**11**) exhibited antibacterial activity with MIC values ranging from 2.5 to 8.4 μg/mL (Schneemann et al. 2010). Streptophenazine K (**12**) was isolated from *Streptomyces* HB202, which showed antibacterial activity against *B. subtilis* and *S. epidermidis* with MIC values of 21.6 and 14.5 μM, respectively (Kunz et al. 2014). *Streptomyces* sp. BCC45596 yielded urdamycinone E (**13**), urdamycinone G (**14**), and dehydroxyaquayamycin (**15**), which were active against *M. tuberculosis* with MIC values of 3.13, 12.50 and 6.25 μg/mL, respectively (Supong et al. 2012). Jiao et al. isolated four new compounds from *Streptomyces* sp. LHW52447, namely actinomycins D1 – D4 (**16–19**), which displayed inhibitory activity against *S. aureus* (MRSA) with MIC values ranging from 0.125 to 1.0 μg/mL (Jiao et al. 2018).

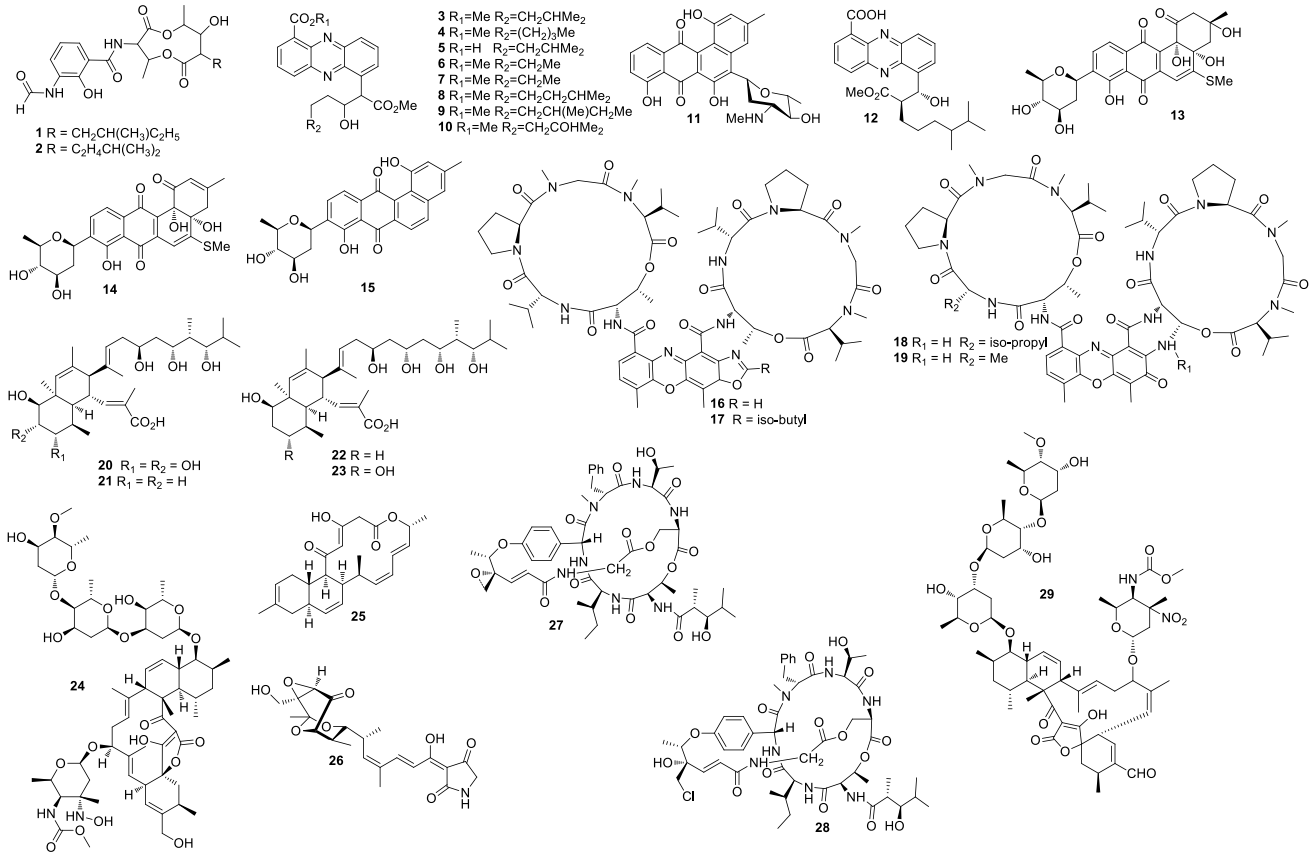

Fig. 1 Structures of compounds **1–29**

Antimicrobial compounds from *Streptomyces* sp. associated with corals

Four nahuoic acids B–E (**20**–**23**) were isolated from *Streptomyces* sp. SCSGAA 0027, which exhibited weak antibiofilm activity against *Shewanella onedensis* MR-1 biofilm (Nong et al. 2016). *Streptomyces* sp. M-207 produced lobophorin K **(24)**, which inhibited *S. aureus* EPI167 (MRSA) with an MIC_{90} value in the range of 40−80 μg/mL (Braña et al. 2017a). Anthracimycin B (**25**) was obtained from a culture of *Streptomyces cyaneofuscatus* M-169, which displayed antimicrobial activity against *S. aureus* MRSA (MB5393), *S. aureus* MSSA (ATCC 29213), *E. faecium* VANS (CL144754) and *E. faecalis* VANS (CL144492) with MICs below the lowest concentration tested at 0.03 μg/mL and inhibited *M. tuberculosis* (H37Ra) with an MIC value of 1−2 μg/mL (Rodríguez et al. 2018). Isotirandamycin B **(26)** was isolated from a culture of *Streptomyces* sp. SCSIO 41399, which displayed antimicrobial activity against *Streptococcus agalactiae* with an MIC value of 11.5 μM (Cong et al. 2019).

Antimicrobial compounds from *Streptomyces* sp. associated with other marine animals

Streptomyces hygroscopicus yielded salinamides A (**27**) and B (**28**). Both compounds were active against *S. pneumoniae* with an equal MIC value of 4 μg/mL. Both compounds were also active against *S. pyrogenes* with MIC values of 4 and 2 μg/mL, respectively (Trischman et al. 1994). *Streptomyces* sp. 1053U.I.1a.3b produced lobophorin I (**29**), which exhibited inhibitory activity against *M. tuberculosis* and *B. subtilis* with MIC values of 2.6 and 10.6 μM, respectively (Lin et al. 2014). Salinamide F (**30**) (Fig. 2) obtained from *Streptomyces* sp. CNB091, had a broad spectrum of antibacterial activity (Hassan et al. 2015). Streptoseomycin (**31**) was isolated from *Streptomyces seoulensis* A01, which exhibited inhibitory activityagainst *H. pylori*, *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Eubacterium brachy*, *Propionibacterium acnes*, *S. aureus*, *Micrococcus luteus* and *B. subtilis* with MIC values ranging from 2 to 64 μg/mL (Zhang et al. 2018a).

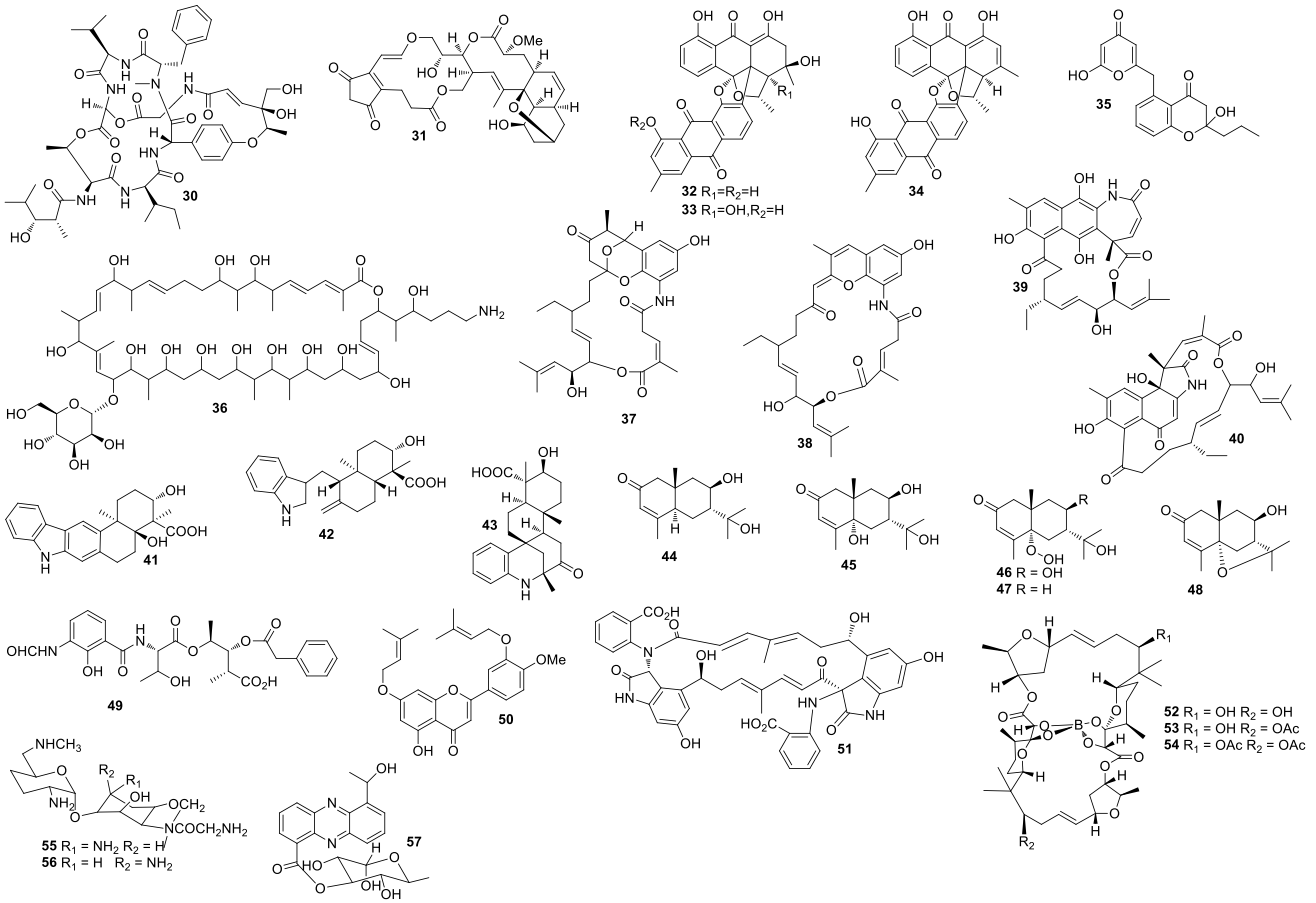

Fig. 2 Structures of compounds **30–57**

Antimicrobial compounds from *Streptomyces* sp. associated with marine algae

Bisanthraquinone derivatives A−C (**32–34**), were isolated from *Streptomyces* sp. N1-78-1, which displayed antimicrobial activity against MRSA with IC_{50} values of 0.15, 0.36 and 31 µM, respectively (Socha et al. 2006). 2-Hydroxy-5-((6-hydroxy-4-oxo-4*H*-pyran-2-yl) methyl)-2-propylchroman-4-one (**35**) was obtained from *Streptomyces* sp. WR1L1S8, which showed antibacterial activity against *E. coli* ATCC 25922 and MRSA ATCC 43300 with MIC values of 16 and 2 µM, respectively (Djinni et al. 2013). Braña et al. isolated desertomycin G (**36**) from *Streptomyces althioticus* MSM3, which exhibited inhibitory activity against a wide spectrum of bacterial strains, with MIC values ranging from 4 to 64 µg/mL (Braña et al. 2019).

Antimicrobial compounds from *Streptomyces* sp. associated with mangrove

Divergolides A–D (**37–40**), were isolated from a culture of *Streptomyces* sp. HKI0576, which displayed antimicrobial activity against *B. subtilis*, *Mycobacterium vaccae* and MRSA with inhibition zone diameters of 10−20 mm (Ding et al. 2011a). Xiamycin B (**41**), indosespene (**42**), and sespenine (**43**) were obtained from *Streptomyces* sp. HKI0595, which exhibited antibacterial activity against MRSA (Ding et al. 2011b). Kandenols A–E (**44–48**) were isolated from *Streptomyces* sp. HKI0595, which showed weak antimicrobial activity against *B. subtilis* ATCC 6633 and *Mycobacterium vaccae* IMET 10,670 (Ding et al. 2012). Antimycin B2 (**49**) was discovered from *S. lusitanus* XM52, which displayed antibacterial activity against *S. aureus* and *L. hongkongensis* with MIC values of 32 and 8 µg/mL, respectively (Han et al. 2012).

Antimicrobial compounds from *Streptomyces* sp. associated with other plants

Streptomyces sp. MA-12 yielded 7,3′-di-(γ, γ-dimethylallyloxy)-5-hydroxy-4′-methoxyflavone (**50**). Compound **50** was active against *C. musae*, *G. zeae* (Schweinitz) Petch, and *P. citrinum* at 0.25 mM with inhibition zone diameters of 12.7, 13.00 and 12.17 mm, respectively

(Ding et al. 2013). Juanlimycin A (**51**) was isolated from a culture of *Streptomyces* sp. LC6, which showed moderate inhibition on the secretion of *Salmonella* Pathogenicity Island-1 effectors, SipA/B/C/D (Zhang et al. 2014).

