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REVIEW ARTICLE

Diversity and Biotechnological Potential of Marine Actinomycetes from India

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Abstract Actinomycetes are potential antibiotic producers that have been isolated from various terrestrial ecosystems and are exploited for their bioactive compounds. On the contrary, the marine environments were less explored and the research on marine actinomycetes had gained momentum only for the past three decades. Marine actinomycetes are one of the most significant producers of diverse groups of secondary metabolites and provide a huge scope for pharmaceutical and other industries. These organisms are proved to be important, both biotechnologically and economically considering their global presence. The marine ecosystem in India is less explored for the isolation of actinomycetes and several ecological niches are left unattended. Compared to the global scenario, the contribution from Indian researchers towards the isolation and exploitation of marine actinomycetes from the Indian sub-continent is noteworthy. Exploration of actinomycetes from these ecosystems will certainly yield new species and metabolites. Considering the declining rate of drug discovery from terrestrial actinomycetes, the marine counterparts, especially from unexplored regions from the Indian coast will hold a promising way ahead. Apart from drugs, these organisms are reported for the production of different industrially important enzymes like cellulase, amylase, protease, lipase, etc. They are also used in environmental applications, agriculture, and aquacultures sectors. With the rapid advancement in the study of actinomycetes from different marine sources in India, new metabolites are being discovered which have an important role from the economic and industrial point of view. As the world is witnessing newer diseases such as Sars-Cov 2 and the pandemic due to its demands drugs and other metabolites are increasing day by day. Therefore, the necessity for the quest for unique and rare marine actinomycetes is enhancing too. This review highlights the research on marine actinomycetes in India and also the challenges associated with its research.

Keywords Marine ecosystem · Actinomycetes · India · Diversity · Bioactive compounds

Introduction

In the biosphere, the marine environment covers 70% of the earth and acts as the largest ecosystem for various living organisms, especially microbes. Marine microbiology has encouraged the interest of researchers to investigate unexplored marine environments from all over the world with a sole focus on the discovery of novel bioactive compounds. The majority of these novel compounds have been obtained from marine actinomycetes thereby attracting considerable attention. They are present on the surface water and also in the deep sea, with varying pH, temperature, salinity, and other extreme physical conditions. Marine actinomycetes hold an important position due to their adaptation capability to various extreme conditions and resultantly the production of different compounds used for various applications. Actinomycetes belonging to different genera like *Streptomyces, Actinomyces, Arthrobacter, Corynebacterium, Frankia, Micrococcus, Micromonospora* are capable of producing several

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compounds that possess a wide range of biological activities. Apart from water and sediments, marine actinomycetes are also present and associated with different sources like fishes, sponges, seaweeds, mangroves, etc. [1]. Evidence also shows the presence of these organisms in different extreme conditions which increases the novelty of the metabolites produced, along with its biological significance. Research on actinomycetes in India started in the early '60s when a detailed isolation process from terrestrial soil samples was explained. Later, in the 1980s, scientists have reported the presence of actinomycetes from different marine sources as well as the production of various bioactive compounds [2]. Research on actinomycetes has seen a surge from the beginning of the 21st century. There are numerous novel actinomycetes strains discovered from marine soil samples collected from all over the Indian coast. Reports have also proven the presence of novel strains among the different marine sources. Several novel secondary metabolites have been purified and characterized from the newly isolated strains. These organisms are efficient producers of a wide range of metabolites possessing biological activities such as antimicrobial, antitumor, anticancer, insecticidal, and different enzymes [3] However, research on marine actinomycetes in India is still considered in its early stage with relatively fewer attempts to explore the vast water bodies covering half the national boundaries. Most of the research deals only with the isolation and identification of strains and the reports on the polyphasic taxonomy and their biotechnological potential are not clear. The last review on marine actinomycetes research in India was published by Sivakumar et al. [4]. Hence in this review, we mostly focus on the research carried out in marine actinomycetes from India and the significance regarding their diversity in the past decade (2009–2019). It also deals with the recent reports regarding the discovery of novel secondary metabolites from these organisms and their significance in pharmaceutical and other industrial needs.

Isolation and Diversity of Marine Actinomycetes in India

India is surrounded by water bodies on its three sides and nine states and four union territories of India consist of coastlines including several extreme habitats such as backwater lakes, lagoons estuaries, mangroves. Despite having various constraints like sample collection, sample transfer, isolation, and maintenance of the isolates, various novel strains have been isolated by Indian researchers to date. Further, diverse marine vertebrates and invertebrates have been investigated to isolate the symbiotic actinomycetes.

