MARINE ACTINOMYCETES: SPECIES DIVERSITY AND POTENTIAL BIOACTIVE COMPOUNDS

Abstract

Marine organisms have evolved diverse structural, physiological and metabolic features that support them to survive under extreme conditions. Marine microorganisms, especially, actinomycetes, are among the most promising sources of bioactive compounds. They are Gram +ve filamentous bacteria that are widely studied for the production of different metabolites with potent bioactivity. The studies on marine actinomycetes for exploration of their diverse compounds intensified with the advancement in technologies that enabled their culture-independent isolation and characterization. Currently, several research groups have purified and characterized various promising compounds from marine actinobacteria associated with sediments, algae, invertebrates, fishes, etc. and several of them are at the final stages of the drug discovery pipeline. The actinomycetes diversity in the marine environment with an emphasis on those associated with marine fauna and their bioactive compounds is focused on in this chapter.

Keywords: Actinomycetes, Marine Environment, Diversity, Bioactive compounds

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I. 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 temperature, pressure and salinity (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 get a better understanding of marine actinomycetes and their secondary metabolite production capability.

Actinomycetes or Actinobacteria are Gram +ve bacteria that have filamentous growth with a high content of Cytosine and Guanosine (G+C) in its DNA [Jensen et al., 2005]. Approximately 70% of antibiotics used in human treatment are produced by actinomycetes, which makes them a powerful natural source of antibiotics and the organism of great interest in drug discovery programs (Bérdy, 2005). In the past, actinomycete natural products were obtained by culturing them in media that were different from their natural environments. The search for natural products from actinomycetes has declined rapidly after 1980s, mainly due to the re-discovery of compounds (Van Middlesworth and Cannell, 1998). Subsequently, the attempts to find and separate new potential 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 the ready availability of actinomycete genome sequences from those widely isolated from different sources, it has become evident that actinomycetes can produce natural products that have never been observed before [Behie et al., 2017]. This has elicited huge interest in exploring them to find new and potent natural products using innovative strategies. The chapter summarizes the Actinomycete diversity in the marine environment and the potent bioactive compounds produced by them.

II. ACTINOMYCETE DIVERSITY IN THE MARINE ECOSYSTEM

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 sediments of a shrimp culture farm by You et al. (2005). Jose and Jha (2017) in their study at Diu Island in Arabian Sea, isolated a total of 148 Actinobacteria from intertidal sediments and based on 16S rRNA gene sequence, found to belong to Glycomycete, Micromonospora, Nocardia, Nocardiopsis, Pseudonocardia, Streptomyceta, and Thermomonospora sp. Actinobacteria (73 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 Kocuria sp., Nocardiopsis sp., Dietzia sp., and Streptomyces sp. Gozari et al. (2019) isolated actinomycetes from their study in the northern part of the Oman sea; from 14 sediment samples collected, they isolated 168 colonies, the majority (66%) of which belonged to Streptomycetaceae and the others 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), 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), Streptomyces sp. (Moran et al. 1995), and *Aeromicrobium marinum* (Bruns et al. 2003).

Invertebrates: Bioactive compounds were isolated from marine invertebrates, such as corals, sponges etc., but their small biomass makes them unreliable sources (Jagannathan et al., 2021). The Marine sponges 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 associated with these invertebrates are the real source of these bioactive natural products (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 actinomycetes from sponges. Pimentel-Elardo et al. (2008) collected the sponge *Axinella polypoides* from Banyuls-surmer, France and isolated an obligate marine actinomycete *Streptomyces axinellae* sp. nov. from them. The knowledge of diversity of actinobacteria in coral reef systems is scant. Mahmoud and Kalendar, (2016) studied the richness and diversity of Actinomycete present in the coral reefs of north of the Arabian Gulf; three types of coral viz., *Platygyra daedalea*, *Coscinaraea columna*, and *Porites harrisoni* were studied. The actinobacterial genera isolated belong to the common Streptomyces as well as Micrococcus, Ornithinimicrobium, Kineococcus, Brevibacterium, Renibacterium, Nocardia, Microbacterium, Dietzia, Cellulomonas, Micromonospora, Rhodococcus, Agrococcus, Devriesea, Arthrobacter, Kocuria, Marmoricola, Brachybacterium, and Dermacoccus. 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

III. 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., (associated with marine sponge *Mycale plumose*)	Metacycloprodigiosin, Undecylprodigiosin	Cytotoxicity	Liu et al., 2005
Micromonospora sp. (associated with marine sponge *Acanthostrongylophora sp.)*	manzamine A, 8-hydroxy manzamine	Antibacterial and Antiviral	Abdelmohsen et al., 2014a
Salinispora sp. strain M403 (associated with 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 (associated with 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	Lomaiviticins A and B	Cytotoxicity	Chen et al.,

(derived from marine ascidian *Polysyncraton lithostrotum*)			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	3,4,6-trisubstituted α-	Cytotoxicity	Shin et al.,

(associated with starfish *Acanthaster planci)*	pyrone derivatives violapyrones H and I		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	Cytotoxicity Antibacterial	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.

IV. 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.

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