Chapter

Actinobacteria Associated with Marine Invertebrates: Diversity and Biological Significance

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Abstract

The ocean harbors a wide diversity of beneficial fauna offering an enormous resource for novel compounds, and it is classified as the largest remaining reservoir of natural molecules to be evaluated for biological activity. The metabolites obtained from marine invertebrate-associated actinobacteria have different characteristics compared to terrestrial actinobacteria as marine environments are exigent and competitive. Actinobacteria produce a wide range of secondary metabolites, such as enzymes, antibiotics, antioxidative, and cytotoxic compounds. These allelochemicals not only protect the host from other surrounding pelagic microorganisms but also ensure their association with the host. The harnessing of such metabolites from marine actinobacteria assures biotechnological, agricultural, and pharmaceutical applications.

Keywords: actinobacteria, marine invertebrates, diversity, biological activity

1. Introduction

Actinobacteria are gram-positive bacteria with high G + C DNA content [1] that can live in different habitats including the marine environment. These bacteria enclose significant biotechnological potential as they produce complex biopolymers, such as polysaccharides, extracellular and intracellular enzymes, antibiotics, inhibitors, and various metabolic products [2]. Since the discovery of streptomycin from **Streptomyces griseus**, actinobacteria are recognized for antibiotic production. Approximately two-thirds of world bioactive compounds are isolated from these phyla. Therefore, actinobacteria are considered as a potential source for the development of new drugs [3]. It has been emphasized that actinobacteria from marine habitats may be valuable for the isolation of novel strains that can potentially produce secondary metabolites like enzymes, cosmetics, antibiotics, anti-parasitic, vitamins, nutritional material, and immunosuppressive agents having great economical and biotechnological importance [4]. Nowadays, research has been diverted toward marine niches to screen that actinobacteria can produce bioactive compounds with different metabolic characteristics as the frequency of novel bioactive compounds from terrestrial actinobacteria decreases with time [5]. Marine flora (mangroves, seaweed, seagrasses, and algae) and fauna (Porifera, coelenterates, ascidians, crustaceans, and mollusks) are part of highly productive ecosystems and are habitats of numerous bioactive compounds producing microorganisms. Bioactive compounds obtained from associated microorganisms are known for a broad range

of biological effects, such as antimicrobial, antifungal, insecticides, antiprotozoal, antiparasitic, anti-inflammatory, and antitumor [6–8]. Sponges (phylum: Porifera) and corals (phylum: Cnidaria) are the most predominant source of marine natural products. Ascidians (phylum: Chordata) have been classified as the second predominant source of natural products [9, 10]. Seaweeds-associated bacterium produces a diverse range of biologically active compounds that specifically target fouling organisms and also show antifungal and antibacterial effects [11]. The rare actinobacterial species are explored from marine environments based on conventional and molecular approaches. The changes in salinity along with the nutrient value within the ocean make the marine environment a good source of novel actinobacteria. Due to the nutrient diversity present in the oceans, one can expect that the organisms that inhabit the marine environment would be very diverse. The different zones of the ocean contain different nutrients and minerals. Therefore, the microorganisms that inhabit various zones generally have metabolites as well as functions that are conducive to their specific zone. It indicates a high probability of microbial diversity that leads to the production of novel antibiotics and enzymes in the marine environment [12, 13]. The present investigation has emphasized invertebrate-associated actinobacteria as a source for novel natural products. The rationale behind this is because invertebrate-associated microorganisms are capable of producing various secondary metabolites and enzymes that can be used in predator defense, antifouling, inhibition of overgrowth, protection from ultraviolet radiation as well as acting as mediators in the competition for settling space [14].

2. Diversity of actinobacteria associated with marine invertebrates

Invertebrate-associated bacterial communities have a significant ability to produce bio-medically relevant micro molecules. Cultivable approaches and metagenomic analysis show that many invertebrates harbor actinobacterial species. These actinobacterial species mainly belong to genera Streptomyces, Nocardiopsis, Kocuria, Salinospora, Nocardia, Rhodococcus, Nonomuraea, Actinokinespora, and Saccharopolyspora [15–17].

