**Marine Actinomycetes: Species Diversity and Potential Bioactive Compounds**

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**Abstract**

Marine organisms have evolved diverse structural, physiological and metabolic characteristics that allow them to survive under extreme conditions. Marine microorganisms, in particular, actinomycetes, are one of the promising sources of bioactive compounds. Actinomycetes are Gram Positive filamentous bacteria that are extensively studied for the production of diverse secondary metabolites. The studies on marine actinomycetes and their bioactive compounds intensified with the advancement in technologies that enabled their culture-independent isolation and characterization. The diversity of actinomycetes in the marine environment with an emphasis on those associated with marine organisms and their bioactive compounds is focused on in this chapter.

**Keywords**: Actinomycetes, Marine Environment, Diversity, Bioactive compounds

**Introduction**

The marine ecosystem entails a rich variety of organisms, both macro and micro with specific and unique morphological and metabolic characteristics that make them capable of surviving under extreme pressure, salinity, and temperature (Abdelmohsen et al., 2014). These diverse microbial communities of marine habitats and the ecology of marine ecosystems remain largely unexplored. Actinomycetes make up a promising group of marine microbes. Novel antimicrobial drugs have been produced by actinomycetes, including the most important classes of tetracyclines, aminoglycosides, macrolides, and glycopeptides. Marine actinomycetes provide a fresh perspective on microbial natural product research with their novel secondary metabolites discovered from unique taxa and isolated rare populations. Actinomycete diversity and the effects of marine adaptations on secondary metabolite production need to be determined in order to better understand the potential of marine actinomycetes.

Actinomycetes are Gram-positive filamentous bacteria with a high G+C content [Jensen et al., 2005]. Approximately 70% of antibiotics used in the human treatment are produced by actinomycetes (Bérdy, 2005) making them the most powerful natural source of antibiotics. In the past, actinomycete natural products were obtained by culturing them in media that were different from their natural environments. Since the 1980s, the search for natural products from actinomycetes has declined rapidly due to the re-discovery of compounds (Van Middlesworth and Cannell, 1998). Subsequently, the efforts to isolate novel compounds from actinomycetes witnessed a massive shutdown, parallel to which there was the rise in antibiotic-resistant pathogenic microbes. Since the advent of omics and high throughput technologies and with thousands of actinomycete genome sequences readily available, it has become evident that actinomycetes can produce NPs that have never been observed before [Behie et al., 2017]. This has elicited huge interest in exploring them for the discovery of novel products using innovative strategies. The chapter provides an overview of the Actinomycete diversity in the marine environment and the potent bioactive compounds produced by them.

**Actinomycete Diversity in the Marine Environment**

There are many unique features of marine environments that distinguish them from other aquatic environments. Extreme environmental conditions like salinity, high temperature, pressure, and pH variations induce bioactive compound production in marine microorganisms in comparison to their terrestrial counterparts (Sarkar and Suthindhiran, 2022). Marine actinomycetes are diverse and inhabit sediment, seawater, and aquatic organisms. The majority of the actinomycetes isolated have been from the sponges, corals, ascidians etc. as well as from the brown algae. There are also reports of isolation of potent actinomycetes from other marine sources like sediments (mangroves, estuaries, coastal areas, lagoons, deep sea lakes) and from marine vertebrates.

Sediments: Marine actinomycetes predominantly Streptomyces sp. were isolated from sediments by several researchers. Ellaiah et al. (1996 and 2004) isolated Streptomyces sps. from marine sediments of Machilipatnam and Kakinada coast in Andra Pradesh, India. About 94 strains of Actinomycetes predominantly Streptomyces sps. were isolated from the marine sediments of a shrimp farm by You et al. (2005). Jose and Jha (2017) in their study isolated a total of 148 Actinobacteria from intertidal marine sediments of Diu Island (India) in Arabian Sea and based on 16S rRNA gene sequence, determined to belong to Glycomycete, Micromonospora, Nocardia, Nocardiopsis, Pseudonocardia, Streptomyceta, and Thermomonospora sp.. A total of 73 actinobacterial strains were isolated from marine soil of East coast regions of Andhra Pradesh, India; 8 of them were characterized and were found to belong to Dietzia sp., Kocuria sp., Nocardiopsis sp. and Streptomyces sp. Gozari et al. (2019) isolated 168 actinomycete colonies from 14 sediment samples of the northern part of the Oman sea. The majority (66%) of the isolates belonged to Streptomycetaceae followed by Micromonosporaceae (14%), Nocardiaceae (6%) and Pseudonocardiaceae (4%). The deep-sea sediment isolates of Actinomycete in the previous studies were not well- characterized (Goodfellow and Williams, 1983). Native marine actinomycetes showed to exist in the oceans from culture-independent studies (Ward and Bora, 2006), which include Dietzia sp., Rhodococcus sp. (Heald et al., 2001), Streptomyces sp. (Moran et al. 1995), Salinispora sp. (Mincer et al., 2005, Jensen et al., 2005, Maldonado et al., 2005) and Marinispora sp. (Jensen et al., 2005, Kwon et al., 2006) and *Aeromicrobium marinum* (Bruns et al. 2003).