Antimicrobial compounds from *Streptomyces* sp. from marine sediments

Aplasmomycins A−C (**52–54**) were isolated from *S. griseus* SS-20, which inhibited the growth of Gram-positive bacteria (Okami et al. 1976; Sato et al. 1978). Istamycins A and B (**55** and **56**) were purified from *S. tenjimariensis* SS-939, which showed inhibition against Gram-positive and Gram-negative bacteria (Okami et al. 1979). Phenazine alkaloid (**57**) was obtained from a culture of *Streptomyces* sp. CNB-253, which displayed antimicrobial activity against *Hemophilus influenza* and *Clostridium perfringens* with MIC values of 1 and 4 μg/mL, respectively (Pathirana et al. 1992). Wailupemycin A (**58**) (Fig. 3) and 3-epideoxyenterocin (**59**) were isolated from *Streptomyces* sp. BD-26 T(20) (Sitachitta et al. 1996). Compound **58** showed antibacterial activity against *S. aureus* with an inhibition zone diameter of 18 mm at 1 mg/6 mm disk. Compound **59** showed antibacterial activity against *E. coli* with an inhibition zone diameter of 15 mm at 0.1 mg/6 mm disk. *δ*-Indomycinone (**60**) was obtained from *Streptomyces* sp. B 8300, which showed antibacterial activity against *B. subtilis* with an MIC value of 100 μg/mL (Biabani et al. 1997). *Streptomyces* sp. CNB-689 produced actinoflavoside (**61**), which exhibited wide antibacterial activity against *S. pneumonia*, *S. pyrogenes*, *S. aureus* and *M. luteus*at with an equal MIC value of 64 μg/mL (Jiang et al. 1997). Dimethyl 5, 10-dihydrophenazine-l,6-dicarboxylate (5, 10-Dihydrophencomycin methyl ester) (**62**) was isolated from *Streptomyces* sp. B 8251, which displayed weak antimicrobial activity against *E. coli* and *B. subtilis* (Pusecker et al. 1997). Lysophosphatidyl inositols A and B (**63** and **64**) were isolated from *Streptomyces sp.* M428, and both compounds showed antifungal activities against *C. albican* with MIC values of 5.0 and 2.5 μg/mL, respectively (Cho et al. 1999). Lornemide A (**65**) was discovered from *Streptomyces* sp. MSTMA190, which demonstrated inhibitory activity against *B. subtilitis* with a LD_{99} value of 50 μg/mL (Capon et al. 2000). 2-Amino-9,13-dimethyl heptadecanoic acid (**66**) was produced by *Streptomyces* sp. 1010, which showed inhibitory activity against *M. luteus* and *B. subtilis* with MIC values of 15 and 50 μg/mL, respectively (Ivanova et al. 2001). A study of *Streptomyces* sp. B7064 led to the identification of chalcomycin B (**67**), which displayed antibacterial activity against *S. aureus*, *E. coli* and *B. subtilis* with inhibition zone diameters of 23, 28, and 21 mm at 10 μg/disk, respectively (Asolkar et al. 2002). Bonactin (**68**) was isolated from *Streptomyces* sp. BD21-2 and was active against *S. aureus*, *B. megaterium* and *S. cerevisiae* with the inhibition zone diameters of 7.0, 8.0 and 7.5 mm at 1 mg/mL, respectively (Schumacher et al. 2003). Lajollamycin (**69**) was discovered from *S. nodosus* NPS007994, which displayed antibacterial activity against *S. pneumonia* and *S. aureus* with MIC values of 1.5 and 5 μg/mL, respectively (Manam et al. 2005). Daryamides A and B (**70** and **71**) was obtained from *Streptomyces* sp. CNQ-085, which exhibited antifungal activity against *C. albicans* with MIC values of 62.5 and 125 μg/mL, respectively (Asolkar et al. 2006). 5,7-Dihydroxy-5,6,7,8-tetrahydroazocin-2(1*H*)-one (**72**) obtained from *Streptomyces* sp.

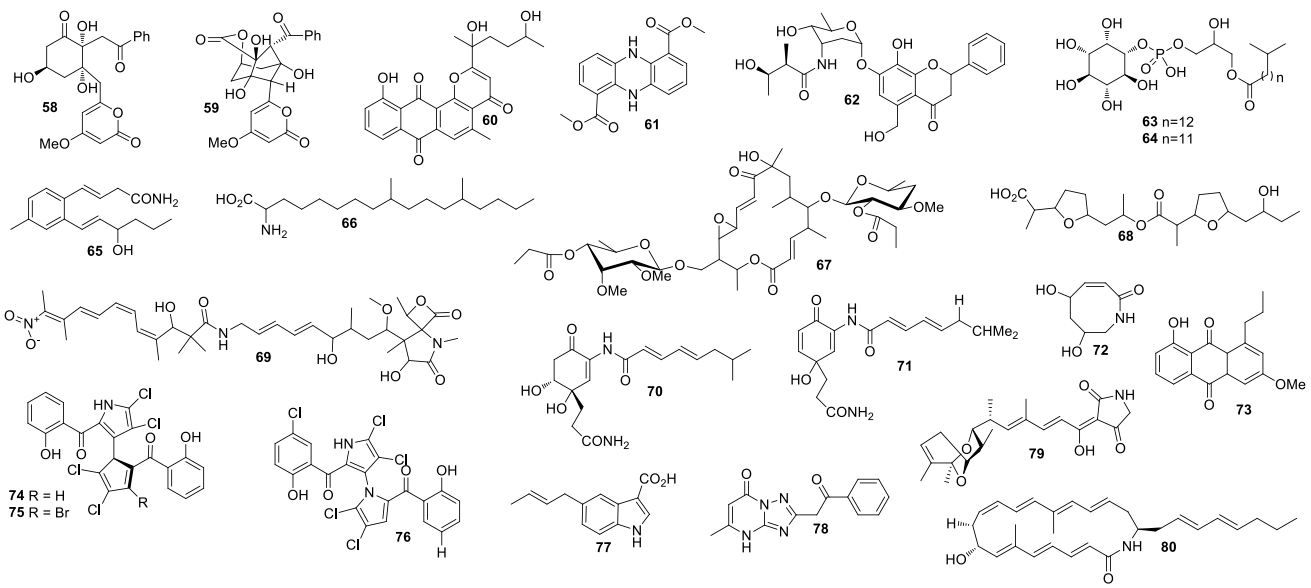

Fig. 3 Structures of compounds **58–80**

QD518 showed inhibitory activity against *S. aureus* at 40 µg/disc with an inhibition zone diameter of 11 mm (Wu et al. 2006). *Streptomyces* sp. B8000 yielded 8-hydroxy-3-methoxy-1-propylanthraquinone (**73**), which was active against *S. aureus and Streptomyces viridochromogenes* at 40 µg/disc with inhibition zone diameters of 14 and 12 mm, respectively (Poumale et al. 2006). Marinopyrroles A (**74**) and B (**75**) were isolated from a culture of *Streptomyces* sp. CNQ-418, which demonstrated antimicrobial activity against MRSA with MICs of 0.61 and 1.10 µM, respectively (Hughes et al. 2008). Marinopyrrole C (**76**) displayed antimicrobial activity against MRSA with an MIC value less than 1 µg/mL (Hughes et al. 2010). *Streptomyces* sp. MS239 produced **77**, which showed weak antibacterial activity against *B. subtilis* ATCC6633 (Motohashi et al. 2008). Essramycin (**78**) was obtained from *Streptomyces* sp. Merv8102, which displayed antibacterial activity against *E. coli* (ATCC 10536), *P.aeruginosa* (ATCC 10145), *B. subtilis* (ATCC6051), *S. aureus* (ATCC 6538), and *M. luteus* (ATCC 9341) with the MIC values of 8.0, 3.5, 1.0, 1.0 and 1.5 µg/mL, respectively (El-Gendy et al. 2008). Tirandamycin C (**79**) was isolated from a culture of *Streptomyces* sp. 307–9, which demonstrated antimicrobial activity against vancomycin-resistant *E. faecalis* with an MIC value of 110 µM (Carlson et al. 2009). 8-Deoxyheronamide C (**80**) was isolated from *Streptomyces* sp. CMB-M0406, which exhibited inhibitory activity against wild-type fission yeast with an MIC value of 5.8 µM (Sugiyama et al. 2014). Heronapyrroles A−C (**81–83**) (Fig. 4) were isolated from *Streptomyces* sp. CMB-M0423, which inhibited the growth of Gram-positive bacteria with MIC values ranging from 0.6 to 6.5 µM (Raju et al. 2010). Antimycins A_{19} and A_{20} (**84** and **85**) were discovered from *S. antibioticus* H74-18, which displayed antifungal activity against *C. albicans* with MIC values of 5 and 10 µg/mL, respectively (Xu et al. 2011). Fijimycins A–C (**86–88**) were obtained from *Streptomyces* sp. CNS-575, which inhibited the growth of MRSA (ATCC33591, Sanger 252, UAMS1182) with MIC values ranging from 4 to 16 µg/mL (Sun et al. 2011). Glucopiericidin C (**89**) isolated from *Streptomyces* sp. B8112 was active against *Mucor miehei* (Shaaban et al. 2011). Lobophorin F (**90**) was produced by *Streptomyces* sp. SCSIO 01127, which demonstrated inhibitory activity against *S. aureus* ATCC 29213 and *E. faecalis* ATCC 29212 with an equal MIC value of 8 µg/mL (Niu et al. 2011). Ansalactams B−D (**91–93**) were purified from *Streptomyces* sp. CNH-189, which exhibited inhibitory activities against MRSA with MIC values of 31.2, 31.2 and 62.5 µg/mL, respectively (Wilson et al. 2011). Three compounds meroindenon (**94**), merochlorins E (**95**) and F (**96**) were produced by *Streptomyces* sp. CNH-189. Compound

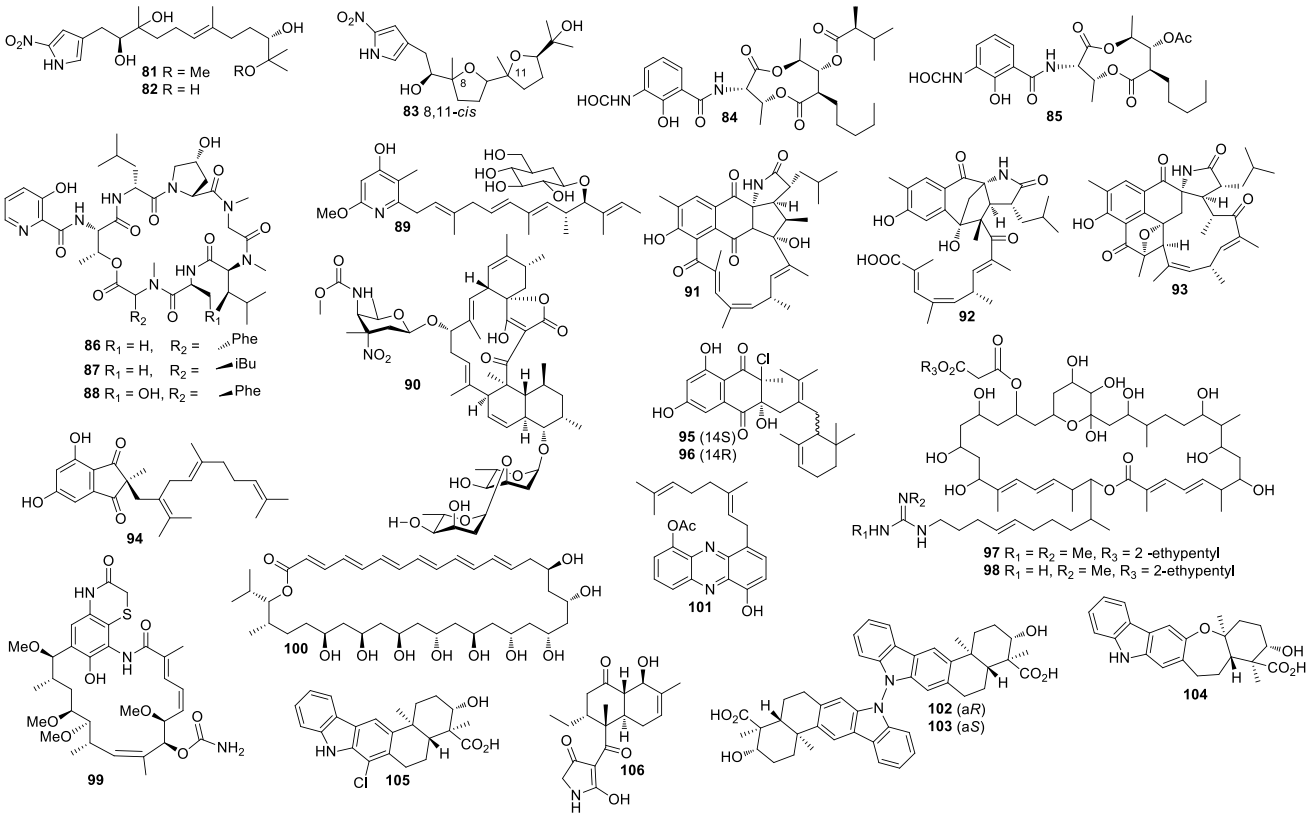

Fig. 4 Structures of compounds **81–106**

94 displayed antibacterial activity against *B. subtilis*, *K. rhizophila* and *S. aureus* with MIC values of 16, 64 and 128 µg/mL, respectively. Compounds **95** and **96** displayed antibacterial activities against *B. subtilis*, *K. rhizophila* and *S. aureus* with MIC values in the range of 1−2 µg/mL (Ryu et al. 2019). Coumpounds **97** and **98** identified from *Streptomyces* sp. 211,726 were active against *C. albicans* with MIC values of 2.34 and 12.50 µg/mL, respectively (Yuan et al. 2011). Heronamycin A (**99**) was produced by *Streptomyces* sp. CMB-M0392, which displayed inhibition against *B. subtilis* ATCC6052 and ATCC6633 with MIC values of 8 and 14 µg/mL, respectively (Raju et al. 2012). Bahamaolide A (**100**) was produced by *Streptomyces* sp. CNQ343, which showed inhibition against *C. albicans* and various pathogenic fungi (Kim et al. 2012). Geranylphenazinediol (**101**) was isolated from *Streptomyces* sp. LB173, which exhibited weak antibacterial activity (Ohlendorf et al. 2012). Dixiamycins A (**102**) and B (**103**), oxiamycin (**104**) and chloroxiamycin (**105**) were purified from *Streptomyces* sp. SCSIO 02999, which demonstrated inhibitory activity against *E. coli* ATCC 25922 with MIC values of 8, 8, 16 and 4 µg/mL, respectively (Zhang et al. 2012). Compounds **102–105** also exhibited inhibitory activity against *S. aureus* ATCC29 213 with MIC values of 8, 16, 16 and 8 µg/mL, respectively. Compounds **102**, **103** and **105** displayed inhibitory activity against *B. subtilis* SCSIO BS01 with MIC values of 64, 128 and 64 µg/mL, respectively. Compounds **102** and **103** showed inhibitory activity against *B. thuringiensis* SCSIO BT01 with MIC values of 64 and 64 µg/mL, respectively. Streptosetin A (**106**) was obtained from *Streptomyces* sp. CP13-10, and it displayed antifungal activity against yeast Sir2p with an MIC value of 2.5 mM (Amagata et al. 2012). *Streptomyces* sp. RJA2961 was reported to produce novobiocin (**107**) (Fig. 5), desmethylnovobiocin (**108**) and 5-hydroxynovobiocin (**109**), which displayed antibacterial activity against MRSA (ATCC 33,591) with MIC values of 0.25, 16 and 8 µg/mL, respectively (Dalisay et al. 2013). Iso-16-deethylindanomycin (**110**), 16-deethylindanomycin methyl ester (**111**) and iso-16-deethylindanomycin methyl ester (**112**) were isolated from a culture of *S. antibioticus* PTZ0016, which showed antimicrobial activity against *S. aureus* ATCC6538 with MIC values of 6.0, 6.0 and 8.0 µg/mL, respectively (Lian et al. 2013). Three compounds marfuraquinocins A (**113**), C and D (**114** and **115**) were produced