2.1 Sponges

The phylum Porifera harbor dense and diverse bacterial communities. According to the literature review, about 40% of the sponge biomass was due to their associated bacteria [18]. The sponges are recognized for their potential source of bioactive metabolites. These bioactive metabolites are generally produced by their associated microbial communities which suggest that associated microorganisms might play a role in the chemical defense of their host [19]. Till today, about 60 actinobacterial genera have been isolated from marine sponges [20]. Sponge-associated actinobacteria dwell in the mesohyl matrix of sponges. They may be true halobiont or taken up from nearby water through the filtration process. About 20 actinobacterial genera belonging to genera *Kocuria*, *Micromonospora*, *Nocardia*, *Nocardiopsis*, *Saccharopolyspora*, *Salinispora*, and *Streptomyces* were isolated from South China sea sponges (Genera: *Haliclona*, *Amphimedon, Phyllospongia, Agelas, Hippospongialachne, Cinachyrsina, Arenosclera, Phakellia, Cliona*) [18, 20].

2.2 Coral reefs

The bacterial communities associated with coral have unique properties. Bacteria inhabit coral in three different parts of the coral body that includes the

surface of the mucus layer, the interior of coral tissue, and the calcium carbonate skeleton. Each of them harbors unique beneficial properties. The skeletons of corals are porous which provides micro niches for a variety of bacterial communities for colonization [21]. Cyanobacteria in the skeleton of *Oculina Patagonica* provide organic compounds to the coral tissue which helps them to survive during losses of endosymbiotic algae [21, 22]. In addition, a recent study shows that bacteria isolated from the mucus of healthy *Acropora palmata* produce antibiotics inhibiting the growth of potentially pathogenic microorganisms. This shows that the diversity of bacterial species that are associated with a particular coral species is high, including many novel species. A number of mutualistic benefits have been suggested [23, 24]. The other microbial lives, such as bacteria are associated with coral halobiont for their nutritional requirement. In return, the associated bacteria protect the host by the production of secondary metabolites, such as antifungal, antibacterial, and antihelminth. The antimicrobial peptide damicornin produced by coral-associated bacteria was active against fungi and selective gram-positive bacteria but not against *Vibrios sp.* while the organic extract of *Siderastrea sidereal* coral showed antibacterial activity against two of the four strains of gram-positive bacterial isolates from coral surfaces [25, 26].

The actinobacterial communities associated with corals can fix nitrogen which explains their dominance in healthy corals [21, 27]. Lampert et al. reported mucus-associated bacterial diversity among which 23% were Actinobacteria [28]. Mahmoud and Kalendar reported *Brachybacterium, Brevibacterium, Cellulomonas, Dermacoccus, Devriesea, Kineococcus, Kocuria, Marmoricola, Micrococcus, Micromonospora, Ornithinimicrobium, Renibacterium,* and *Rhodococcus* actinobacterial genera that belong to three corals (*Coscinaraea columna, Platygyra daedalea*, and *Porites harrisoni*) among which *Kocuria* and *Brevibacterium* were dominant genera [22]. Kuang et al. reported *Fridmanniella* and *Propionibacterium* as major groups associated with *P. lutea* while genera *Demetria, Fodinicola, Friedmanniella, Geodermatohilus, Iamia, Modestobacter, Ornithinimicrobium, Tersicoccus,* and *Yonghaparikia* were detected for the first time from *P. lutea* through culture-independent study [23]. The novel actinobacterial species *Nocardiopsis coralli* HNM0947^T isolated from Hainan province, PR China inhabitants of coral *Galaxeaastreata* show optimum growth at pH 7, temperature 28°C, and 3% NaCl(w/v). The strain HNM0947^T contained 71.3% mol G + C, MK-10(H8), MK-10(H6), and MK-10(H4) as major menaquinones, iso-C16:0, anteiso-C17:0, C18:0, C18:0 10-methyl (TBSA), and anteiso-C15:0 as major fatty acids [29]. Among the cultivable actinobacterial genera *Jiangella, Micromonospora, Nocardia*, *Nocardiopsis, Rhodococcus, Verrucosispora, Salinispora,* and *Streptomyces* showed potential actinobacterial activity against various test pathogens consequently contributing to coral health [23].