Invertebrates: Bioactive compounds have been derived from marine invertebrates, such as sponges and corals, but their small biomass makes them unreliable sources (Jagannathan et al., 2021). The Marine sponges belong to the phylum Porifera and are among the primitive multicellular animals (Love et al., 2009) on Earth which inhabit diverse microbes, and their symbiotic relationships with bacteria are among the most complex (Taylor et al., 2007; Sun et al., 2015). Studies suggest the microorganisms within these invertebrates are the true sources of these bioactive compounds (El Samak et al., 2018). Rare actinomycete genera such as Actinokinetospora, Amycolatopsis, Nonomuracea, Saccharomonospora, Saccharopolyspora, Pseudonocardia, Pseudonocardia, Actinomadura, Knoellia and Verrucosispora have been isolated from marine sponges which could be targeted for novel lead compounds (Abdelmohsen et al., 2014). Several studies evidenced the isolation of new marine actinomycete genera from sponges. Pimentel-Elardo et al. (2008) isolated an obligate marine marine actinomycete *Streptomyces axinellae* sp. nov. from the sponge Axinella polypoides collected from Banyuls-surmer, France. The knowledge of actinobacterial diversity in coral reef systems is scant. Mahmoud and Kalendar, (2016) studied the richness and diversity of Actinomycete present in three types of coral viz., *Coscinaraea columna*, *Platygyra daedalea* and *Porites harrisoni* surviving in the coral reef system north of the Arabian Gulf. The actinobacterial genera isolated belong to the common Streptomyces as well as Micrococcus, Brevibacterium, Renibacterium, Nocardia, Microbacterium, Dietzia, Cellulomonas, Ornithinimicrobium, Micromonospora, Rhodococcus, Agrococcus, Kineococcus, Dermacoccus, Devriesea, Kocuria, Marmoricola, Brachybacterium and Arthrobacter. Several researchers have also isolated rare actinomycetes which are the non-streptomyces actinomycete from the marine environment with the ability to produce novel compounds (Ezeobiora et al., 2022). Table 1 shows some of the rare actinomycetes isolated from marine sponges and corals.

Table 1. Rare actinomycetes isolated from marine sponges & corals

|  |  |  |  |
| --- | --- | --- | --- |
| Host species | Identified actinomycete genera | Location of sample collection | Reference |
| **Sponge-associated actinomycete** |
| *Xestospongia* sp. | *Nocardia xestospongiae* | Andaman sea | Thawai et al., 2017 |
| *Speciospongia vagabunda* | *Actinokinespora spheciospongiae* | Red sea | Kampfar et al., 2014 |
| *Amphimedon viridis* | *Williamsia spongiae* | Praia Guaecá (São Paulo, Brazil) | Afonso et al., 2017 |
| *Glodia corticostylifera* | *Marmoricola aquaticus* | São Paulo, Brasil | De Memezes, et al. 2015 |
| Unidentified marine sponge | *Micromonospora spongicola* | Gulf of Thailand | Supong et al., 2013a |
| Xestospongia sp. | *Verrucosispora andamanensis* | Phuket Province of Thailand | Supong et al., 2013b |
| **Coral-associated actinomycete** |
| *Galaxea fascicularis* | *Prauserella corallicola* | - | Wu et al., 2014 |
| *Nocardiopsis coralliicola* | *Gorgonian coral, Menella praelonga* | Weizhou Island, Guangxi province, China | Li et al., 2012 |

**Marine Actinomycetes producing Bioactive Compounds**

The advancement in technologies provided us with different ways and methods to determine microbial diversity and determine the biosynthesis ability of potent marine microorganisms (Chen et al., 2021) which are unculturable. The actinomycete-derived bioactive compounds of marine origin are mainly isolated from marine sponges. The actinomycete genera belonging to Micrococcineae are reported to be the predominant sponge symbionts but with limited potential for secondary metabolism. In contrast, those belonging to Streptomycetaceae, Micromonosporaceae, and Pseudonocardiaceae which are less abundant in sponges show more potential for secondary metabolite production and have prospects to produce novel drug / bioactive leads (Chen et al., 2021). The symbiotic actinomycete in the marine environment are potent sources of novel natural products (El Samak et al., 2018).