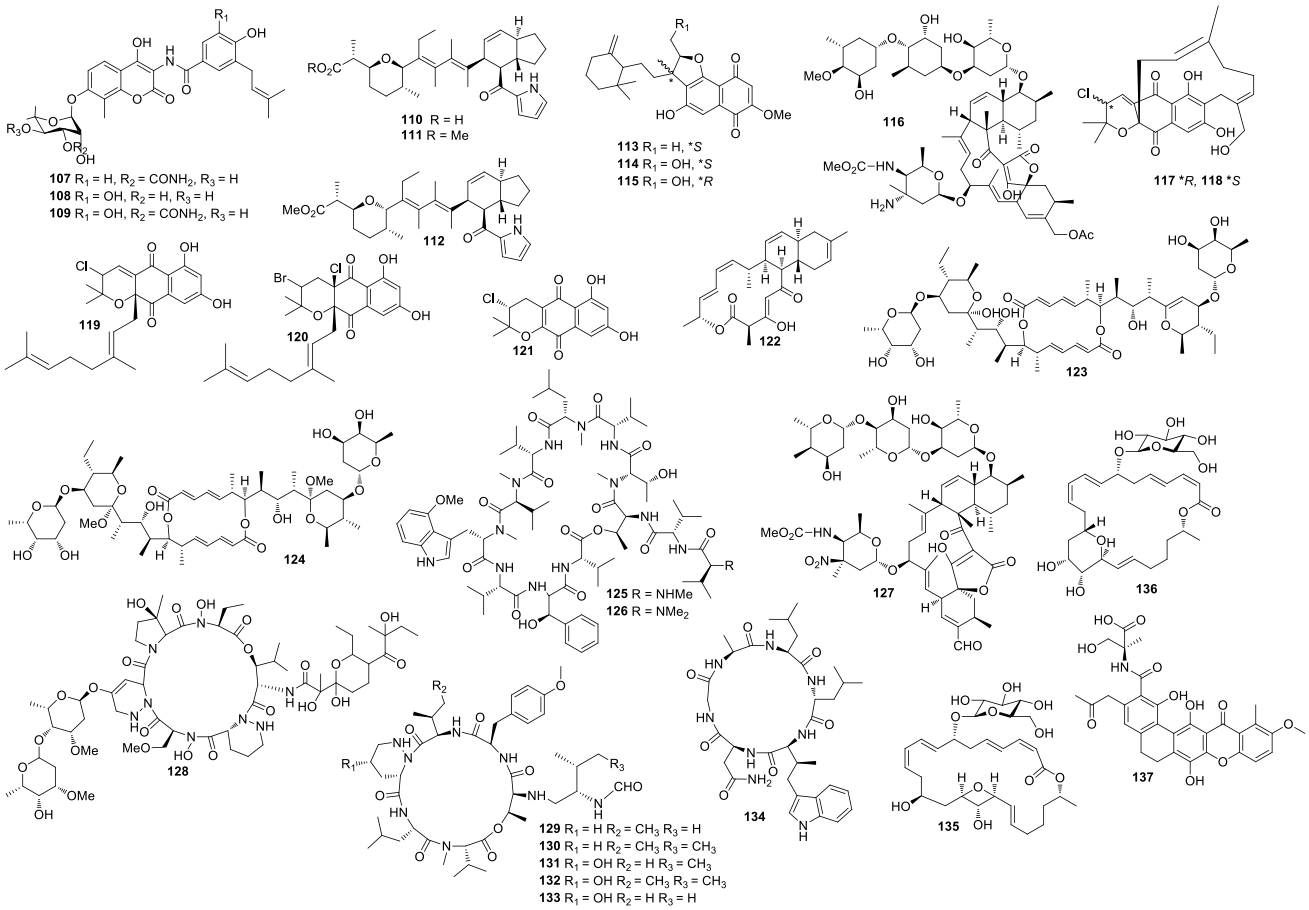

Fig. 5 Structures of compounds **107–137**

by *S. niveus* SCSIO 3406, and they displayed antibacterial activities against *S. aureus* ATCC 29,213 with an equal MIC value of 8 μg/mL. Compounds **114** and **115** showed antibacterial activities against methicillin-resistant *Staphylococcus epidermidis* shhs-E_1 with an equal MIC value of 8 μg/mL (Song et al. 2013). *Streptomyces* sp. MS100061 yielded lobophorin G1 (**116**), which inhibited the growth of *B. subtilis* and *M. tuberculosis* H37Rv with MIC values of 3.1 and 32 μg/mL, respectively (Chen et al. 2013). Napyradiomycins A and B (**117** and **118**) were produced by *Streptomyces* sp. CNQ-329, which possessed inhibitory activity against MRSA with MIC values of 16 and 64 μg/mL, respectively (Cheng et al. 2013). Designated 4-dehydro-4a-dechlorona pyradiomycin A1 (**119**), 3-dechloro-3-bromonapyradiomycin A1 (**120**), and 3-chloro-6,8-dihydroxy-8-α-lapachone (**121**) from *Streptomyces* sp. SCSIO 10,428 exhibited antibacterial activity against *B. thuringensis* SCSIO BT01 with MIC values of 8, 1 and 16 μg/mL, respectively. They exhibited antibacterial activity against *B. subtilis* SCSIOBS01 with MIC values of 4, 1 and 8 μg/mL, respectively (Wu et al. 2013a). Compounds **119** and **120** showed antibacterial activity against *S. aureus* ATCC 29,213 with MIC values of 4.0 and 0.5 μg/mL, respectively. *Streptomyces* sp. CNH365 afforded anthracimycin (**122**), which exhibited antibacterial activity against *B. anthracis* UM23C1-1, *S. aureus* ATCC, *E. faecalis* ATCC 29,212, *S. pneumoniae* ATCC 51,916 and *H. influenzae* ATCC 31,517 with MIC values of 0.03125, 0.0625, 0.125, 0.25 and 4 μg/mL, respectively (Jang et al. 2013). 11′,12′-Dehydroelaiophylin (**123**) and 11,11′-O-dimethyl-14′-deethyl-14′-methylelaiophylin (**124**) were isolated from *Streptomyces* sp. 7–145, which displayed good inhibitory activity against MRSA and vancomycin-resistant *enterococci* pathogens (Wu et al. 2013b). Two new compounds ohmyungsamycins A (**125**) and B (**126**) were isolated from *Streptomyces* sp. SNJ042. Compound **125** exhibited inhibitory activity against *B. subtilis* ATCC6633, *K. rhizophila* NBRC12708 and *P. hauseri* NBRC3851 with MIC values of 4.28, 1.07 and 2.14 μM, respectively, while compound **126** was active against *K. rhizophila* NBRC12708 with an MIC value of 8.5 μM (Umet al. 2013). Lobophorin H (**127**) was discovered from *Streptomyces* sp. 12A35, which displayed inhibitory activity against *S. aureus* ATCC29213 and *B. subtilis* CMCC63501 with MIC values of 50 and 1.57 μg/mL, respectively (Pan et al. 2013). Mollemycin A (**128**) was identified from *Streptomyces* sp. CMBM0244 and it was active against *S. aureus* ATCC 25293 and ATCC 9144, *S. epidermidis* ATCC 12228, *B. subtilis* ATCC 6051 and ATCC 6633, *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853 and *Mycobacterium bovis* (BCG) with MIC values of 50, 10, 50, 10, 10, 10, 50 and 3200 nM, respectively (Raju et al. 2014). Marformycins A−E (**129–133**) exhibited inhibitory activities against *M. luteus* with MIC values of 0.25, 4.0, 0.25, 0.063 and 4.00 μg/mL, respectively (Zhou et al. 2014). Desotamide B (**134**) was obtained from a culture of *S. scopuliridis* SCSIO ZJ46, which demonstrated antimicrobial activity against *S. aureus* ATCC29213, *S. pnuemoniae* NCTC 7466 and MRSA with MIC values of 16.0, 12.5 and 32.0 μg/mL, respectively (Song et al. 2014). Glycosylated macrolactins A1 (**135**) and B1 (**136**) were isolated from *Streptomyces* sp. 06CH80, which displayed antibacterial activities against *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. aureus* and *S. cerevisiae* with MIC values in the range of 0.027 to 0.22 μM/mL (Mondol and Shin 2014). Buanmycin (**137**) was isolated from *Streptomyces* sp. SNR69, and compound **137** exhibited antibacterial activity against five bacterial strains with MIC values ranging from 0.7 to 21.1 μg/mL (Moon et al. 2015). Chemical investigation of a culture extract of *Streptomyces* sp. CMB-M0150 led to the discovery of aranciamycins I (**138**) (Fig. 6) and J (**139**). **138** and **139** showed inhibitory activity against *M. tuberculosissurrogate* with MIC values in the range of 0.7 to 1.7 μM, respectively (Khalil et al. 2015). A fermentation broth of *Streptomyces* sp. SNM5 yielded mohangamides A (**140**) and B (**141**), which exhibited inhibitory activity against *C. albicans* ICL with IC_{50} values of 4.4 and 20.5 μM, respectively (Bae et al. 2015a). Hormaomycins B (**142**) and C (**143**) from *Streptomyces* sp. SNM5 displayed broad antibacterial activities with MIC values ranging from 0.23 to 114 μM (Bae et al. 2015b). *Streptomyces zhaozhouensis* CA-185989 yielded isoikarugamycin (**144**), 28-*N*-methylikarugamycin (**145**), and 30-oxo-28-*N*-methylikarugamycin (**146**). **144**– **146** were active against MRSA with MIC values of 1–4, 1–4, 32–64 μg/mL, respectively. Compound **144** was active against *C. albicans* and *A. fumigatus* with MIC values of 2–4 and 4–8 μg/mL, respectively, and **145** was active against *C. albicans* and *A. fumigatus* with MIC values of 4 and 4–8 μg/mL, respectively (Lacret et al. 2015). *S. rochei* 06CM016 yielded compounds **147** and **148**. **147** showed antimicrobial activity against *E. coli* O157:H7 RSKK 234, MRSA DSM 11729 and *C. albicans* DSM 5817 with MIC values of 16, 8 and 4 μg/mL, respectively (Aksoy et al. 2016). **148** exhibited antimicrobial activity against *E. coli* O157:H7 RSKK 234, MRSA DSM 11729 and *C. albicans* DSM 5817 with MIC values of 16, 16 and 8 μg/mL, respectively (Aksoy et al. 2016). *N*-acetyl-*N*-demethylmayamycin (**149**) was obtained from *Streptomyces* sp. 182SMLY, which was active against MRSA with an MIC of 20.0 μM (Liang et al. 2016). Neo-actinomycins A (**150**) and B (**151**) were discovered from *Streptomyces* sp. IMB094, which displayed antibacterial activity against MRSA and vancomycin-resistant *Enterococci* with MIC values in the range of 16 to 64 μg/mL (Wang et al. 2017). Strepchazolin A (**152**) was obtained from *Streptomyces chartreusis* NA02069, which showed antibacterial activity against *B. subtilis* with an MIC value of 64 μM (Yang et al. 2017). Jiang et al. isolated four new naphthoquinone derivatives from *Streptomyces* sp. XMA39,

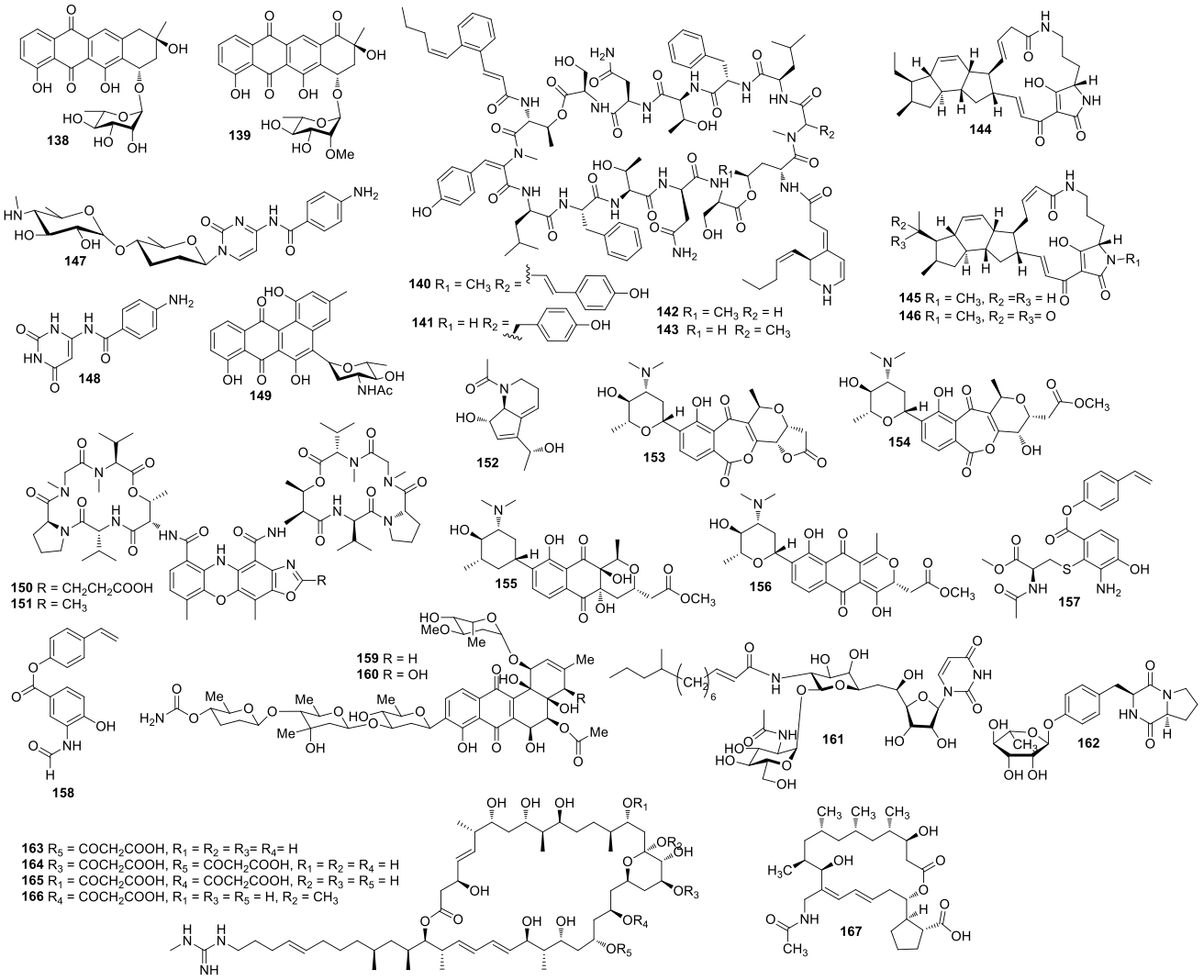

Fig. 6 Structures of compounds **138–167**

namely strepoxepinmycins A–D (**153–156**), which displayed inhibitory activity against a wide spectrum of strains with MIC values ranging from 6.0 to 10.0 μg/mL (Jiang et al. 2018). Bagremycins F (**157**) and G (**158**) were obtained from *Streptomyces* sp. ZZ745 and they showed inhibitory activities against *E. coli* with MIC values of 41.8 and 67.1 μM, respectively (Zhang et al. 2018b). *Streptomyces Pratensis* NA-ZhouS1 yielded stremycins A (**159**) and B (**160**). **159** and **160** were active against *P. aeruginosa,* MRSA, *K. pneumonia* and *E. coli* with the same MIC value of 16 μg/mL. Both were also active against *B. subtilis* with MIC values from 8 to 16 μg/mL (Akhter et al. 2018). Tunicamycin E (**161**) was obtained from *Streptomyces xinghaiensis* SCSIO S15077, which exhibited inhibitory activity against *B. thuringiensis* BT01, *B. thuringiensis*, *C. albicans* (ATCC 96901) and *C. albicans* CMCC (F) 98001 with MIC values of 2.0, 0.5, 32 and 8 μg/mL, respectively (Zhang et al. 2018c). A fermentation broth of *Streptomyces* sp. ZZ446 yielded a new compound maculosin-*O*-*α*-*L*-rhamnopyranoside (**162**), which showed antimicrobial activity against MRSA, *E. coli* and *C. albicans* with MIC values of 37.0, 28.0 and 26.0 μg/mL, respectively (Chen et al. 2018a). Niphimycins C−E (**163−165**) and 17-*O*-methylniphimycin (**166**) were isolated from a culture of *Streptomyces* sp. IMB7-145, which displayed antimicrobial activity against *C. albican* with MIC values of 8−32 μg/mL (Hu et al. 2018). Compound **163** showed anti-bacterial activity against MRSE, MRSA and *M. tuberculosis* with MIC values ranging from 4 to 64 μg/mL. *Streptomyces mutabilis* sp. MII yielded N-acetylborrelidin B (**167**), which was active against *B. subtilis*, *B. cereus* and *S. aureus* with inhibition zone diameters of 8−11 mm. Compound **167** was also active against *S. warneri* with an inhibition zone diameter of 18 mm (Hamed et al. 2018a). Nivelactam B (**168**) (Fig. 7), a new biphenyl derivative, was