2.3 Shrimps

Shrimps are considered one of the most famous seafood consumed worldwide. They belong to the phylum Arthropoda, subphylum Crustacea. The exoskeleton of Shrimps contains chitin, structural proteins, and mineral deposits, and its construction is an energy-demanding process. Till today, very few studies regarding actinobacterial diversity associated with Shrimps are published. The *Streptomyces californicus* isolated from Shrimp farming displayed the ability to inhibit the growth of *Vibrio sp.,* one of the disease-causing pathogens [30]. You et al. demonstrated the significance of actinobacteria in shrimp farming due to their antimicrobial, antifungal, and antioxidative ability [31]. Kumar et al. prepared extract from actinobacterial sp. and observed its in vivo effect by supplementing extract with feed to black

tiger shrimp having white sport syndrome [32]. You et al. reported actinobacteria with the ability to inhibit the formation of biofilm produced by *Vibrio sp*. All these studies indicate the significance of actinobacteria in aquaculture [33].

2.4 Ascidians

Ascidians belong to phylum Chordata, subphylum Tunicate. More than 1000 bioactive metabolites have been isolated from ascidians and their associated microbial communities. The indolocarbazoles having anticancer ability were produced by *E. toealensis* associated with actinobacterial genera *Salinispora* and *Verrucosispora* [34]. Lee et al. reported actinobacterial species, including *Arthrobacter rhomb,* Brachybacterium muris*,* Micrococcus lylae*,* and *Nocardiopsissynnemataformans* from squid collected from Jumunjin, Gangwon-do, Korea [35].

3. Biological significance of actinobacteria associated with marine invertebrates

The actinobacteria are omnipresent in all environmental conditions. They produce a wide range of metabolites having biotechnological applications as described in **Table 1**. Actinobacteria is a group of organisms having the ability to produce inhibitors, **immunomodifiers**, **biosurfactants, antioxidative, anti-inflammatory,** antimicrobial, antifungal, and anticancer compounds along with intracellular and extracellular enzymes with unique characteristics in terms of substrate selectivity, stability in presence of salts, temperature tolerance, pH variation, etc. The significance of host-associated marine actinobacteria is also described in **Table 1**.

3.1 Antimicrobial ability

The **Micrococcus luteus** isolated from sponge shows strong inhibition against **Staphylococcus aureus***,* **Vibrio anguillarum***,* and **Candida albicans** [53]. Mayamycin and Microluside isolated from sponge-associated *Streptomyces sp*. HB202 and *Micrococcus sp.* EG45 inhibited **S. aureus** with IC50 (1.16 μg/mL) and (12.42 μg/mL) respectively [54, 55]. *Salinispora sp*. isolated from *Pseudoceratina clavate*, as well as *Micromonospora sp*. *CPI 12 and Saccharomonospora sp. CPI 13* isolated from *Callyspongia diffusa* showed antibacterial activity against **S. epidermidis** [56]. Actinobacterial genera *Pseudonocardia, Streptomyces, Kocuria, Aeromicrobium, Brachybacterium*, and *Nocardiopsis* were isolated from sponges, such as *Haliclona sp., Callyspongia sp.*, and *Desmacella sp*. Among 92 isolated actinobacterial strains, 52 actinobacterial strains exhibited antibacterial activity against **E. coli***,* **P. fluorescens***,* **V. alginolyticus***,* and **V. splendidus***.* Further analysis revealed that 18% of actinobacterial strains contained NRPS gene clusters while 10% harbor PKS-KS gene and 6% have PKS-NRPS gene clusters [57]. Different actinobacterial genera of marine origin consist of nontoxic antibiotics able to inhibit the growth of *Vibrio sp.* resulting in a potential source for aqua culturing [58, 59].