Table 2. Natural products / Bioactive compounds (Alkaloids, Polyketides, Peptides and Steroids from Actinomycete associated with Marine organisms (Adapted from Chen et al., 2021)

|  |  |  |  |
| --- | --- | --- | --- |
| Actinomycete sp. | Bioactive compound | Bioactivity | Reference |
| **Alkaloids** |
| Micromonospora sp. L-31-CLCO-002 (associated with marine sponge *Clathrina coriacea*) | 4’-N-methyl-5’-hydroxystaurosporine, 5’-hydroxystaurosporine, staurosporine | Cytotoxicity | Abdelmohsen et al., 2014a; Hernandez et al., 2000 |
| Saccharopolyspora sp. nov., (associatedwith marine sponge *Mycale plumose*) | Metacycloprodigiosin, Undecylprodigiosin  | Cytotoxicity | Liu et al., 2005 |
| Micromonospora sp. (associatedwith marine sponge *Acanthostrongylophora sp.)* | manzamine A, 8-hydroxy manzamine | Antibacterial and Antiviral | Abdelmohsen et al., 2014a |
| Salinispora sp. strain M403 (associatedwith marine sponge *Pseudoceratina clavate*)  | Rifamycins B and SV | Antibacterial | Abdelmohsen et al., 2014a; Kim et al., 2006 |
| Streptomyces sp. strain Ni-80 (associated with unidentified Sponge) | Urauchimycins A and B | Antifungal | Abdelmohsen et ala., 2014; Imamura et al., 1993 |
| Streptomyces sp. strain HB202 (associated with marine sponge *Halichondria panicea*) | Streptophenazines A-H | Antibacterial | Mitova et al., 2008 |
| Salinispora sp.FS-0034 (associated with marine sponge *Theonella* sp.) | Rifamycin W | Antibacterial | Singh et al., 2014 |
| Streptomyces sp. strain RV15 (associated with marine sponge *Dysidea tupha*) | Naphthacene glycoside SF2446 A2 | Antibacterial | Reimer et al., 2015 |
| Strain MCCB267 (associatedwith marine sponge *Mycale* sp.) | Ikarugamycin (IK), clifednamide A (CF), 30-oxo-28-N-methylikarugamycin and 28-N-methylikarugamycin (MI) | Cytotoxicity | Dhaneesha et al., 2019 |
| Streptomyces sp. OUCMDZ-1703 (associated with soft coral) | Watasemycin A, pulicatin G, aerugine | Antibacterial | Peng et al., 2013 |
| Streptomyces sp. (associated with *Lophelia pertusa*) | Lobophorin K | Cytotoxicity | Brana et al., 2017 |
| Salinispora pacifica LL-371366 (derived from marine ascidian *Polysyncraton lithostrotum*) | Lomaiviticins A and B | Cytotoxicity | Chen et al., 2018; Janso et al., 2014; He et al., 2001 |
| **Polyketides** |
| Micromonospora sp. L-25-ES25-008 (associated with Marine sponge) | IB-96212 (26-membered spiroketal macrolide) | Cytotoxicity | Abdelmohsen et al., 2014a; Canedo et al., 2000 |
| Saccharopolyspora taberi PM070747 (associated with Marine sponge)  | Angucyclinone PM070747 | Cytotoxicity | Perez et al., 2009 |
| Streptomyces sp. Sp080513GE-26 (associated with Marine sponge) | Tetracenoquinocin | Cytotoxicity | Abdelmohsen et al., 2014a; Motohashi et al., 2010 |
| Nocardiopsis strain HB383 (associated with Marine sponge *Halichondria panacea*) | γ-pyrones nocapyrones A-D | Antibacterial | Abdelmohsen et al., 2014a; Pimentel-Elardo et al., 2011 |
| Streptomyces sp. BCC45596 (associated with Marine sponge *Xestospongia sp.*) | Urdamycinone E, Uramycinone G and dehydroxyaquayamycin  | Antibacterial, Antiparasitic | Wang et al., 2020; Supong et al., 2012  |
| Actinokineospora sp. EG49 (associated with Marine sponge *Spheciospongia vagabunda*) | Actinosporin C and D | Antioxidant | Abdelmohsen et al., 2014b; Grkovic et al., 2014 |
| Micrococcus sp. EG45 (associated with Red Sea sponge) | Microluside A | Antibacterial | Vicente et al., 2015 |
| Streptomyces sp. PG-19 (associated with Cortez gorgonian octocoral Pacifigorgia sp.) | Octalactins A and B | Cytotoxicity | Tapiolas et al., 1991 |
| Streptomyces sp. SCSIO 41399 (Coral associated) | Araciamycin K | Cytotoxicity | Cong et al., 2019 |
| *Streptomyces variabilis* (associated with Scleractinia coral *Acropora formosa*) | 1-hydroxy-1-norresistomycin (HNM) | Cytotoxicity | Ramalingam et al., 2019 |
| *Streptomyces sp.* #N1-78-1 (associated with sea squirt *Ecteinascidia turbinata*) | Bisanthraquinones 1 and 2 | Antibacterial | Chen et al., 2018; Socha et al., 2006 |
| *Pseudonocardia sp.* HS7 (associated with sea cucumber *Holothuria moebii)* | Curvularin macrolides (5) | Cytotoxicity | Cao et al., 2019 |
| *Streptomyces sp.* 112CH148 (associated with starfish *Acanthaster planci)* | 3,4,6-trisubstituted α-pyrone derivatives violapyrones H and I | Cytotoxicity | Shin et al., 2014 |
| *Micromonospora* (associated with marine mammals*)* | Glycosylated polyketide phocoenamicin | Antibacterial | Ochoa et al., 2018 |
| **Peptides** |
| Streptomyces sp. DA18 (associated with marine sponge *Craniella australiensis*)  | Diketopiperazines (DKPs) | Antifouling | Gao et al., 2010 |
| Streptomyces sp. strains 22 and 23 (associated with marine sponge *Aplysina aerophoba* and *Axinella polypoides* ) | Cyclic depsipeptide Valinomycin | Antiparasitic | Abdelmohsen et al., 2014a; Pimentel-Elardo et al., 2011 |
| *Kocuria palustris* (associated with marine sponge) | Kocurin | Antibacterial | Palomo et al., 2013; Martin et al., 2013 |
| Streptomyces sp. SBT348 (associated with marine sponge) | Petrocidin A (cyclic dipeptide) | Cytotoxicity | Kitani et al., 2017 |
| Micromonospora sp. L-13ACM2-092 (associated with soft coral) | Thiocoraline | CytotoxicityAntibacterial | Boger et al., 2000; Qi et al., 2020 |
| **Steroids** |
| Actinomadura sp. SBMs009 (associated with marine sponge *Suberites japonicus*) | 3-keto sterols bendigoles D-F | Antiinflammatory | Abdelmohsen et al., 2014a; Simmons et al., 2011 |
| *Streptomyces seoulensis* IFB-A01 | Streptolactone | Antiviral | Jiao et al., 2013 |
| *Streptomyces seoulensis* sp. RM66 (associated with marine sponge) | Manadoperoxide H and acanthosterol sulfate F  | Antiprotozoal | Alkhalifah, 2021 |