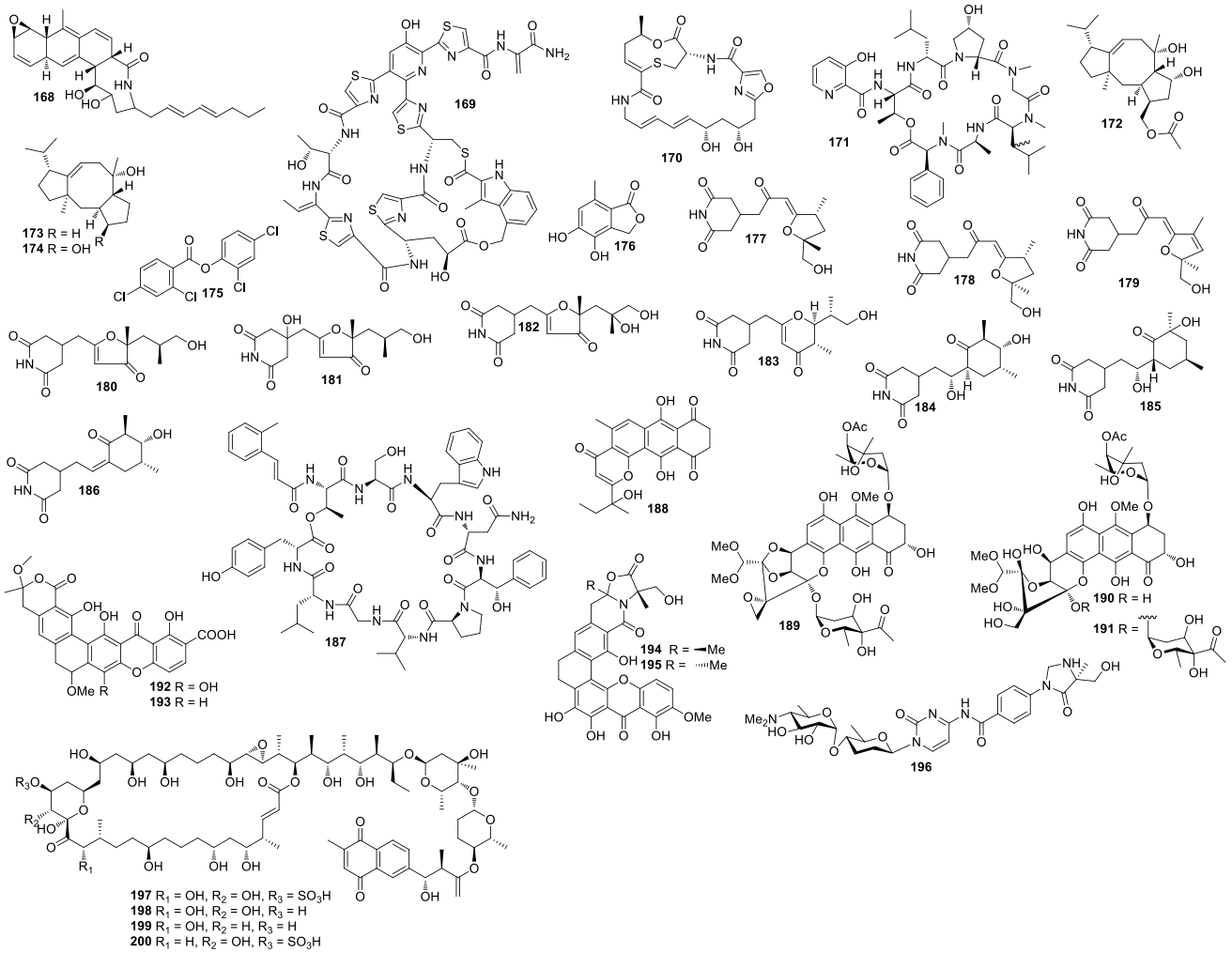

Fig. 7 Structures of compounds **168–200**

obtained from *S. varsoviensis* HF-11225, which exhibited inhibitory activity against *Sclerotinia sclerotiorum* with an inhibition zone diameter of 9 mm at 100 µg per 7 mm paper disks (Chen et al. 2018b). Nosiheptide (**169**), griseoviridin (**170**) and etamycin (**171**) were produced by *Streptomyces* sp. OPMA 1245. Compound **169** displayed antibacterial activity against *M. avium* JCM15430, *M. intracellulare* JCM6384 and *M. bovis* BCG Pasteur with MIC values of 0.024, 0.024 and 0.012 µg/mL, respectively. Compound **170** showed antibacterial activity against *M. avium* JCM15430, *M. intracellulare* JCM6384 and *M. bovis* BCG Pasteur with MIC values of 1.56, 1.56 and 6.25 µg/mL, respectively. Compound **171** was active against *M. avium* JCM15430, *M. intracellulare* JCM6384 and *M. bovis* BCG Pasteur with MIC values of 0.097, 0.190 and 0.780 µg/mL, respectively (Hosoda et al. 2019). *Streptomyces* sp. ZZ820 yielded diterpenoids 18-acetyl-cyclooctatin (**172**), 5,18-dedihydroxy-cyclooctatin (**173**) and 5-dehydroxy-cyclooctatin (**174**), which inhibited the growth of MRSA and *E. coli* with MIC values ranging from 24.11 to 55.12 µM (Yi et al. 2019). *Streptomyces* sp. G212 produced 2,4-dichlorophenyl 2,4-dichloro benzoate (**175**) and 4,5-dihydroxy-7-methyl-phthalide (**176**). Compound **175** exhibited inhibitory activity against *C. albicans* with an MIC value of 64 µg/mL, and compound **176** inhibited *E. faecalis* with the same MIC value of 64 µg/mL (Cao et al. 2019). Streptoglutarimides A–J (**177–186**) were obtained from *Streptomyces* sp. ZZ741. **177–186** showed antifungal activity against *C. albicans* with MIC values in the range of 8−20 µg/mL. They showed inhibitory activity against MRSA with MIC values ranging from 9 to 11 µg/mL, and against *E. coli* with MIC values in the range of 8−12 µg/mL (Zhang et al. 2019a). Atratumycin (**187**) was produced by *Streptomyces atratus* SCSIOZH16, which displayed inhibition against *M. tuberculosis* H37Ra and H37Rv with MIC values of 3.8 and 14.6 µM, respectively (Sun et al. 2019).

Antimicrobial compounds from *Streptomyces* sp. from marine seawater

Parimycin (**188**) and trioxacarcins D–F (**189**–**191**) obtained from *Streptomyces* sp. B8652 had a broad spectrum of antibacterial activity (Maskey et al. 2002, 2004). *Streptomyces caelestis* afforded new antibacterial citreamicins A (**192**), B (**193**), citreaglycon A (**194**) and dehydrocitreaglycon A (**195**). **192**–**195** showed broad spectrum of antibacterial activity against bacterial strains (Liu et al. 2012). Streptcytosine A (**196**) was discovered from *Streptomyces* sp. TPU1236A, and it exhibited antibacterial activity against *M. smegmatis* with an MIC value of 32 μg/mL (Bu et al. 2014).

Antimicrobial compounds from *Streptomyces* sp. from other marine sources

Streptomyces caniferus CA-271066 afforded caniferolides A–D (**197**–**200**). They showed a broad spectrum of antifungal activity against *A. fumigatus* ATCC46645 and *C. albicans* MY1055 with MIC values ranging from 0.5 to 8.0 μg/mL (Pérez-Victoria et al. 2019).

Antimicrobial compounds from *Micromonospora* species

Antimicrobial compounds from *Micromonospora* sp. associated with ascidians

Lomaiviticins A (**201**) (Fig. 8) and B (**202**) were isolated from *Micromonospora lomaivitiensis* LL-37I366 and showed inhibitory activities against *S. aureus* and *E. faecium* with MIC values in the range of 6 to 25 ng/spot (He et al. 2001). Diazepinomicin (**203**) was obtained from *Micromonospora* sp. DPJ12, which exhibited antibacterial activity against Gram-positive bacteria with MICs of about 32 μg/mL (Charan et al. 2004). Micromonohalimane B (**204**) was isolated from *Micromonospora* sp. WMMC-218, and **204**

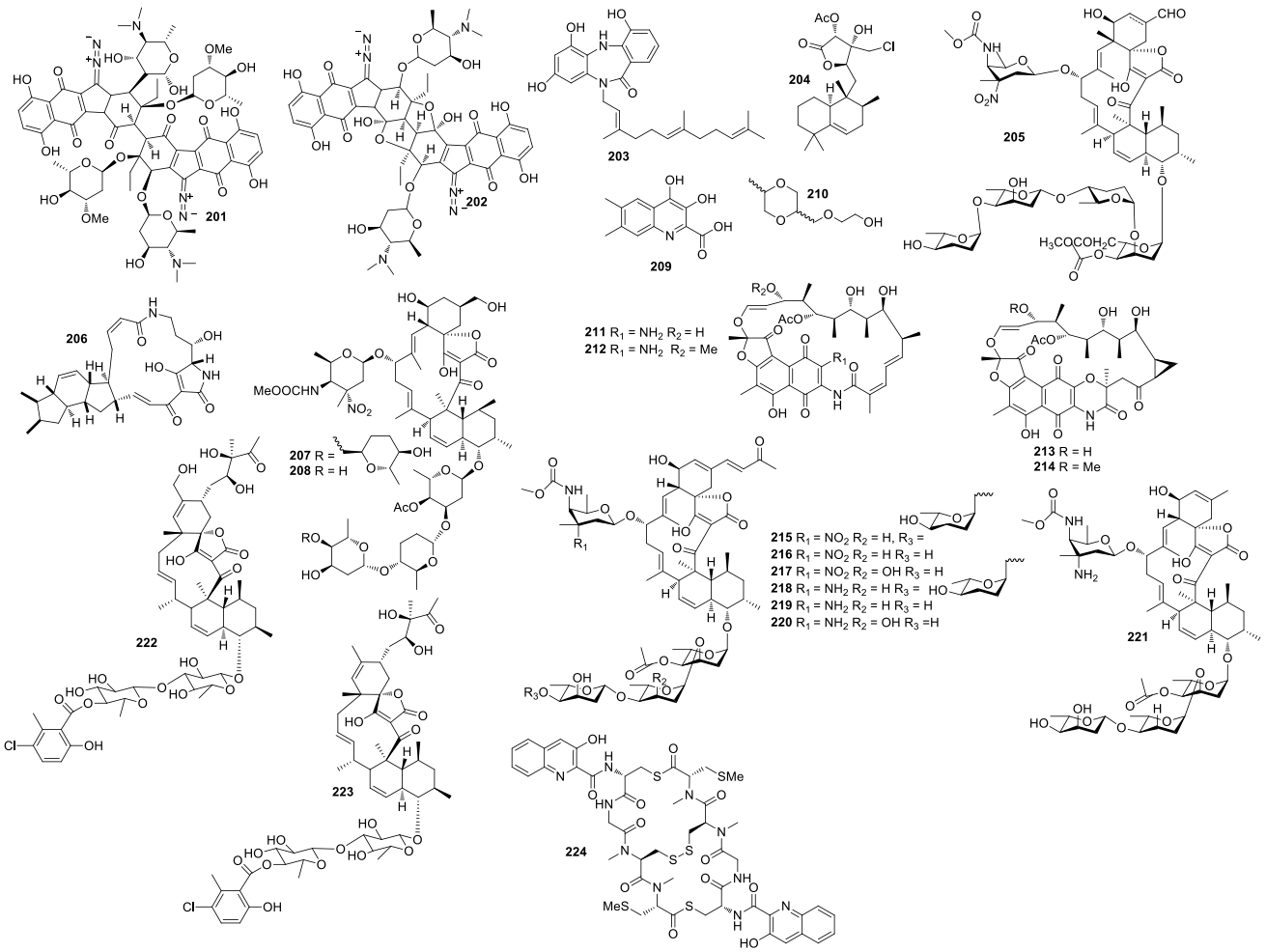

Fig. 8 Structures of compounds **201**–**224**

inhibited MRSA with an MIC value of 40 µg/mL (Zhang et al. 2016a).

Antimicrobial compounds from *Micromonospora* sp. associated with sponges

Tetrocarcin Q (**205**) was discovered from *Micromonospora carbonacea* LS276, which displayed antibacterial activity against *B. subitlis* ATCC 63501 with an MIC value of 12.5 µM (Gong et al. 2018).

Antimicrobial compounds from *Micromonospora* sp. from marine sediments

Butremycin (**206**) was isolated from *Micromonospora* sp. K310, which exhibited weak antibacterial activity against *S. aureus* ATCC 25923, *E. coli* ATCC 2592 and MRSA (Kyeremeh et al. 2014). Chemical investigation of a culture extract of *Micromonospora* sp.5–297 led to the discovery of two glycosidic spirotetronates tetrocarcins N (**207**) and O (**208**). **207** and **208** showed inhibitory activity against *B. subtilis* with MIC values of 2 and 64 µg/mL, respectively (Tan et al. 2016). 3,4-Dihydroxy-6,7-dimethyl-quinoline-2-carboxylic acid (**209**) were isolated from *Micromonospora* sp. G019, which demonstrated inhibitory activity against *E. coli*, *S. enterica* and *E. faecalis* with the MIC values of 48, 96 and 128 µg/mL, respectively (Thi et al. 2016a). 2-[(5-Methyl-1,4-dioxan-2-yl)methoxy]ethanol (**210**) showed inhibitory activity against *E. faecalis* and *C. albican* with MIC values of 32 and 64 µg/mL, respectively (Thi et al. 2016a). 3-amino-27-demethoxy-27-hydroxyrifamycin S (**211**), 3-amino-rifamycin S (**212**), sporalactams A (**213**) and B (**214**) were produced by *Micromonospora* sp. RJA4480. Compounds **211–214** displayed antibacterial activities against MRSA, *E. coli* and *M. tuberculosis* with MIC values of 0.0009, 0.0003 and 0.0009; 0.0008, 0.0001 and 0.0008; 7.0, 1.8 and 0.8; and 1.80, 0.40 and 0.06 µg/mL, respectively (Williams et al. 2017). Microsporanates A–F (**215–220**) and tetrocarcin P (**221**) obtained from *Micromonospora harpali* SCSIO GJ089 displayed a wide range of antibacterial activities (Gui et al. 2017). Phocoenamicins B (**222**) and C (**223**) were isolated from *Micromonospora* sp. CA-214671, both compounds showed a broad spectrum of antibacterial activities with MIC values ranging from 2 to 64 µg/mL (Pérez-Bonilla et al. 2018).