3.2 Antioxidative ability

Ferric reducing antioxidant power (FRAP), nitric oxide (NO) scavenging, and DPPH radical scavenging activity were extensively used to measure antioxidant capacity. *Nocardiopsis sp.*PU3 isolated from the coral reef of the Pullivasal Island, Gulf of Mannar, and India was detected as a potential source of antioxidative agent that can be used to treat various oxidative stress-related disorders with 53.6%

Actinobacteria	Host	Location	Significance	References
Sponge				
Nocardiopsis dassonvillei MAD08	D. nigra	Southwest coast, India	Antibacterial activity and anticandidal activity	[36]
Nocardiopsis sp., *Micromonospora sp.*, *Rhodococcus sp.* and *Streptomyces sp.*	*Iotrochota sp.,* and *Hymeniacidonperleve*	Eastern Mediterranean coast, Turkey	15 strains exhibited antimicrobial activity against methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus faecium and *three strains* showed anticandidal activity against Candida albicans	[37]
Actinoalloteichus sp. Micrococcus sp., Micromonospora sp., Nocardiopsis sp., Streptomyces sp.	*Halichondriapanicea*	Baltic Sea, Germany	Presence of polyketide synthases (PKS) and nonribosomal peptide synthases (NRPS)	[38]
Streptomyces poriferorum sp. nov	*Geodiabarretti* and *Anthodichotoma*	Tautra island, Trondheim fjord of Norway	Anti MRSA activity	[39]
Salinispora arenicola and *Salinispora pacifica*	Sponges	Great Barrier Reef	N-acyl homoserine lactones	[40]
]Actinobacterial strains	*Callyspongia sp*., *Callyspongiaaerizusa, Carteriospongia contorta, Chelanoplysilla sp*., and *Diacarnusbismarckensis*	Panggang Island, Taman Nasional KepulauanSeribu, Indonesia	Plant growth promoting bioactivity: Indolacetic acid production, HCN production, phosphate solubilization, and antimicrobial activity against Xanthomonas oryzae and *Pyricularia oryzae*	[41]
Williamsiaaurantiacus sp. nov	*Glodiacorticostylifera*	Praia Guaeca, Sao Paulo, Brazil	Antimicrobial activity against S. aureus and *Colletotrichum gloeosporioides*	[42]
Streptomyces olivaceus	*Dysideaavara*	Larak Island, Persian Gulf	Olivomycin A: cytotoxic activity against SW480, HepG2, and MCF7 cell line	[43]
Corals				
S. arenicola	P. lobata and P. panamensis	Tropical central Pacific	Promotes plant growth in salt stress conditions	[44]
Micromonospora marina	Soft coral	Indian Ocean coast, Mozambique	Thiocoraline: anticancer activity against LoVo and SW620 human colon cancer cell lines	[45]

Actinobacteria	Host	Location	Significance	References
Mycobacterium sp	Coral	Kurusadai Island, Gulf of Mannar	Antioxidant Activity: Scavenging of Hydrogen peroxide, Nitric Oxide Radical	[46]
Actinobacterial sp.	*Sarcophyton glaucum*	Red sea	Antibacterial activity against S. aureus, *K. pneumonia,* P. aeruginosa, V. fluvialis, *antifungal activity against* A. niger, *Penicillium sp.,* and *C. albicans*	[47]
Myceligeneranscantabricum sp. nov	Fam. Caryophillidae	Aviles Canyon, Cantabrian Sea, Asturias, Spain	Antimicrobial activity against *E. coli*, Micrococcus luteus, and Saccharomyces cerevisiae	[48]
Micromonosporaaurantiaca, Nocardiopsisdassonvillei subsp. Albirubida, Nocardiopsissynnemataformans, Streptomyces rutgersensis, Streptomyces viridodiastaticus	Scleractinian corals	Luhuitou fringing reef	Presence of NRPS, PKS type I and II biosynthetic gene cluster	[49]
Ascidians				
*Salinispora*sp. and *Verrucosispora sp.*	*E. toealensis*	Micronesian Islands, Chuuk	Antibiotic: Indolocarbazoles and Staurosporines	[34]
Mollusks				
Streptomyces sp. CP32	*Conus pulicarius*	Mactan Island, Philippines	Derivatives of Pulicatins with neurological activity	[50]
*Nocardiopsis alba*CR167	*C. rolani,*	Mactan Island, Philippines	Nocapyrones with neurological activity	[51]
Streptomyces sp.	*Crassostrea sikamea*	Bahia de La Paz, Baja California Sur, Mexico	—	[52]