As is evident from Table 2 that several actinomycetes associated with marine organisms are characterized and have pronounced bioactive compound production potential. Molecules with apparent activities have entered clinical trials. Further investigations of marine actinomycetes could uncover new compounds not known to date from these versatile microbes.

**Conclusion**

 Given the vast diversity of the marine environment, it is increasingly obvious that the oceans contain numerous unique chemical compounds. Novel metabolites with pharmaceutical and industrial applications are generated by actinomycetes. Actinomycetes inhabiting extreme environments like the ocean have rich metabolic diversity, making them ideal candidates as sources of novel bioactive compounds. In light of the rise of antibiotic resistance and the need for alternatives, it is essential to expand research on actinomycetes and explore their potential. As highlighted in this chapter, there have been several breakthroughs in bioactive leads from marine actinomycetes in the past decade which are to be harnessed to find potential applications.

**References**

1. Abdelmohsen U. R., Yang C., Horn H., Hajjar D., Ravasi T., Hentschel U. (2014). Actinomycetes from Red Sea sponges: sources for chemical and phylogenetic diversity. Mar. Drugs 12, 2771–2789. 10.3390/md12052771
2. Abdelmohsen, U.R.; Bayer, K.; Hentschel, U. Diversity, abundance and natural products of marine sponge-associated actinomycetes. Nat. Prod. Rep. 2014, 31, 381–399.
3. Afonso CB, Afonso RS, Souza WR, Parma M, Melo IS, Zucchi TD, Fantinatti GF (2017) Williamsia spongiae sp. nov., an actinomycete isolated from the marine sponge Amphimedon viridis. Int J Syst Evol Microbiol 67:1260–1265
4. Alkhalifah, D.H.M. Sponge-associated sp. RM66 metabolome induction with N-acetylglucosamine: Antibacterial, antifungal and anti-trypanosomal activities. Saudi J. Biol. Sci. 2021, 28, 4691–4698.
5. Behie S. W., Bonet B., Zacharia V. M., McClung D. J., Traxler M. F. (2017). Molecules to ecosystems: actinomycete natural products in situ. Front. Microbiol. 7:2149. 10.3389/fmicb.2016.02149
6. Bérdy, J. Bioactive Microbial Metabolites. J Antibiot 58, 1–26. 2005. <https://doi.org/10.1038/ja.2005.1>
7. Boger, D.L.; Ichikawa, S. Total Syntheses of Thiocoraline and BE-22179: Establishment of Relative and Absolute Stereochemistry. J. Am. Chem. Soc. 2000, 122, 2956–2957.
8. Braña, A.F.; Sarmiento-Vizcaíno, A.; Osset, M.; Pérez-Victoria, I.; Martín, J.; de Pedro, N.; de la Cruz, M.; Díaz, C.; Vicente, F.; Reyes, F.; et al. Lobophorin K, a New Natural Product with Cytotoxic Activity Produced by Streptomyces sp. M-207 Associated with the Deep-Sea Coral Lophelia pertusa. Mar. Drugs 2017, 15, 144.
9. Bruns A, Philipp H, Cypionka H, Brinkhoff T. Aeromicrobium marinum sp. nov., an abundant pelagic bacterium isolated from the German Wadden sea. Antonie Van Leeuwenhoek 2003;53:1917–23.
10. Cañedo, L.M.; Puentes, J.L.F.; Baz, J.P.; Huang, X.-H.; Rinehart, K.L. IB-96212, a Novel Cytotoxic Macrolide Produced by a Marine Micromonospora. II. Physico-chemical Properties and Structure Determination. J. Antibiot. 2000, 53, 479–483.
11. Cao, D.D.; Trinh, T.T.V.; Mai, H.D.T.; Vu, V.N.; Le, H.M.; Thi, Q.V.; Nguyen, M.A.; Duong, T.T.; Tran, D.T.; Chau, V.M.; et al. Antimicrobial lavandulylated flavonoids from a sponge-derived Streptomyces sp. G248 in east vietnam sea. Mar. Drugs 2019, 17, 529.
12. Chen J, Xu L, Zhou Y, Han B. Natural Products from Actinomycetes Associated with Marine Organisms. Mar Drugs. 2021 Nov 10;19(11):629. doi: 10.3390/md19110629. PMID: 34822500; PMCID: PMC8621598.