Antimicrobial compounds from *Micromonospora* sp. from other marine sources

Thiocoraline (**224**) was isolated from *Micromonospora* sp. L-13-ACM2–092, which inhibits the growth of Gram-positive bacteria (Perez et al. 1997).

Antimicrobial compounds from *Nocardiopsis* species

Antimicrobial compounds from *Nocardiopsis* sp. from marine sediments

Nocardiopsis dassonvillei produced kahakamide A (**225**) (Fig. 9), which showed weak antibacterial activity against *B. subtilis* (Schumacher et al. 2001). Thiopeptide TP-1161 (**226**) from *Nocardiopsis* sp. TFS65-07 displayed broad antibacterial activity with MIC values ranging from 0.25 to 1.0 µg/mL (Engelhardt et al. 2010). Nocapyrones E−G (**227–229**), were isolated from *Nocardiopsis dassonvillei* HR10-5, which exhibited inhibitory activities against *B. subtilis* with MIC values of 26, 14 and 12 µM, respectively (Fu et al. 2011). Nocarimidazoles A (**230**) and B (**231**), were produced by *Nocardiopsis* sp. CNQ115. They displayed antimicrobial activities against *B. subtilis* with an equal MIC value of 64 µg/mL. Compound **231** displayed antimicrobial activity against *S. epidermidis* with an MIC value of 64 µg/mL (Leutou et al. 2015). Three α-pyrones 4-deoxyphomapyrone C (**232**), 4-deoxy-11-methylphomapyrone C (**233**) and 10-hydroxymucidone (**234**) were produced by *Nocardiopsis* sp. SCSIO 10419. Compound **232** displayed antibacterial activity against *B. subtilis* SCSIO BS01 with an MIC value of 64 µg/mL. Compound **233** and **234** displayed antibacterial activities against *M. luteus* with the same MIC value of 64 µg/mL (Zhang et al. 2016b). 2-[(2*R*-Hydroxypropanoyl)amino] benzamide (**235**) was isolated from *Nocardiopsis* sp. G057, which displayed inhibitory activity against *E. coli* with an MIC value of 16 µg/mL (Thi et al. 2016b). Nocazine G (**236**) was produced by *Nocardiopsis* sp. YIM M13066, which possessed inhibitory activity against *B. subtilis* ATCC 6051 with an MIC value of 25.8 µM (Sun et al. 2017). Fluvirucin B6 (**237**) was isolated from *Nocardiopsis* sp. CNQ-115, which exhibited inhibitory activity against *B. subtilis*, *K. rhizophila* and *S. aureus* with MIC values of 64, 32 and 32 µg/L, respectively (Leutou et al. 2018). Terretonin N (**238**) obtained from *Nocardiopsis* sp. LGO5 had a broad spectrum of antibacterial activity against bacteria (Hamed et al. 2018b).

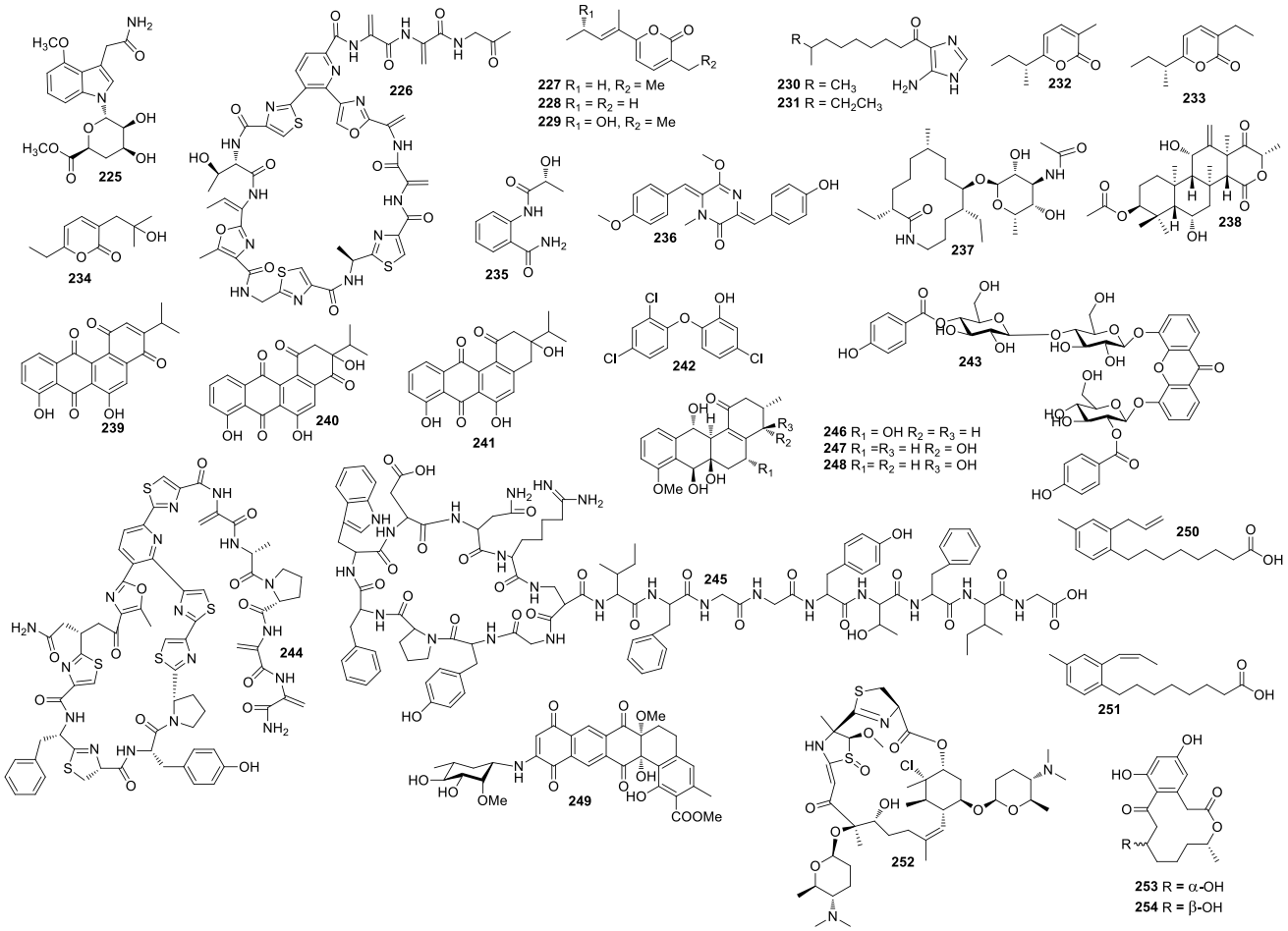

Fig. 9 Structures of compounds **225–254**

Antimicrobial compounds from *Nocardiopsis* sp. associated with sponges

Nocardiopsistins A−C (**239–241**), were isolated from *Nocardiopsis* sp. HB-J378, which showed antibacterial activity against MRSA with MIC values ranging from 3.12 to 12.5 μg/mL (Xu et al. 2018).

Antimicrobial compounds from other marine actinomycetes

Antimicrobial compounds from other actinomycetes associated with sponges

2,4,4′-Trichloro-28-hydroxydiphenylether (**242**) was isolated from *Micrococcus luteus*, which showed a broad spectrum of antibacterial activity with MIC values ranging from 16 to 64 μg/mL (Bultel-Poncé et al. 1998). Microluside A (**243**) was obtained from a culture of *Micrococcus* sp. EG45, which displayed antimicrobial activity against *E. faecalis* JH212 and *S. aureus* NCTC 8325 with MIC values of 10 and 13 μM, respectively (Eltamany et al. 2014). PM18110448 (Kocurin) (**244**) discovered from *Kocuria palustris* demonstrated a broad spectrum of antibacterial activity (Martín et al. 2013). A study of *Actinokineospora spheciospongiae* DSM45935^T led to the identification of actinokineosin (**245**), which exhibited antibacterial activity against *M. luteus* with an inhibition zone diameter of 8.0 mm at 50 μg/disk (Takasaka et al. 2017).

Antimicrobial compounds from other actinomycetes associated with other marine animals

Saccharothrix espanaensis An 113 produced saccharothrixins A−C (**246–248**), which showed modest antibacterial activity (Kalinovskaya et al. 2008). Arenjimycin (**249**) from *Salinispora arenicola* CNR-647 displayed broad antibacterial activity (Asolkar et al. 2010). *Solwaraspora* sp. WMMB329 yielded solwaric acids A and B (**250** and **251**). Both compounds were active against *E. coli,* MRSA, MSSA and *P. aeruginosa* with MIC values

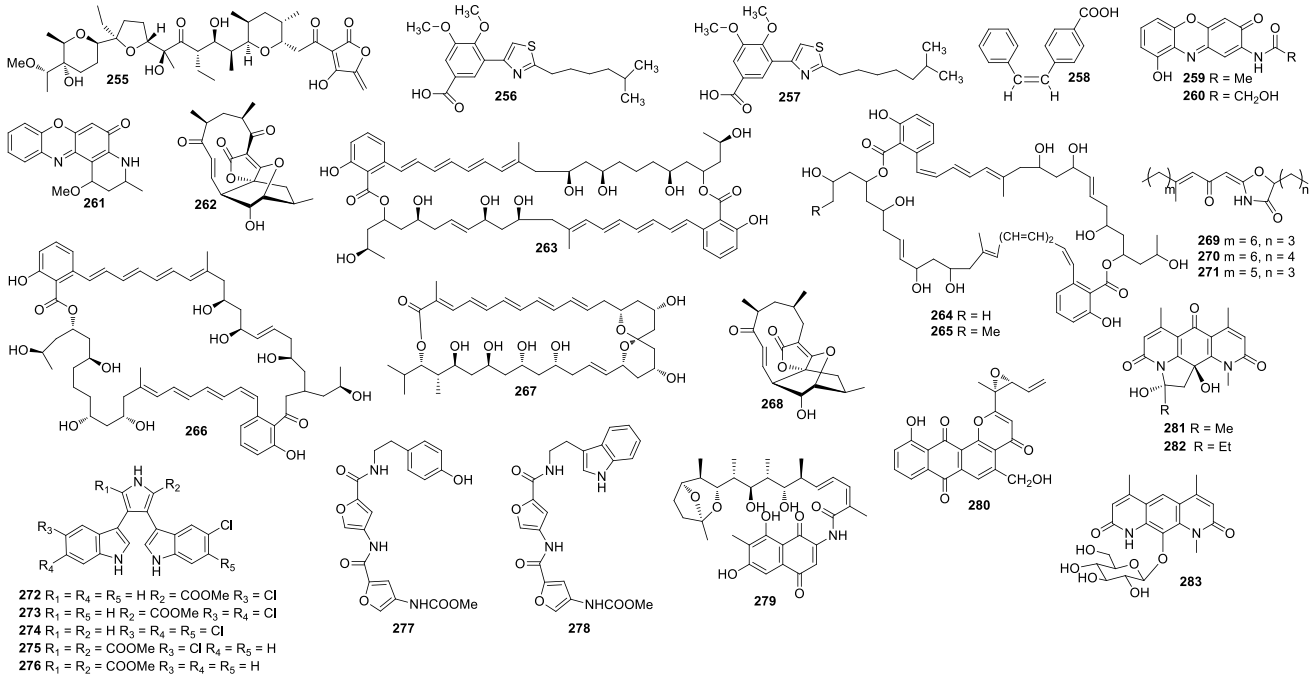

Fig. 10 Structures of compounds **255–283**

of 128, 32, 64, 128 µM and 128, 32, 64, 128 µM, respectively (Ellis et al. 2014). Forazoline A (**252**) was isolated from *Actinomadura* sp. WMMB-499, which exhibited inhibitory activity against *C. albicans* with an MIC value of 16 µg/mL (Wyche et al. 2014). (11*S*,15*R*)-11-Hydroxycurvularin (**253**) and (11*R*,15*R*)-11-hydroxycurvularin (**254**) were obtained from *Pseudonocardia* sp. HS7. They showed antibacterial activity against *E. coli* with an equal MIC value of 20 µg/mL (Ye et al. 2016). *Actinomadura* sp. WMMB499 yielded ecteinamycin (**255**) (Fig. 10), which showed antibacterial activity against *E. coli*, *S. aureus* (MRSA and MSSA), and *P. aeruginosa* with MIC values of 16, 0.125 and 8 µg/mL, respectively. Compound **255** exhibited inhibition against *C. difficile* with an MIC value of 0.059−0.117 µg/mL (Wyche et al. 2017).

Antimicrobial compounds from other actinomycetes associated with mangroves and algae

Lechevalieria aerocolonigenes K10-0216 afforded pyrizomicins A and B (**256**, **257**). They showed broad spectrum of antimicrobial activity (Kimura et al. 2018). *Kocuria marina* CMG S2 afforded kocumarin (**258**), which showed activity against MRSA with an MIC value of 10−15 µg/mL (Uzair et al. 2018).

Antimicrobial compounds from other actinomycetes associated with marine sediments

Cultivation of *Actinomadura* sp. M045 produced three new phenoxazin-3-one antibiotics chandrananimycins A–C (**259–261**). Compounds **259** and **260** exhibited inhibitory activity against *Mucor meihei* with inhibition zone diameters of 11 and 12 mm at 20 µg/platelet, respectively. Compound **261** showed activity at 20 µg/platelet against *B. subtilis*, *Mucor meihei* and *S. aureus* with inhibition zone diameters of 23, 27 and 22 mm, respectively (Maskey et al. 2003). Abyssomicin C (**262**) was obtained from *Verrucosispora* sp. AB-18-032, which exhibited antibacterial activity against *S. aureus* N315 and *S. aureus* Mu50s with MIC values of 4 and 13 µg/mL, respectively (Bister et al. 2004). Chemical investigation of a culture extract of *Marinispora* sp. CNQ-140 led to the discovery of marinomycins A−D (**263−266**). These compounds showed inhibitory activity against MRSA with MIC_{90} values of 0.13, 0.25, 0.25 and 0.25 µM, respectively. Compound **264** showed inhibitory activity against VRFE and *C. albicans* with MIC_{90} values of 0.13 and 7.8 µM, respectively (Kwon et al. 2006). *Marinispora* sp. CNQ-140 produced marinisporolide A (**267**). **267** displayed antifungal activity against *C. albicans* with an MIC value of 22 µg/mL (Kwon et al. 2009). Atropabyssomicin C (**268**) was obtained from *Verrucosispora* sp.