Table 1.
Significance of actinobacteria associated with marine invertebrates.

DPPH, 74.2% hydrogen peroxide, and 56% nitric oxide radical scavenging activity at 100 μg/mL concentration [60]. Recently, 54.50% ABTS free radical scavenging activity with 100 μg/mL was reported from coral reef-associated *Saccharopolyspora sp.* IMA1 [16]. While *Streptomyces sp.* NMF6 associated with marine sponge *Diacarnus ardoukobae* possessed significant phosphomolybdenum, ferric-reducing power, and DPPH free radical scavenging activity [61]. Ser et al. reported *Streptomyces malaysiense sp.* having 27.24% DPPH radical scavenging activity at 2 mg/mL of 0.016% DPPH solution [62].

3.3 Cytotoxic activity

Cancer treating drugs have elevated toxic effects with undesirable side effects. Therefore, the reach of new and less harmful drugs has a high demand. Progress had been made recently to reach antitumor compounds from marine actinobacteria [63]. Violapyrone H and I were isolated from *Streptomyces sp.* associated with starfish. Violapyrone exhibited cytotoxicity against 10 human cancer cell lines with a GI_{50} value from 1.10 M to 26.12 M. This is the first report of violapyrones tested for their cytotoxicity potential [64]. *Streptomyces sp*. isolated from *Acanthaster planci* collected from the Federated States of Micronesia produced violapyrone H, Iα pyrones derivatives that displayed cytotoxicity against 10 human cancer cell lines with GI_{50} value from 1.10 μM to 26.12 μM [63]. *Donaxtrunculus anatinus*-associated Actinobacterial genera *Nocardioides, Kitasatosporia*, and *Streptomyces* showed strong antitumor activity against human carcinoma of the liver (HEPG2), cervix (HELA), and breast (MCF7) cell line with IC_{50}: 3.89, 9.4, and 10 μg/ml, respectively [65]. Steffimycin produced by *Streptomyces* sp. 0630 exhibited cytotoxic effect against a panel of human cancer cells MCF-7, HepG-2, and A2780 with IC_{50} values of 5.05, 5.57, and 1.91 μM, respectively [66]. *Streptomyces sp*. TMKS8 associated with sea slug exhibited cytotoxicity against murine leukemia P388 cells with IC_{50} 9.8 μM [67, 68].

3.4 Enzymes

The significance of enzymes in food, textile, detergent, and pharmaceutical has been known for a long. The harnessing of actinobacterial-derived enzymes comprises of cost-effective and eco-friendly nature due to its mild fermentation condition, such as the use of agricultural waste as a source of nutrients, temperature, pH, agitation, and less production time [69]. Actinobacteria associated with marine hosts produce various enzymes including amylase, protease, keratinase, lipase, L asparaginase, Xylanase, chitinase, cellulase, and dextranase that embrace industrial significance [70].