13. Chen, L.; Hu, J.-S.; Xu, J.-L.; Shao, C.-L.; Wang, G.-Y. Biological and Chemical Diversity of Ascidian-Associated Microorganisms. Mar. Drugs 2018, 16, 362.
14. Chen, M.-H.; Zhang, W.-L.; Chen, L.; Lin, R.; Xie, Y.; Fang, D.-S.; Lian, Y.-Y.; Jiang, H. Isolation, purification and identification of two new alkaloids metabolites from marine-derived Verrucosispora sp. FIM06025. Nat. Prod. Res. 2018, 33, 2897–2903.
15. Cong, Z.; Huang, X.; Liu, Y.; Liu, Y.; Wang, P.; Liao, S.; Yang, B.; Zhou, X.; Huang, D.; Wang, J. Cytotoxic anthracycline and antibacterial tirandamycin analogues from a marine-derived Streptomyces sp. SCSIO 41399. J. Antibiot. 2019, 72, 45–49.
16. Dhaneesha, M.; Hasin, O.; Sivakumar, K.C.; Ravinesh, R.; Naman, C.B.; Carmeli, S.; Sajeevan, T.P. DNA Binding and Molecular Dynamic Studies of Polycyclic Tetramate Macrolactams (PTM) with Potential Anticancer Activity Isolated from a Sponge-Associated Streptomyces zhaozhouensis subsp. mycale subsp. nov. Mar. Biotechnol. 2019, 21, 124–137.
17. e Menezes CB, Tonin MF, Silva LJ, De Souza WR, Parma M, Melo IS, Zucchi TD, Destefano SA, Fantinatti GF (2015) Marmoricola aquaticus sp. nov., an actinomycete isolated from marine sponge. Int J Syst Evol Microbiol 65:2286–2291
18. El Samak M, Solyman SM, Hanora A. Antimicrobial activity of bacteria isolated from Red Sea marine invertebrates. Biotechnol Rep (Amst). 2018 Jul 20;19:e00275. doi: 10.1016/j.btre.2018.e00275. PMID: 30197871; PMCID: PMC6127373.
19. Ellaiah P., Ramana T., Bapiraju K.V.V.S., Sujatha P., Uma Sankar A. Investigation on marine actinomycetes from Bay of Bengal near Kakinada coast of Andhra Pradesh. Asian. J. Microbiol. Biotech. Env. Sci. 2004;6:53–56.
20. Ellaiah, D. Kalyan, V.S. Rao, B.V. Rao Isolation and characterization of bioactive actinomycetes from marine sediments Hindustan Antibiot Bull, 38 (1996), pp. 48-52.
21. Ezeobiora, C.E., Igbokwe, N.H., Amin, D.H. et al. Uncovering the biodiversity and biosynthetic potentials of rare actinomycetes. Futur J Pharm Sci 8, 23 (2022). <https://doi.org/10.1186/s43094-022-00410-y>
22. Gao, Y.; Yu, L.; Peng, C.; Li, Z.; Guo, Y. Diketopiperazines from two strains of South China Sea sponge-associated microorganisms. Biochem. Syst. Ecol. 2010, 38, 931–934.
23. Goodfellow M, Williams ST. Ecology of actinomycetes. Annu Rev Microbiol. 1983;37:189-216. doi: 10.1146/annurev.mi.37.100183.001201. PMID: 6357051.
24. Gozari, M., Zaheri, A., Jahromi, S.T. et al. Screening and characterization of marine actinomycetes from the northern Oman Sea sediments for cytotoxic and antimicrobial activity. Int Microbiol 22, 521–530 (2019). <https://doi.org/10.1007/s10123-019-00083-3>
25. Grkovic, T.; Abdelmohsen, U.R.; Othman, E.M.; Stopper, H.; Edrada-Ebel, R.; Hentschel, U.; Quinn, R.J. Two new antioxidant actinosporin analogues from the calcium alginate beads culture of sponge-associated Actinokineospora sp. strain EG49. Bioorganic Med. Chem. Lett. 2014, 24, 5089–5092.
26. He, H.; Ding, W.D.; Bernan, V.S.; Richardson, A.D.; Ireland, C.M.; Greenstein, M.; Ellestad, G.A.; Carter, G.T. Lomaiviticins A and B, potent antitumor antibiotics from Micromonospora lomaivitiensis. J. Am. Chem. Soc. 2001, 123, 5362–5363.
27. Heald SC, Brandao PFB, Hardicre R, Bull AT. Physiology, biochemistry and taxonomy of deep-sea nitrile metabolising Rhodococcus strains. Antonie Van Leeuwenhoek 2001;80:169–83.