AB-18-032, which showed antibacterial activity against MRSA N315 with an MIC value of 2.67 μg/mL (Keller et al. 2007). *Marinispora* NPS008920 yielded lipoxazolidinones A–C (**269–271**). These three compounds were active against *S. aureus* ATCC 29213 (MSSA) and *E. faecalis* ATCC 29212 (VSE) with MIC values of 0.9, 6.0 and 4.0; and 1.0, 3.0 and 2 μg/mL, respectively. Compound **269** was also active against *H. influenza* with an MIC value of 12 μg/mL (Macherla et al. 2007). Lynamicins A–E (**272–276**) were isolated from *Marinispora* sp. NPS12745, which exhibited inhibitory activity against MRSA and vancomycin-resistant *E. faecium* with MIC values ranging from 1.8 to 57.0 μg/mL (McArthur et al. 2008). Cultivation of *Verrucosispora maris* AB-18–032 produced proximicins B and C (**277** and **278**). Compound **277** showed antibacterial activity against *Brevibacillus brevis* DSM with an inhibition zone diameter of 12 mm at 0.3 mg/mL, Compound **278** exhibited a slight inhibition against *Brevibaccillus brevis* DSM30 (Fiedler et al. 2008). Salinisporamycin (**279**) was isolated from a culture of *Salinispora arenicora* YM23-082, which displayed antimicrobial activity against *B. subtilis* IFO 3134 and *Salinispora aureus* IFO12732 with MIC values of 4.1 and 0.46 μg/mL, respectively (Matsuda et al. 2009). Culture of *Salinispora arenicola* yielded saliniquinone A (**280**), which showed weak activity against MRSA (Murphy et al. 2010). Pseudonocardians A–C (**281–283**) were ontained from *Pseudonocardia* sp. SCSIO 01299, which exhibited inhibitory activities against *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212 and *B. thuringensis* SCSIO BT01 with MIC values ranging from 1 to 4 μg/mL (Li et al. 2011). *Actinoalloteichus* sp. NPS702 afforded neomaclafungins A–I (**284–292**) (Fig. 11). These compounds showed antifungal activity against *Trichophyton mentagrophytes* (ATCC 9533) with MIC values ranging from 1 to 3 μg /mL (Sato et al. 2012). Marthiapeptide A (**293**) was isolated from *Marinactinospora thermotolerans* SCSIO 00652, which inhibited the growth of Gram-positive bacteria with MIC values ranging from 2 to 8 μg/mL (Zhou et al. 2012). 1-(10-aminodecyl) pyridinium salt antibiotic (**294**) was purified from *Amycolatopsis alba var. nov.* DVR D4, which demonstrated inhibitory activity against Gram-positive and Gram-negative bacteria with MIC values ranging from 70 to 160 μg/mL (Dasari et al. 2012). 3-[(6-Methylpyrazin-2-yl)methyl]-1*H*-indole (**295**) was obtained from *Serinicoccus profundi* sp. nov., which displayed weak antibacterial activity against *S. aureus* ATCC 25923 with an MIC value of 96 μg/mL (Yang et al. 2013). Glycerol 1-hydroxy-2,5-dimethyl benzoate (**296**) was isolated from *Verrucosispora* sp. MS100047, which exhibited inhibitory activity against MRSA with an MIC value of 12.5 μg/mL (Huang et al. 2016). Kribellosides A–D (**297–300**) were discovered from *Kribbella* sp. MI481-42F6 and they inhibited *S. cerevisiae* with MICs ranging

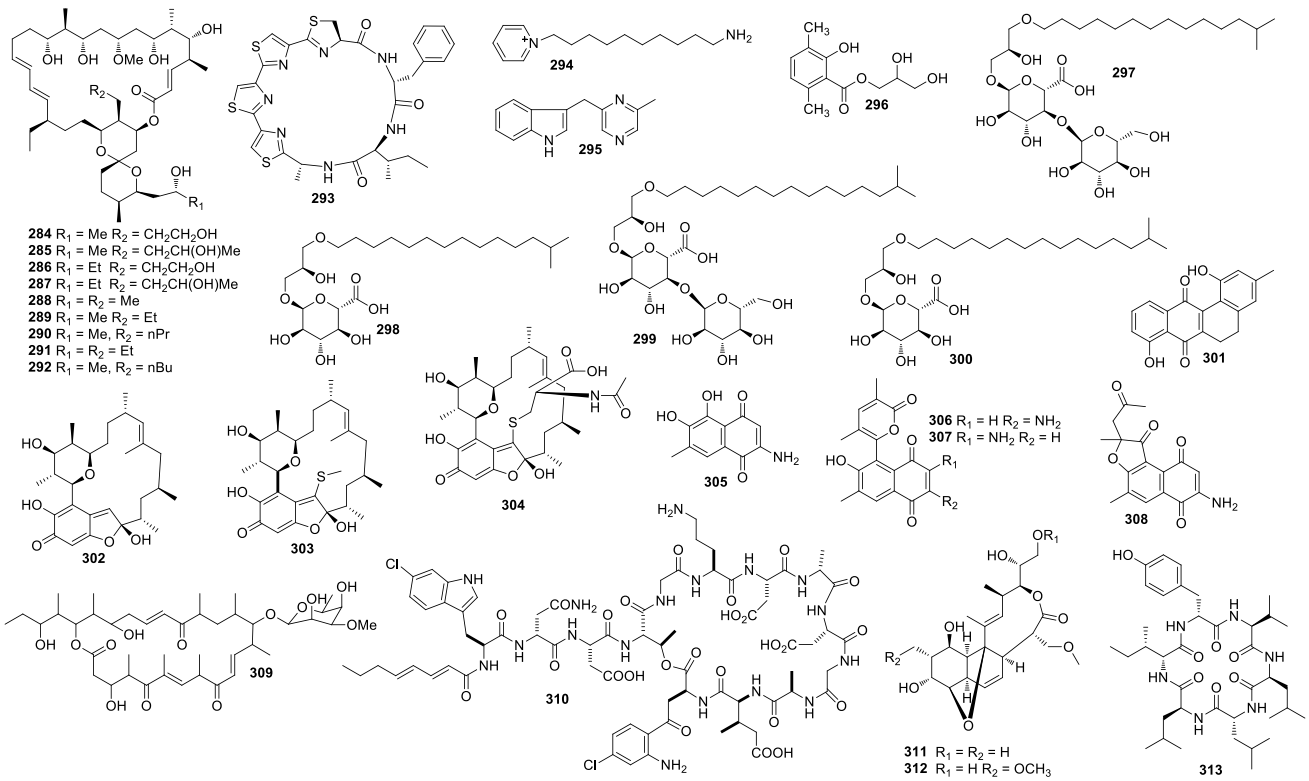

Fig. 11 Structures of compounds **284–313**

from 3.12 to 100 µg/mL (Igarashi et al. 2017). 5,6-Dihydro-1,8-dihydroxy-3-methylbenz[a]anthracene-7,12-quinone (**301**) was separated from *Actinomadura* sp. DS-MS-114, which was active against *S. aureus* NBRC12732 with an inhibition zone diameter of 12.7 mm at 100 µg/mL (Kurata et al. 2017). Kendomycins B–D (**302–304**) obtained from *Verrucosispora* sp. SCSIO 07399 had a broad spectrum of antibacterial activity against *S. aureus* ATCC 29213, *S. aureus* 745524, MRSA shhs-A1, *E. faecalis* ATCC 29212, *B. subtilis* BS01 and *B. thuringiensis* BT01 with MIC values ranging from 0.5 to 8.0 µg/mL (Zhang et al. 2019b). Salinaphthoquinones A–D (**305–308**) were isolated from *Salinispora arenicola* BRA-213, they showed antibacterial activities against *S. aureus* and *E. faecalis* with MIC values ranging from 16 to 125 µg/mL (da Silva et al. 2019).

Antimicrobial compounds from other actinomycetes from other marine sources

Maduralide (**309**) was obtained from an unidentified marine bacterium of the order Actinomycetales, which displayed weak antibacterial activity against *B. subtilis* (Pathirana et al. 1991). Taromycin A (**310**) was isolated from *Saccharomonospora* sp. CNQ-490, which exhibited inhibitory activity against MRSA and *Enterococcus faecalis* 613D with MIC values ranging from 6 to 100 µM (Yamanaka et al. 2014). *Pseudonocardia carboxydivorans* M-227 afforded branimycins B (**311**) and C (**312**). They showed a broad spectrum of antibacterial activities (Braña et al. 2017b). Thermoactinoamide A (**313**) was discovered from *Thermoactinomyces vulgaris* ISCAR 2354 and was active against *S. aureus* ATCC 6538 with an MIC value of 35 µM (Teta et al. 2017).

Conclusion

According to the statistic results (Table 1, Fig. 12), the investigation of antimicrobial compounds from marine-derived actinomycetes could be dated back to 1976 when aplasmomycin A (**52**) was isolated from *Streptomyces griseus* SS-20 (Table 2) (Okami et al. 1976). Until the end of 2019, 313 new antimicrobial compounds derived from marine actinomycetes have been reported. Since 2016, more secondary metabolites have been isolated from marine actinomyces than ever before except 2007 and 2009.

These new marine natural products from actinomycetes have different types of structural skeletons including nitrogen-containing compounds, sterols and terpenoids, polyketides, and others (Fig. 13). Polyketides and nitrogen-containing compounds (e.g., alkaloids and peptides) are the two main classes (Fig. 13). Because of high halogen concentrations in the Ocean when compared with that on Land, marine actinomyces produced more halogen-containing compounds than their terrestrial counterparts. None of the terpenoids and steroids among the 313 compounds cited in this review article showed potent antimicrobial activity when compared with the other classes of compounds. Compounds **74** and **76**, halogenated alkaloids each with two pyrrolphenone moieties inhibited MRSA with an MIC value less than 1 µg/mL (Hughes et al. 2008, 2010). Compounds **201**, **202** and **211–214** are polyketides-derived 1,4-naphthoquinone alkaloids. Compounds **201** and **202** inhibited *S. aureus* and *E. faecium* with MIC values ranging from 6 to 25 ng/spot (He et al. 2001). Compounds **211–214** inhibited MRSA, *E.coli* and *M. tuberculosis* with MIC values in the range of 0.3–0.9, 0.1–0.8, and 60–1800 ng/mL, respectively (Williams et al. 2017). Compounds **16–19** are bicyclic nitrogen-containing compounds each with a phenoxazine bridge. One cyclic peptide fragment (threonine-valine-proline-glycine-valine) was connected to one aromatic ring through an amide bond, and another cyclic peptide fragment (threonine-valine-proline-glycine-valine) was connected to another aromatic ring also through an amide bond. Compounds **16–19** inhibited MRSA with MIC values less than 1.0 µg/mL (Jiao et al. 2018). Compound **128**, a cyclic peptide, exhibited potent antibacterial activity at nanomolar concentrations (Raju et al. 2014). Cyclic peptides **129–133** inhibited *M. luteus* with MIC values in the range of 0.061–4.00 µg/mL (Zhou et al. 2014). Compounds **169–171** are cyclic peptides with some nonstandard amino acids (**169** and **171**) or hybrids of polyketide and peptide (**170**). Compounds**169** and **171** strongly inhibited *M. avium* JCM15430, *M. intracellulare* JCM6384 and *M. bovis* BCG Pasteur with MIC values in the range of 12 to 780 ng/mL (Hosoda et al. 2019). Besides **170** (hybrids of polyketide and peptide), **201**, **202** and **211–214** (1,4-naphthoquinone alkaloids derived from polyketides), some other polyketides (for examples, **25**, **32–34**, **122**, **255**, and **263–266**) also demonstrated potent antimicrobial activity. Compounds **32–34** are polyketide anthraquinone derivatives, among which compounds **32** and **33** inhibited MRSA with IC_{50} values of 0.15 and 0.36 µM, respectively (Socha et al. 2006). Compound **255** is a polyketide derived polyether. It inhibited MRSA, MSSA and *C. difficile* with MIC values in the range of 59–125 ng/mL (Wyche et al. 2017). The macrolides **263–266** are polyketide polyenes, and they inhibited MRSA with MIC_{90} values in the range of 0.13–0.25 µM. Other two macrolides **25** (Rodríguez et al. 2018) and **122** (Jang et al. 2013) also exhibited antibacterial activity at ng/mL level. Glycosylated macrolides **135** and **136** inhibited *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. aureus* and *S. cerevisiae* with MIC values in the range of 0.027 to 0.22 µM (Mondol and Shin 2014).

Marine actinomycetes are efficient producers of new secondary metabolites. The numbers of antimicrobial compounds from marine *Streptomyces* sp., *Micromonospora* sp., *Nocardiopsis* sp. and the other actinomycetes except

Table 1 Antimicrobial compounds isolated from marine actinomycetes (1976–2019)

Compound	Producing strain	Environmental source	Bioactivity	Refs.
1–2	*Streptomyces* sp. Ni-80	Unidentified sponge, urauchic-ove, iriomote, Japan	Antifungal activity	Imamura et al. (1993)
3–12	*Streptomyces* sp. HB202	*Halichondria panicea* sponge, Baltic Sea (Germany)	Antibacterial activity	(Mitova et al. 2008; Schnee-mann et al. 2010; Kunz et al. 2014)
13–15	*Streptomyces* sp. BCC45596	*Xestospongia* sp. sponge, Thailand	Antibacterial activity	Supong et al. (2012)
16–19	*Streptomyces* sp. LHW52447	*Phyllospongia foliascens* sponge, Xisha Islands, South China Sea	Antibacterial activity	Jiao et al. (2018)
20–23	*Streptomyces* sp. SCSGAA 0027	Gorgonian coral *Melitodes squamata*, the South China Sea	Antibacterial activity	Nong et al. (2016)
24	*Streptomyces* sp. M-207	Coral *Lophelia pertusa*, subma-rine canyon	Antibacterial activity	Braña et al. (2017a)
25	*Streptomyces cyaneofuscatus* M-169	Gorgonian coral (order gor-gonacea), avilés submarine Canyon	Antibacterial activity	Rodríguez et al. (2018)
26	*Streptomyces* sp. SCSIO 41,399	*Porites* sp. coral, Wenchang, Hainan, C	Antibacterial activity	Cong et al. (2019)
27–28	*Streptomyces hygroscopicus*	Jellyfish *Cassiopeia xam-achana*, Florida Keys	Antibacterial activity	Trischman et al. (1994)
29	*Streptomyces* sp. 1053U.I.1a.3b	*L. totopotens*, Mactan Island, Cebu, Philippines	Antibacterial activity	Lin et al. (2014)
30	*Streptomyces* sp. CNB091	A jellyfish *(C. xamachana)*, Florida Keys	Antibacterial activity	Hassan et al. (2015)
31	*Streptomyces seoulensis* A01	Marine prawn, Yellow Sea, in China	Antibacterial activity	Zhang et al. (2018a)
32–34	*Streptomyces* sp. # N1-78–1	Unidentified green algae, Rhode Island	Antibacterial activity	Socha et al. (2006)
35	*Streptomyces* sp. WR1L1S8	The brown marine algae *Fucus* sp., Bejaia coastline	Antibacterial activity	Djinni et al. (2013)
36	*Streptomyces althioticus* MSM3	Seaweed *Ulva* sp., Cantabrian Sea (Northeast Atlantic Ocean)	Antibacterial activity	Braña et al. (2019)
37–40	*Streptomyces* sp. HKI0576	Mangrove tree B*ruguiera gymnorrhiza*	Antibacterial activity	Ding et al. (2011a)
41–48	*Streptomyces* sp. HKI0595	Mangrove tree *Kandelia can-del*, Xiamen, China	Antibacterial activity	(Ding et al. 2011a, 2012)
49	*S. lusitanus* XM52	Mangrove root, Fujian, China	Antibacterial activity	Han et al. (2012)
50	*Streptomyces* sp. MA-12	Myoporum root, Leizhou Peninsula	Antibacterial and antifungal activity	Ding et al. (2013)
51	*Streptomyces sp.* LC6	Leaves of kandelia candel, Longhai, Fujian, China	Antibacterial activity	Zhang et al. (2014)
52–54	*Streptomyces griseus* SS-20	Shallow sea sediment, Sagami Bay	Antibacterial activity	(Okami et al. 1976; Sato et al. 1978)
55–56	*S.tenjimariensis* SS-939	Sea mud sample, Tenjin-island, Sagami-Bay	Antibacterial activity	Okami et al. (1979)
57	*Streptomyces* sp. CNB-253	Sediment, Bodega Bay, CA	Antibacterial activity	Pathirana et al. (1992)
58–59	*Streptomyces* sp. BD-26 T(20)	Sediment, Hawaii	Antibacterial activity	Sitachitta et al. (1996)
60	*Streptomyces* sp. B 8300	Sediment, Gulf of Mexico	Antibacterial activity	Biabani et al. (1997)
61	*Streptomyces* sp. CNB-689	Sediment, Christchurch, New Zealand	Antibacterial activity	Jiang et al. (1997)
62	*Streptomyces* sp. strain B 8251	Sediment, Gulf of Mexico	Antibacterial activity	Pusecker et al. (1997)
63–64	*Streptomyces* sp. M428	Sediment, Geomun island	Antifungal activity	Cho et al. (1999)