Proteases hydrolyze protein molecules to peptides and eventually to free amino acids. Protease plays a significant role in the metabolic cycles of all living forms. There are several types of proteases including serine, carboxy serine, cystine, metallo, carboxy metallo, and aspartic proteases [71]. The application of protease includes animal fodder preparation, silk degumming, detergent formulation (stain remover), dehairing and dewooling (leather industry), and silver recovery from X-ray film [72–74]. Actinobacterial genera *Microbacterium* isolated from stony coral *Pocillopora sp.* and *Faviia sp.* produced proteases [75]. Similarly, *Micrococcus sp.* and *Brevibacterium sp.* isolated from *Faviia sp.* produced proteases [75, 76]. Whereas 12.6% and 10.9% of bacteria associated with marine sponge **D. granulosa** and *S. fibulata,* respectively produced proteases [77].

Amylase is one of the most demanding enzymes used mainly for scarification of starch, pulp processing, bread dough making, winery, and detergent industry whereas solvent tolerant amylase was used mainly for bioremediation and

improvement of detergent [78, 79]. Meena et al. isolated 10 actinobacterial genera associated with *Phallusia nigra* ascidian. Among them, *Kinecoccus mangrovi, Kocuria polaris, Salinospora sp.,* and *Nocardiopsis exalbidus* were amylase positive with 12.29, 8.85, 6.61, and 5.13 U/mL activity, respectively [80]. According to the earlier report, bacteria associated with sponges exhibited a higher percentage of amylase production followed by phosphatase and protease while the least urease-positive isolates were obtained from *Dysidea granulose* and *Sigmadocia fibulata* sponge [81].

Chitinase involves in hydrolyses of chitin polymer by cleaving β 1–4 linkages. Chitin is a polymer present in the cell wall of fungi, shells of marine invertebrates, and few insects. The use of chitinase involves the development of pesticides, management of marine wastes, biofuel production, and food and pharma industries [82]. Many actinobacterial genera, including *Streptomyces, Micromonospora, Nocardiopsis,* and *Nocardia* have been reported [83]. Recombinant chitinase from **S. griseus** showed enhanced hydrolysis of α and β chitin with a higher rate of activity using shrimp shells as substrate [84]. SaChiB chitinase isolated and cloned from *S. alfalfa* ACCC400021 showed maximal activity at 45°C temperature with pH 8 while SaChiB exhibited antifungal activity so considered as a biocontrol agent in agriculture [85].

The pharmaceutical demand for L-asparaginase is high due to its anti-carcinogenic ability. L-asparaginase inhibits the growth of cancerous cells by cleaving L-asparagine into ammonia and aspartic acid. Mainly L-asparaginase is produced by fungi while few actinobacterial species are also reported [86]. *Streptomyces noursei* MTCC 10469 associated with marine sponge *Callyspongia diffusa* produced 102 kDa of L-asparaginase that displayed optimum activity in pH 8 at 50°C [87]. Also, **S. fradiae** NEAE-82-derived L-asparaginase showed anti-proliferative activity on cancer cells (HepG2, Hep2, and Caco2) [88]. Currently, *Aspergillus* and *Bacillus*-derived L-asparaginase are available commercially while actinobacterial-derived L-asparaginase is under investigation [86].

Actinobacteria are a distinctive group of prokaryotes having similarities to both fungi and bacteria. The actinobacterial-derived cellulase has unique features in terms of adaptation to extreme environmental parameters and degradation of plant-based biomass. Cellulase is a carbohydrate degrading enzyme that hydrolyzes cellulose into mono- and oligosaccharides [89]. The *Kineococcus mangrove, Kocuria Polaris, Nocarciopsis exalbidus, and Salinispora sp.* belonging to the phylum Actinobacteria were isolated from marine ascidian *Phallusia nigra* exhibited cellulase production [80]. Most terrestrial microbial-derived cellulase showed an inhibitory effect in presence of glucose whereas marine halophilic *Streptomyces*-derived cellulase retained more than 60% activity in presence of 0.5 M glucose which makes the enzyme feasible to conduct high biomass saccharification [90]. Also, *Actinoalloteichus cyanogriseus* strain MHA15 isolated from marine habitat showed higher cellulase activity 14.378 U/mL in carboxy methyl cellulose medium suggesting ideal bacteria for cellulose bioconversion [89].