28. Hernández, L.M.C.; Blanco, J.A.D.L.F.; Baz, J.P.; Puentes, J.L.F.; Millán, F.R.; Vázquez, F.E.; Fernández-Chimeno, R.I.; Grávalos, D.G. 4’-N-Methyl-5’-hydroxystaurosporine and 5’-Hydroxystaurosporine, New Indolocarbazole Alkaloids from a Marine Micromonospora sp. Strain. J. Antibiot. 2000, 53, 895–902.
29. Imamura, N.; Nishijima, M.; Adachi, K.; Sano, H. Novel antimycin antibiotics, urauchimycins A and B, produced by marine actinomycete. J. Antibiot. 1993, 46, 241–246.
30. Jagannathan SV, Manemann EM, Rowe SE, Callender MC, Soto W. Marine Actinomycetes, New Sources of Biotechnological Products. Mar Drugs. 2021 Jun 25;19(7):365. doi: 10.3390/md19070365. PMID: 34201951; PMCID: PMC8304352.
31. Janso, J.E.; Haltli, B.; Eustaquio, A.; Kulowski, K.; Waldman, A.J.; Zha, L.; Nakamura, H.; Bernan, V.S.; He, H.; Carter, G.T.; et al. Discovery of the lomaiviticin biosynthetic gene cluster in Salinispora pacifica. Tetrahedron 2014, 70, 4156–4164.
32. Jensen, P. R., T. J. Mincer, P. G. Williams and W. Fenical, 2005. Marine actinomycete diversity and natural product discovery. Antonie van Leeuwenhoek 87: 43-48.
33. Jiao, W.H.; Yuan, W.; Li, Z.Y.; Li, J.; Li, L.; Sun, J.B.; Gui, Y.H.;Wang, J.; Ye, B.P.; Lin, H.W. Anti-MRSA actinomycins D1-D4 from the marine sponge-associated Streptomyces sp. LHW52447—ScienceDirect. Tetrahedron 2018, 74, 5914–5919.
34. Jose, P.A., Jha, B. Intertidal marine sediment harbours Actinobacteria with promising bioactive and biosynthetic potential. Sci Rep 7, 10041 (2017).
35. Kampfar P, Glaeser SP, Busse H, Abdelmohsen UR, Hentschet U (2014) Rubrobacter aplysinae sp. Nov., isolated from the marine sponge Aplysina aerophoba. Int J Syst Evol Microbiol 3:64
36. Kim, T.K.; Hewavitharana, A.K.; Shaw, N.; Fuerst, J.A. Discovery of a New Source of Rifamycin Antibiotics in Marine Sponge Actinobacteria by Phylogenetic Prediction. Appl. Environ. Microbiol. 2006, 72, 2118–2125.
37. Kitani, S.; Ueguchi, T.; Igarashi, Y.; Leetanasaksakul, K.; Thamchaipenet, A.; Nihira, T. Rakicidin F, a new antibacterial cyclic depsipeptide from a marine sponge-derived Streptomyces sp. J. Antibiot. 2017, 71, 139–141.
38. Kwon HC, Kauffman CA, Jensen PR, Fenical W. Marinomycins A-D, antitumor antibiotics of a new structure class from a marine actinomycete of the recently discovered genus Marinispora. J Am Chem Soc 2006;128:1622–32.
39. Li HW, Zhi XY, Yao JC, Zhou Y, Tang SK, Klenk HP, Zhao J, Li WJ. Comparative genomic analysis of the genus Nocardiopsis provides new insights into its genetic mechanisms of environmental adaptability. PLoS One. 2013 Apr 23;8(4):e61528. doi: 10.1371/journal.pone.0061528. PMID: 23626695; PMCID: PMC3634020.
40. Liu, R.; Cui, C.B.; Duan, L.; Gu, Q.Q.; Zhu,W.M. Potent in vitro anticancer activity of metacycloprodigiosin and undecylprodigiosin from a sponge-derived actinomycete Saccharopolyspora sp. Nov. Arch. Pharm. Res. 2005, 28, 1341–1344.
41. Love G. D., Grosjean E., Stalvies C., Fike D. A., Grotzinger J. P., Bradley A. S., et al.. (2009). Fossil steroids record the appearance of Demospongiae during the Cryogenian period. Nature 457, 718–721. 10.1038/nature07673
42. Mahmoud HM and Kalendar AA (2016) Coral-Associated Actinobacteria: Diversity, Abundance, and Biotechnological Potentials. Front. Microbiol. 7:204. doi: 10.3389/fmicb.2016.00204
43. Maldonado LA, Fenical W, Jensen PR, Kauffman CA, Mincer TJ, Ward AC, et al. Salinispora arenicola gen. nov., sp. nov. and Salinispora tropica sp. nov., obligate marine actinomycetes belonging to the family Micromonosporaceae. Int J Syst Evol Microbiol 2005a;55:1759–66.