Table 1 (continued)

Compound	Producing strain	Environmental source	Bioactivity	Refs.
65	*Streptomyces*MSTMA190	Sediment, Victorian	Antibacterial activity	Capon et al. (2000)
66	*Streptomyces* sp. 1010	Sediment, Livingston	Antibacterial activity	Ivanova et al. (2001)
67	*Streptomyces* sp. B7064	Sediment, Hawaii	Antibacterial activity	Asolkar et al. (2002)
68	*Streptomyces* sp. BD21-2	Sediment,Kailua Beach, Oahu, Hawaii	Antibacterial and antifungal activity	Schumacher et al. (2003)
69	*S. nodosus* NPS007994	Sediment, Scripps Canyons, La Jolla	Antibacterial activity	Manam et al. (2005)
70–71	*Streptomyces* sp.CNQ-085	Sediment, San Diego, CA	Antifungal activity	Asolkar et al. (2006)
72	*Streptomyces* sp.QD518	Sediment, Jiaozhou Bay, China	Antibacterial activity	Wu et al. (2006)
73	*Streptomyces* sp.B8000	Sediment, Gulf of Mexico	Antibacterial activity	Poumale et al. (2006)
74–76	*Streptomyces* sp CNQ-418	Sediment, La Jolla, CA	Antibacterial activity	Hughes et al. 2008; Hughes et al. (2010)
77	*Streptomyces* sp. MS239	Sediment, Tokushima, Japan	Antibacterial activity	Motohashi et al. (2008)
78	*Streptomyces* sp. Merv8102	Sediment, Mediterranean Sea, Egypt	Antibacterial activity	El-Gendy et al. (2008)
79	*Streptomyces* sp. 307–9	Sediment,Salt Cay, U.S. Virgin Islands	Antibacterial activity	Carlson et al. (2009)
80	*Streptomyces* sp. CMB-M0406	Sediment, Heron island, Australai	Antifungal activity	Sugiyama et al. (2014)
81–83	*Streptomyces* sp. CMB-M0423	Sediment Heron Island, Queensland	Antibacterial activity	Raju et al. (2010)
84–85	*S. antibioticus* H74-18	Sediment, South China Sea	Antifungal activity	Xu et al. (2011)
86–88	*Streptomyces* sp. CNS-575	Sediment, Figi island	Antibacterial activity	Sun et al. (2011)
89	*Streptomyces* species B8112	Sediment, Gulf of Mexico	Antifungal activity	Shaaban et al. (2011)
90	*Streptomyces* sp. SCSIO 01,127	Sediment, South China Sea	Antibacterial activity	Niu et al. (2011)
91–96	*Streptomyces* sp. CNH-189	Marine sediments, retrieved off shore of Oceanside, California	Antibacterial activity	(Wilson et al. 2011; Ryu et al. 2019)
97–98	*Streptomyces* sp. 211,726	Rhizosphere soil of *Heritiera globose*, Wenchang, China	Antifungal activity	Yuan et al. (2011)
99	*Streptomyces* sp. CMB-M0392	Sediment, Heron Island, Queensland	Antibacterial activity	Raju et al. (2012)
100	*Streptomyces* sp. CNQ343	Sediment, North Cat Cay, Bahamas	Antifungal activity	Kim et al. (2012)
101	*Streptomyces* sp. LB173	Sediment, Baltic Sea, Germany	Antibacterial activity	Ohlendorf et al. (2012)
102–105	*Streptomyces* sp. SCSIO 02,999	Sediment, South China Sea	Antibacterial activity	Zhang et al. (2012)
106	*Streptomyces* sp. CP13-10	Sediment, SanFrancisco Bay, CA	Antifungal activity	Amagata et al. (2012)
107–109	*Streptomyces* sp. RJA2961	Sediment, British Columbia coast	Antibacterial activity	Dalisay et al. (2013)
110–112	*S. antibioticus* PTZ0016	Sediment, unknown place	Antibacterial activity	Lian and Zhang (2013)
113–115	*S. niveus* SCSIO 3406	Sediment, South China Sea	Antibacterial activity	Song et al. (2013)
116	*Streptomyces* sp. MS100061	Sediment, South China Sea	Antibacterial activity	Chen et al. (2013)
117–118	*Streptomyces* sp.CNQ-329	Sediment, San Diego, CA	Antibacterial activity	Cheng et al. (2013)
119–121	*Streptomyces* sp. SCSIO 10,428	Sediment, Beihai, Guangxi, China	Antibacterial activity	Wu et al. (2013a)
122	*Streptomyces* sp. CNH365	Sediment, Santa Barbara, CA	Antibacterial activity	Jang et al. (2013)
123–124	*Streptomyces* sp. 7–145	Sediment, Heishijiao Bay, China,	Antibacterial activity	Wu et al. (2013b)
125–126	*Streptomyces* sp. SNJ042	Sediment, jeju Island	Antibacterial activity	Um et al. (2013)
127	*Streptomyces* sp. 12A35	Sediment, South China Sea	Antibacterial activity	Pan et al. (2013)
128	*Streptomyces* sp. CMBM0244	Sediment, Molle Island, Queensland	Antibacterial activity	Raju et al. (2014)

Table 1 (continued)

Compound	Producing strain	Environmental source	Bioactivity	Refs.
129–133	*S. drozdowiczii* SCSIO 10,141	Sediment, South China Sea	Antibacterial activity	Zhou et al. (2014)
133	*S. scopuliridis* SCSIO ZJ46	Sediment, South China Sea	Antibacterial activity	Song et al. (2014)
135–136	*Streptomyces* sp. 06CH80	Sediment, Chuuk, Federated States of Micronesia and Ieodo, Korea	Antibacterial activity	Mondol and Shin (2014)
137	*Streptomyces* sp. SNR69	Tidal mudflat in Buan, Korea	Antibacterial activity	Moon et al. (2015)
138–139	*Streptomyces* sp. CMB-M0150	Sediment collected off the Sunshine Coast, Queensland, Australia	Antibacterial activity	Khalil et al. (2015)
140–143	*Streptomyces* sp. SNM5	Intertidal zone mudflat, Mohang, Korea	Antibacterial:**142–143** antifungal activity: **140–141**	Bae et al. (2015a, 2015b)
144–146	*Streptomyces zhaozhouensis* CA-185989	Sediment, Utonde, Equatorial Guinea	Antibacterial:**144–146** antifungal activity: **144–145**	Lacret et al. (2015)
147–148	*S. rochei* 06CM016	Sediment sample, Kaş, Turkey	Antibacterial and antifungal activity	Aksoy et al. (2016)
149	*Streptomyces* sp. 182SMLY 06CM016	Sediment, East China Sea	Antibacterial	Liang et al. (2016)
150–151	*Streptomyces* sp. IMB094	Marine sediment, Heishijiao Bay, Dalian, China	Antibacterial activity:	Wang et al. (2017)
152	*Streptomyces chartreusis* NA02069	Marine sediment, Hainan Island, Dalian, China	Antibacterial activity:	Yang et al. (2017)
153–156	*Streptomyces chartreusis* XMA39	Marine sediment, Xiamen Island, Fujian, China	Antibacterial and antifungal activity	Jiang et al. (2018)
157–158	*Streptomyces* sp. ZZ745	Marine sediment, Zhejiang, China	Antibacterial activity	Zhang et al. (2018b)
159–160	*Streptomyces Pratensis* NA-ZhouS1	Marine sediment, Zhoushan, China	Antibacterial activity	Akhter et al. (2018)
161	*Streptomyces xinghaiensis* SCSIO S15077	Marine sediment, South China Sea, China	Antibacterial and antifungal activity	Zhang et al. (2018c)
162	*Streptomyces* sp. ZZ446	coastal soil	Antibacterial and antifungal activity	Chen et al. (2018a)
163–166	*Streptomyces* sp. IMB7-145	Marine sediment, Daliang, China	Antibacterial: **163** antifungal activity:**163–166**	Hu et al. (2018)
167	*Streptomyces mutabilis* sp. MII	Marine sediment, Red Sea, Hurghada Coast	Antibacterial activity	Hamed et al. (2018a)
168	*S. varsoviensis* HF-11225	Marine sediment, East Sea, Hurghada Coast	Antifungal activity	Chen et al. (2018b)
169–171	*Streptomyces* sp. OPMA 1245	Marine sediment, Okinawa prefecture, Japan	Antibacterial activity	Hosoda et al. (2019)
172–174	*Streptomyces* sp. ZZ820	coastal soil	Antibacterial activity	Yi et al. (2019)
175–176	*Streptomyces* sp. G212	Sediment, Quang Binh-Vietnam	Antibacterial:**176** Antifugal: **175**	Cao et al. (2019)
177–186	*Streptomyces* sp. ZZ741	marine mud, the coastal area of Jintang Island, Zhoushan, China	Antibacterial and Antifungal activity	Zhang et al. (2019a)
187	*Streptomyces atratus* SCSI-OZH16	Sediment sample	Antibacterial activity	Sun et al. (2019)
188–191	*Streptomyces* sp. B8652	Sediment, Laguna de Terminos, Gulf of Mexico	Antibacterial activity	(Maskey et al. 2002, 2004)
192–195	*Streptomyces caelestis*	Coastal water of the Red Sea, near Jeddah	Antibacterial activity	Liu et al. (2012)
196	*Streptomyces* sp. TPU1236A	Seawater, Okinawa, Japan	Antibacterial activity	Bu et al. (2014)
197–200	*Streptomyces caniferus* CA-271066	Unknown source	Antifugal activity	Pérez-Victoria et al. (2019)

Table 1 (continued)

Compound	Producing strain	Environmental source	Bioactivity	Refs.
201–202	*Micromonospora lomaivitiensis* LL-37I366	Ascidian	Antibacterial activity	He et al. (2001)
203	*Micromonospora* sp. DPJ12	*Didemnum proliferum* Kott, Japan	Antibacterial activity	Charan et al. (2004)
204	*Micromonospora* sp.WMMC-218	Ascidian, Florida	Antibacterial activity	Zhang et al. (2016a)
205	*Micromonospora carbonacea* LS276	Sponge, Hainan, China	Antibacterial activity	Gong et al. (2018)
206	*Micromonospora* sp. K310	Sediment, Ghanaian	Antibacterial activity	Kyeremehet al. (2014)
207–208	*Micromonospora* sp.5–297	Sediment, Dalian, China	Antibacterial activity	Tan et al. (2016)
209–210	*Micromonospora* sp. G019	Sediment, Viet Nam	Antibacterial activity:**209–210** Antifugal: **210**	Thi et al. (2016a)
211–214	*Micromonospora* sp. RJA4480	Marine sediment Barkley-Sound, British Columbia	Antibacterial activity	Williams et al. (2017)
215–221	*Micromonospora harpali* SCSIO GJ089	Marine sediment, South China Sea	Antibacterial activity	Gui et al. (2017)
222–223	*Micromonospora* sp. CA-214671	Marine sediment, Canary Island	Antibacterial activity	Pérez-Bonilla et al. (2018)
224	*Micromonospora* sp. L-13-ACM2–092	Unknown source	Antibacterial activity	Perez et al. (1997)
225	*Nocardiopsis dassonvillei*	Sediment sample, island of Kauai, Hawaii	Antibacterial activity	Schumacher et al. (2001)
226	*Nocardiopsis* sp. TFS65-07	Sediment sample, Trondheim Fjord, Norway	Antibacterial activity	Engelhardt et al. (2010)
227–229	*Nocardiopsis dassonvillei* HR10-5	Marine sediment, Yellow River	Antibacterial activity	Fu et al. (2011)
230–231	*Nocardiopsis* sp. CNQ115	Marine sediment, the coast of southern California	Antibacterial activity	Leutou et al. (2015)
232–234	*Nocardiopsis* sp. SCSIO 10419	Marine sediment, Xieyang Island, Beihai, Guangxi, China	Antibacterial activity	Zhang et al. (2016b)
235	*Nocardiopsis* sp. G057	Marine sediment, Cô Tô-Quảng Ninh in Vietnam	Antibacterial activity	Thi et al. (2016b)
236	*Nocardiopsis* sp. YIM M13066	Marine sediment, Cô Tô-Quảng Ninh in Vietnam	Antibacterial activity	Sun et al. (2017)
237	*Nocardiopsis* sp. CNQ-115	Marine sediment, Southern California	Antibacterial activity	Leutou et al. (2018)
238	*Nocardiopsis* sp. LGO5	Marine sediment, Helwan, Egypt	Antibacterial activity	Hamed et al. (2018b)
239–241	*Nocardiopsis* sp. HB-J378	Marine sponge *Theonella* sp.	Antibacterial activity	Xu et al. (2018)
242	*Micrococcus luteus*	Sponge *Xestospongia* sp., New Caledonia	Antibacterial activity	Bultel-Poncé et al. (1998)
243	*Micrococcus* sp. EG45	Red Sea sponge Spheciospongia vagabunda	Antibacterial activity	Eltamany et al. (2014)
244	*Kocuria Palustris*	Sponge, Florida Keys	Antibacterial activity	Martín et al. (2013)
245	*Kocuria Palustris*	Sponge	Antibacterial activity	Takasaka et al. (2017)
246–248	*Saccharothrix espanaensis* An 113	A marine mollusc the Great Bay, Sea of Japan, Russia	Antibacterial activity	Kalinovskaya et al. (2008)
249	*Salinispora arenicola* CNR-647	Ascidian *Ecteinascidia turbinata*, Sweetings Cay, Grand Bahama Island	Antibacterial activity	Asolkar et al. (2010)
250–251	*Solwaraspora* sp. WMMB329	Ascidian *Tridemnum orbiculatum*	Antibacterial activity	Ellis et al. (2014)

Table 1 (continued)