3.5 Helometabolites

Halometabolites produced by marine organisms play a significant role in host defense mechanisms by quorum sensing and production of toxins, growth hormones, or antibiotics. Helometabolites, such as chloride, bromide, and iodine are omnipresent in marine environments whereas fluoride is present in Earth's crust [91]. *Micromonospora echinospora*-derived Calicheamicin is a group of enediyne metabolites with iodine and has remarkable anticancer activity [92]. Whereas, halogenated glycopeptide Vancomycin produced by *S. lavendulae* showed antibacterial activity against various test pathogens [93] followed by the production of indimicine A-E chlorinated bisindolie alkaloid from deep-sea *Streptomyces sp.* showed

strong antimicrobial activity along with cytotoxic activity against MCF-7 cell line with IC_{50} 10 μM [94]. FU et al. reported chlorinated streptochlorides derived from coral-associated *Streptomyces sp.* with antimicrobial activity against proteobacteria and cytotoxicity against breast cancer cell line MCF-7 [95]. The research of halo metabolites through genome mining resulted in 26 $FADH_2$dependanthalogenase positive actinobacterial strains associated with mangroves [96]. The antifungal kutzneride involves in dichlorination at C6 and C7 position of tryptophan has been isolated from *Kutzneria sp.* whereas pyrroindomycin isolated from *S. rugosporus* involves tryptophan dichlorination at position 5 [97]. Further, three novel halogenase gene clusters were identified from sponge-associated actinobacteria that suggest the importance of actinobacteria as a remarkable source for harnessing halometabolites [98].

3.6 Enzymes inhibitors

Enzyme inhibitors have a pivotal position in agriculture to protect crops from predators. Allosamidin derived from *Streptomyces sp.* can inhibit chitinase and shows potent insecticidal activity against *Bombyx mori* and Silkworm [99]. Several α-glucosidase and α-amylase inhibitor has been reported from marine habitat, for instance, *Streptomyces* sp.PW638-derived Acarviostatin 103 inhibit α-amylase with IC50 value 12.23 μg/mL and α-glucosidase with IC_{50} 1.25 μg/mL [100]. Whereas amino-oligosaccharide α-glucosidase inhibitors produced by *Streptomyces sp.* CKD-711 showed potent inhibitory activity against **Comamonas terrigena** [101]. Protease inhibitor has valuable antiviral activity against Zika, Dengue, hepatitis C virus, and many more. Kamarudheen et al. reported protease inhibitor from marine sponge *Callyspongiasp*-associated **S. griseoincarnatus** HK12 having antiviral activity against Chikungunya [102]. Leupeptin, Pepstatin, Antipain, Phosphoramidon, Talopeptin, and Diketopiperazine are well-known actinobacteria-derived protease inhibitors having remarkable pharmaceutical significance [103, 104].

4. Conclusion

The marine actinobacterial provides vast scope for therapeutically active macromolecules, such as antibiotics and halometabolites with the addition of industrially significant enzymes, such as amylase, protease, asparaginase, xylanase, cellulase, chitinase, and lipase. The presence of actinobacteria in marine habitats plays a pivotal role in their associated organisms by providing protection against harmful moieties. Harnessing host-specific actinobacterial diversity from the marine ecosystem will result in novel species with the ability to produce new and diverse secondary metabolites which will be beneficial for detergent, food, medicine, agriculture, cosmetics, paper, and pulp industries. Furthermore, the exploitation of bioactive compounds from marine microorganisms will fulfill the current demand for drug-resistant microorganisms as many more marine niches are still unexplored.

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Conflict of interest

The authors declare no conflict of interest.

Acronyms and abbreviations

FRAP	Ferric reducing antioxidant power
NO	Nitric oxide
VCPO	Vanadium dependant chloroperoxidase
MRSA	Methicillin-resistant Staphylococcus aureus
PKS	Polyketide synthases
NRPS	Nonribosomal peptide synthases
IC_{50}	Half maximal inhibitory concentration

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