44. Martin, J.; Sousa, T.D.S.; Crespo, G.; Palomo, S.; González, I.; Tormo, J.R.; De La Cruz, M.; Anderson, M.; Hill, R.T.; Vicente, F.; et al. Kocurin, the True Structure of PM181104, an Anti-Methicillin-Resistant Staphylococcus aureus (MRSA) Thiazolyl Peptide from the Marine-Derived Bacterium Kocuria palustris. Mar. Drugs 2013, 11, 387–398.
45. Mincer TJ, Fenical W, Jensen PR. Culture-dependent and culture-independent diversity within the obligate marine actinomycete genus Salinispora. Appl Environ Microbiol 2005;71:7019–28.
46. Mitova, M.I.; Lang, G.; Wiese, J.; Imhoff, J.F. Subinhibitory Concentrations of Antibiotics Induce Phenazine Production in a Marine Streptomyces sp. J. Nat. Prod. 2008, 71, 824–827.
47. Moran MA ,Rutherfford LT, HodsonRE. Evidence for indigenous Streptomycespopulations in a marine environment determined with a 16S rRNA probe. Appl Environ Microbiol 1995;61:3695–700.
48. Motohashi, K.; Takagi, M.; Shin-Ya, K. Tetrapeptides possessing a unique skeleton, JBIR-34 and JBIR-35, isolated from a sponge derived actinomycete, Streptomyces sp. Sp080513GE-23. J. Nat. Prod. 2010, 73, 226–228.
49. Ochoa, J.L.; Sanchez, L.M.; Koo, B.-M.; Doherty, J.S.; Rajendram, M.; Huang, K.C.; Gross, C.A.; Linington, R.G. Marine Mammal Microbiota Yields Novel Antibiotic with Potent Activity Against Clostridium difficile. ACS Infect. Dis. 2018, 4, 59–67.
50. Palomo, S.; González, I.; De La Cruz, M.; Martínez, I.G.; Tormo, J.R.; Anderson, M.; Hill, R.; Vicente, F.; Reyes, F.; Genilloud, O. Sponge-Derived Kocuria and Micrococcus spp. as Sources of the New Thiazolyl Peptide Antibiotic Kocurin. Mar. Drugs 2013, 11,1071–1086.
51. Peng, F.; Fandong, K.; Yuanfei,W. Antibiotic Metabolites from the Coral-Associated Actinomycete Streptomyces sp. OUCMDZ-1703. Chin. J. Chem. 2013, 31, 100–104.
52. Perez, M.; Schleissner, C.; Rodriguez, P.; Zuniga, P.; Benedit, G.; Sanchez-Sancho, F.; de la Calle, F. PM070747, a new cytotoxic angucyclinone from the marine-derived Saccharopolyspora taberi PEM-06-F23-019B. J. Antibiot. Tokyo 2009, 62, 167–169.
53. Pimentel-Elardo SM. Dissertation thesis. University of Würzburg; Würzburg, Germany: 2008. Novel Anti-infective secondary metabolites and biosynthetic gene clusters from actinomycetes associated with marine sponges.
54. Pimentel-Elardo, S.M.; Buback, V.; Gulder, T.A.; Bugni, T.S.; Reppart, J.; Bringmann, G.; Ireland, C.M.; Schirmeister, T.; Hentschel, U. New Tetromycin Derivatives with Anti-Trypanosomal and Protease Inhibitory Activities. Mar. Drugs 2011, 9, 1682–1697.
55. Qi, S.; Gui, M.; Li, H.; Yu, C.; Li, H.; Zeng, Z.; Sun, P. Secondary Metabolites from Marine Micromonospora: Chemistry and Bioactivities. Chem. Biodivers. 2020, 17, 2000024.
56. Ramalingam, V.; Mahamuni, D.; Rajaram, R. In vitro and in silico approaches of antibiofilm activity of 1-hydroxy-1-norresistomycin against human clinical pathogens. Microb. Pathog. 2019, 132, 343–354.
57. Reimer, A.; Blohm, A.; Quack, T.; Grevelding, C.G.; Kozjak-Pavlovic, V.; Rudel, T.; Hentschel, U.; Abdelmohsen, U.R. Inhibitory activities of the marine streptomycete-derived compound SF2446A2 against Chlamydia trachomatis and Schistosoma mansoni. J. Antibiot. 2015, 68, 674–679.
58. Sarkar G, Suthindhiran K. Diversity and Biotechnological Potential of Marine Actinomycetes from India. Indian J Microbiol. 2022 May 15:1-19. doi: 10.1007/s12088-022-01024-x.
59. Shin, H.J.; Lee, H.-S.; Lee, J.S.; Shin, J.; Lee, M.A.; Lee, H.-S.; Lee, Y.-J.; Yun, J.; Kang, J.S. Violapyrones H and I, New Cytotoxic Compounds Isolated from Streptomyces sp. Associated with the Marine Starfish Acanthaster planci. Mar. Drugs 2014, 12, 3283–3291.