Compound	Producing strain	Environmental source	Bioactivity	Refs.
252	*Actinomadura* sp. WMMB-499	Ascidian *Ecteinascidia turbinata*	Antifungal activity	Wyche et al. (2014)
253–254	*Pseudonocardia* sp HS7	The cloacal aperture of sea cucumber *Holothuria moebii*	Antibacterial activity	Ye et al. (2016)
255	*Actinomadura* sp.	Ascidian *Ecteinascidia turbinata*	Antibacterial activity	Wyche et al. (2017)
256–257	*Lechevalieria aerocolonigenes* K10-0216	Mangrove, Iriomote island	Antibacterial and antifungal activity	Kimura et al. (2018)
258	*Lechevalieria aerocolonigenes* K10-0216	Brown seaweed *Pelvetia canaliculata* (Linnaeus),the rocks of Sonmiani Beach (Karachi, Pakistan)	Antibacterial activity	Uzair et al. (2018)
259–261	*Actinomadura* sp. M045	Sediment, Jiaozhou Bay	Antifugal:**259–261** Antibacterial activity:**261**	Maskey et al. (2003)
262	*Verrucosispora* sp. AB-18–032	Sediment	Antibacterial activity	Bister et al. (2004)
263–267	*Marinispora* sp. CNQ-140	Sediment, La Jolla, California	Antibacterial activity:**263–266** Antifugal:**263** and **267**	(Kwon et al. 2006, 2009)
268	*Verrucosispora* sp. AB-18–032	Sediment, Sea of Japan	Antibacterial activity	Keller et al. (2007)
269–271	*Marinispora* NPS008920	Sediment, Cocos Lagoon, Guam	Antibacterial activity	Macherla et al. (2007)
272–276	*Marinispora* sp. NPS12745	Sediment, the coast of San Diego, California	Antibacterial activity	McArthur et al. (2008)
277–278	*Verrucosispora maris* AB-18–032	Sediment, Raune Fjord, Norway	Antibacterial activity	Fiedler et al. (2008)
279	*Salinispora arenicora* YM23-082	Sediment, Yap, Micronesia	Antibacterial activity	Matsuda et al. (2009)
280	*Salinispora arenicola*	Sediment, Palau	Antibacterial activity	Murphy et al. (2010)
281–283	*Pseudonocardia* sp. SCSIO 01,299	Sediment, the South China Sea	Antibacterial activity	Li et al. (2011)
284–292	*Actinoalloteichus* sp. NPS702	Sediment, Usa Bay, Kochi Prefecture, Japan	Antifungal activity	Sato et al. (2012)
293	*Marinactinospora thermotolerans* SCSIO 00,652	Sediment, the South China Sea	Antibacterial activity	Zhou et al. (2012)
294	*Amycolatopsis alba var. nov.* DVR D4	Sediments from, Bay of Bengal	Antibacterial activity	Dasari et al. (2012)
295	*Serinicoccus profundi* sp. nov	A deep-sea sediment, Indian Ocean	Antibacterial activity	Yang et al. (2013)
296	*Verrucosispora* sp. MS100047	Sediment, the South China Sea	Antibacterial activity	Huang et al. (2016)
297–300	*Kribbella* sp. MI481-42F6	Sediment, Japna	Antifungal activity	Igarashi et al. (2017)
301	*Actinomadura* sp. DS-MS-114	Sediment, Sagami Bay	Antibacterial activity	Kurata et al. (2017)
302–304	*Verrucosispora* sp. SCSIO 07,399	Sediment, the South China Sea	Antibacterial activity	Zhang et al. (2019b)
305–308	*Salinispora arenicola* BRA-213	Sediment, St.Peter and St. Paul Archipelago, Brazil	Antibacterial activity	da Silva et al. (2019)
309	unidentified marine bacterium of the order Actinomycetales	The shallow waters of Bodega Bay	Antibacterial activity	Pathirana et al. (1991)
310	*Saccharomonospora* sp. CNQ-490	Unknown source	Antibacterial activity	Yamanaka et al. (2014)
311–312	*Pseudonocardia carboxydivorans* M-227	Deep seawater of the Aviles submarine Canyon	Antibacterial activity	Braña et al. (2017b)
313	*Thermoactinomyces vulgaris* ISCAR 2354	Coastal hot spring, Icelandic marine waters	Antibacterial activity	Teta et al. (2017)

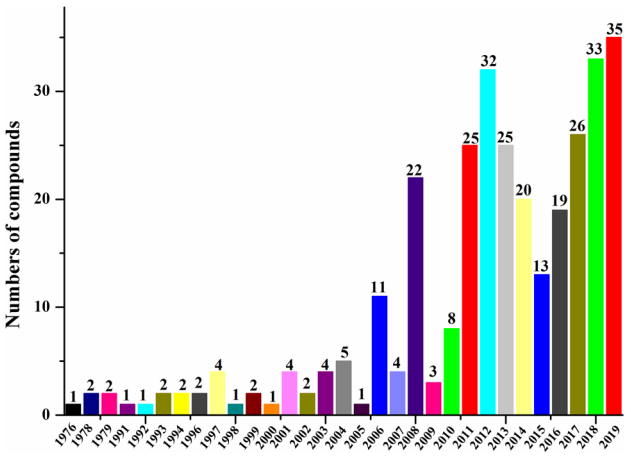

Fig. 12 Annual numbers of antimicrobial compounds identified (1976–2019)

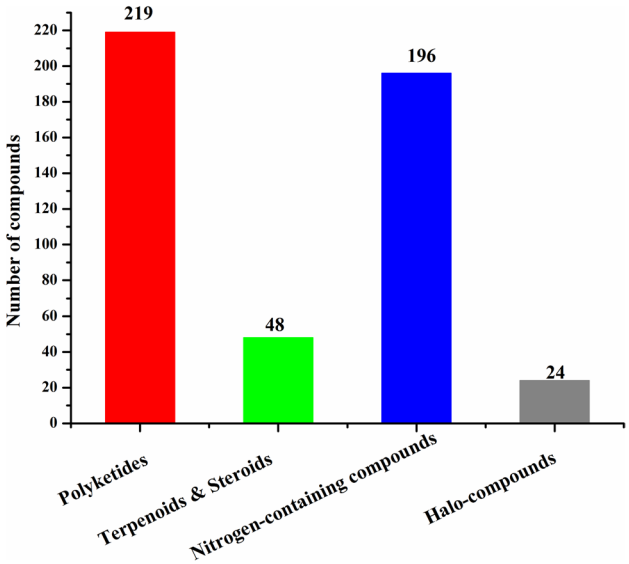

Fig. 13 Structural classes of antimicrobial compounds isolated from marine actinomycetes (1976–2019)

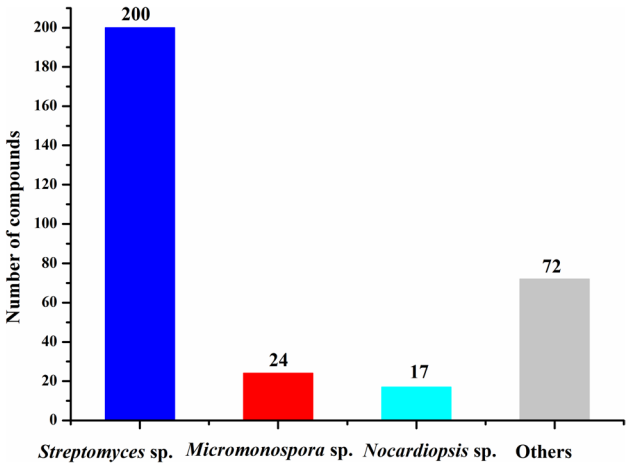

Fig. 14 Numbers of antimicrobial compounds from different marine actinomycetes (1976–2019)

Streptomyces sp., *Micromonospora* sp., and *Nocardiopsis* sp. were 200, 24, 17 and 72, respectively (Fig. 14), among which about 64% were produced by *Streptomyces* sp. Other actinomycetes (for examples, *Micromonospora*, *Nocardiopsis*, *Salinispora* and *Pseudonocardia*) are also prolific producers of secondary metabolites in the marine environment. The numbers of antibacterial and anti-fungal compounds identified from marine actinomycetes are 272 and 70, respectively (Fig. 15).

Scholars in Europe and America, China and other Asian countries published 145, 106 and 50 antimicrobial compounds, respectively (Fig. 16). Different from the antimicrobial study of marine fungi in which Chinese scientists are the most productive in recent years, researchers in Europe and America published 156 antimicrobial compounds from marine actinomycetes, slightly more than scholars in Asia who reported 145 antimicrobial compounds.

J. Nat. Prod. attracted the most contributions (35 articles), followed by *J. Antibiot.* (29 articles) and *Mar. Drugs* (24 articles), which accounts for 83% (=88/107) of all the published papers (Fig. 17). Nearly one-third (31.6%) of all the new antimicrobial compounds were pubished in *J. Nat. Prod.* followed by *Mar. Drugs* (12.2%) and by *J. Antibiot.* (12.1%) (Fig. 18). The dominant host of actinomycetes was marine sediment with a ratio of 69.6% (Fig. 19). Marine animals were also good hosts for actinomycetes (16.9%). Rare marine actinomycetes (for example, *Salinispora* sp. from deep-sea sediments) in combination of new screening approach will provide more antimicrobial agents.

Table 2 The initial research on antimicrobial active compounds from actinomycetes

Fist producing strain	Environment source	Compound	Time
Streptomyces griseus SS-20	Shallow sea sediment, Sagami Bay	Aplasmomycin A	1976
Micromonospora sp. L-13-ACM2–09	Unknown source	Thiocoraline	1997
Nocardiopsis dassonvillei	Sediment sample, island of Kauai, Hawaii	Kahakamide A	2001
Other actinomycetes (unidentified marine bacterium of the order Actinomycetales)	The shallow waters of Bodega Bay	Maduralide	1991

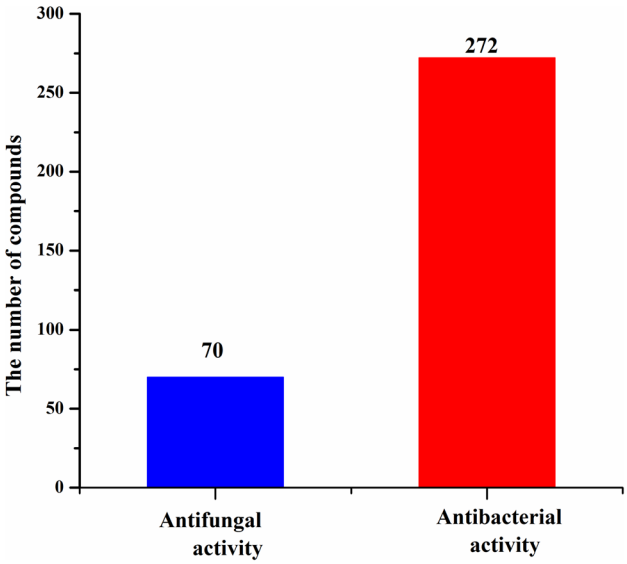

Fig. 15 Numbers of antibacterial and anti-fungal compounds from marine actinomycetes (1976–2019)

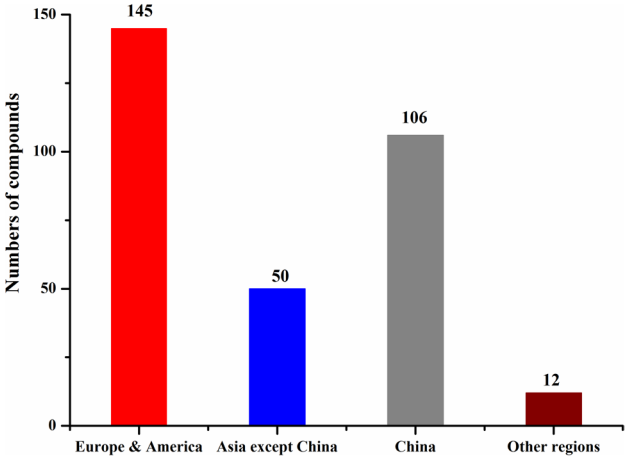

Fig. 16 Numbers of antimicrobial marine metabolites by different countries (1976–2019)

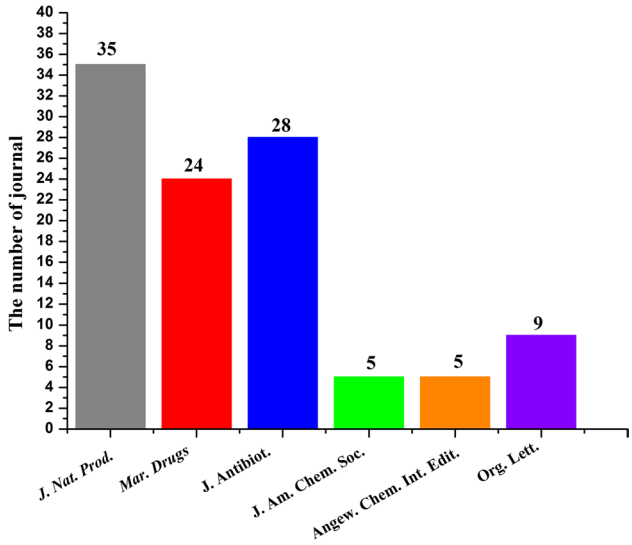

Fig. 17 Journals and numbers of papers that published antimicrobial compounds (1976–2019)

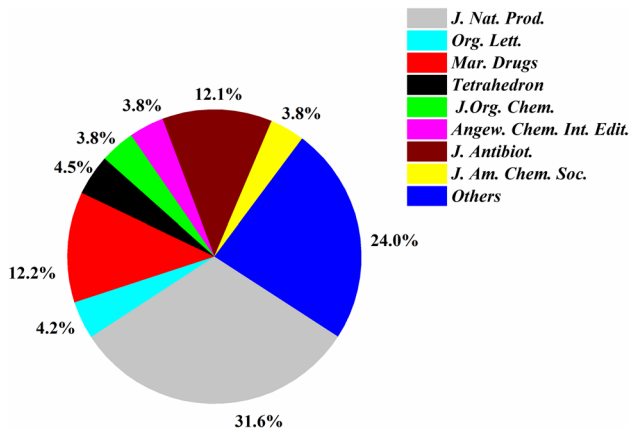

Fig. 18 Percentages of antimicrobial compounds published in different journals (1976–2019)

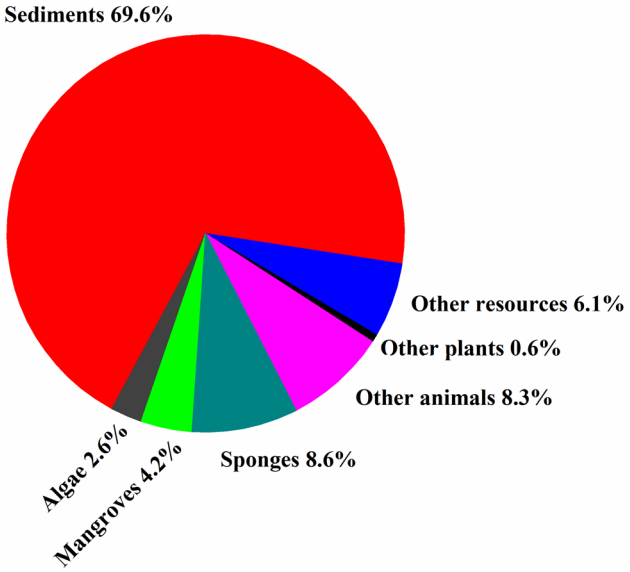

Fig. 19 Percentages of antimicrobial compounds on the basis of the hosts of actinomycetes (1976–2019)

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Compliance with ethical standards

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

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