60. Simmons, L.; Kaufmann, K.; Garcia, R.; Schwär, G.; Huch, V.; Müller, R. Bendigoles D–F, bioactive sterols from the marine sponge-derived Actinomadura sp. SBMs009. Bioorg Med. Chem. 2011, 19, 6570–6575.
61. Singh, S.; Prasad, P.; Subramani, R.; Aalbersberg, W. Production and purification of a bioactive substance against multi-drug resistant human pathogens from the marine-sponge-derived Salinispora sp. Asian Pac. J. Trop. Biomed. 2014, 4, 825–831.
62. Socha, A.M.; Garcia, D.; Sheffer, R.; Rowley, D.C. Antibiotic Bisanthraquinones Produced by a Streptomycete Isolated from a Cyanobacterium Associated with Ecteinascidia turbinata. J. Nat. Prod. 2006, 69, 1070–1073.
63. Sun W, Zhang F, He L, Karthik L, Li Z. Actinomycetes from the South China Sea sponges: isolation, diversity, and potential for aromatic polyketides discovery. Front Microbiol. 2015 Oct 1;6:1048. doi: 10.3389/fmicb.2015.01048. PMID: 26483773; PMCID: PMC4589764.
64. Supong K, Suriyachadkun C, Pittayakhajonwut P, Suwanborirux K, Thawai C 2013a Micromonospora spongicola sp. nov., an actinomycete isolated from marine sponge in the gulf of Thailand. J Antibiot 66:505–509
65. Supong K, Suriyachadkun C, Suwanborirux K, Pittayakhajonwut P, Thawai C. Verrucosispora andamanensis sp. nov., isolated from a marine sponge. Int J Syst Evol Microbiol. 2013b 63(Pt 11):3970-3974. doi: 10.1099/ijs.0.050906-0. Epub 2013.
66. Supong, K.; Thawai, C.; Suwanborirux, K.; Choowong, W.; Supothina, S.; Pittayakhajonwut, P. Antimalarial and antitubercular C-glycosylated benz[α]anthraquinones from the marine-derived Streptomyces sp. BCC45596. Phytochem. Lett. 2012, 5, 651–656.
67. Tapiolas, D.M.; Roman, M.; Fenical, W.; Stout, T.J.; Clardy, J. Octalactins A and B: Cytotoxic eight-membered-ring lactones from a marine bacterium, Streptomyces sp. J. Am. Chem. Soc. 1991, 113, 4682–4683.
68. Taylor M. W., Radax R., Steger D., Wagner M. (2007). Sponge-associated microorganisms: evolution, ecology, and biotechnological potential. Microbiol. Mol. Biol. Rev. 71, 295–347. 10.1128/mmbr.00040-06
69. Thawai C, Rungjindamai N, Klanbut K, Tanasupawat S (2017) Nocardia Xestospongiae sp. nov., isolated from a marine sponge in the Andaman sea. Int J Syst Evol Microbiol 67:1451–1456
70. Van Middlesworth, F., and Cannell, R. P. (1998). “Dereplication and partial identification of natural products,” in Natural Products Isolation Methods in Biotechnology, ed. R. P. Cannell (Totowa, NJ: Humana Press), 279–327. doi: 10.1007/978-1-59259-256-2\_10
71. Vicente, J.; Stewart, A.K.; VanWagoner, R.M.; Elliott, E.; Bourdelais, A.J.;Wright, J.L.C. Monacyclinones, New Angucyclinone Metabolites Isolated from Streptomyces sp. M7\_15 Associated with the Puerto Rican Sponge Scopalina ruetzleri. Mar. Drugs 2015, 13, 4682–4700.
72. Wang, C.; Lu, Y.; Cao, S. Antimicrobial compounds from marine actinomycetes. Arch. Pharmacal Res. 2020, 43, 677–704.
73. Ward AC, Bora N. Diversity and biogeography of marine actinobacteria. Curr Opin Microbiol. 2006 Jun;9(3):279-86. doi: 10.1016/j.mib.2006.04.004. Epub 2006 May 3. PMID: 16675292.
74. Wu JF, Li J, You ZQ, Zhang S (2014) Prauserella coralliicola sp. nov., isolated from the coral Galaxea fascicularis. Int J Syst Evol Microbiol 64:3341–3345
75. You JL, LX Cao, GF Liu, SN Zhou, HM Tan & YC Lin. 2005. Isolation and characterization of actinomycetes antagonistic to pathogenic Vibrio spp. from nearshore marine sediments. World Journal of Microbiology and Biotechnology 21: 679-682.