The presence of different genera of actinomycetes has been detected in different sediment samples collected from coastal areas, beaches, mangroves, estuaries, lagoons, and lakes (Fig. 1). Additionally, novel strains have been isolated from extreme environments like hot springs, salt pans. Further, reports also show the isolation of new actinomycetes from marine organisms. Among the isolates, genera like *Streptomyces, Micromonospora*, and *Rhodococcus* are predominantly reported. These species are responsible for producing a wide range of secondary metabolites, mainly antibiotics. These compounds have antagonist effects against different pathogens, including multiple drug-resistant organisms. Marine actinomycetes especially showed diverse production of bioactive compounds better than their terrestrial counterparts (Table 1). Manikandan and Vijayakumar have studied six different samples (Point Calimere, Athirampattinam, Mallipattinam, Manora seashores, Vedharanyam saltpan, and Muthupet mangroves) collected along the Palk Strait of Bay of Bengal and identified 55 morphologically distinct strains [5]. Other than *Streptomyces*, these isolates belong to different rare genera like *Actinoplanes, Actinobispora, Actinopolyspora, Actinokineospora, Saccaropolyspora, Streptosporangium, Actinosynnema, Catellospora, Micromonospora, Strptoverticillium, Micromonospora, Dactylosporangium, Actinomadura*, and *Kitasatospora*.

The isolation and exploitation of actinomycetes from normal marine environments have led to the rediscovery of known compounds. However, various actinomycetes from extreme environments promise an increase in the prospect of discovering new compounds with potential activities that can be commercialized. Extreme environments are defined as the physio-chemical conditions that are significantly different from the optimum conditions that help in

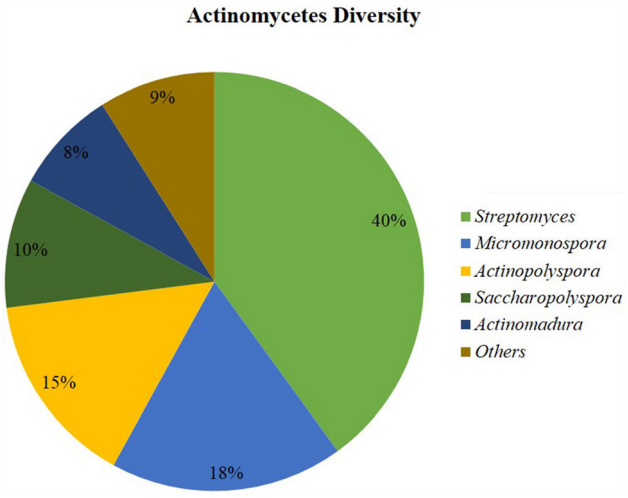

Fig. 1 Percentage of the actinomycetes diversity in India

Table 1 Reports on different genera of actinomycetes reported from India in the past decade (2008–2017)

	Isolates	Location	Significance
Streptomyces	*Streptomyces longwoodensis*	Beaches from Ernakulam to Kannur (Payambalam, Puthiyangadi, Butt road, Calicut, Muzhuppilangadi h, Fort Cochin, Beypore)	Antimicrobial Compound Production
	Streptomyces viridiviolaceus.	Calicut Mangrove sediment	Antimicrobial Compound Production
	Streptomyces sp. DPTB16	Cuddalore coast	antifungal compound (4' phenyl-1-naphthyl-phenyl acetamide) production
	Streptomyces sp. D1	The coastal region of Goa, Alibagh, and Mumbai	α-amylase production
	Streptomyces VITSDK1 spp.	Marakkanam Coast	Hemolytic activity
	Streptomyces fungicidicus MML1614	Bay of Bengal coastal areas, Pulicat lake, and Pichavaram mangrove	Thermostable alkaline protease production
	Streptomyces sp (AQBWWS1)	Marine sponge *Callyspongia diffusa* at Kovalam Coast	Food-grade pigments production
	Streptomyces orientalis	Ennore saltpan	Acts as biosurfactant and exhibits heavy metal resistance
	Streptomyces aureomonopodiales	Ennore saltpan	Acts as biosurfactant and exhibits heavy metal resistance
	Streptomyces VITSVK9 spp	Puducherry and Marakkanam Coast	Antimicrobial activity
	Streptomyces olivochromogenes	Parangipettai coast	L-glutaminase Production
	Streptomyces gedanensis	Nicobar Islands	Biosurfactant Production
	Streptomyces VITSVK5 spp	Marakkanam coast	Antifungal compound Production
	Streptomyces rochei	Visakhapatnam Coast	Antimicrobial Activity
	Streptomyces noursei	Marine sponge *Callyspongia diffusa* at Kovalam Coast	L-asparaginase production
	Streptomyces sp. VITSTK7	Bay of Bengal coast of Puducherry	Anti-Aspergillus activity
	Streptomyces sp.-SBU1	Cape Comorin coast	L-glutaminase production
	Streptomyces afghaniensis VPTS3-1	Palk Strait, East Coast of India	Antimicrobial Compound Production
	Streptomycesstrain A3	Goa, Alibagh, and Mumbai coastal region	α-amylase production
	Streptomyces albidoflavus	Visakhapatnam Coast	Synthesis of Silver Nanoparticles
	Streptomyces species B3	Western Coast of India	Biosurfactant Production
	Streptomyces parvulus	Kothapattanam Coast	Antibacterial activity against Multidrug resistance *Staphylococcus aureus*
	Streptomyces sp. VPTSA18	Vedaranyam Saltpans	Antimicrobial Activity
	Streptomyces sp. (SS7)	Bay of Bengal Coast	L-asparaginase production
	Streptomyces sp. VITAN1	Elephanta, Radhanagar, and Havelock Beach, Andaman, and the Nicobar Islands	Antibacterial activity
	Streptomyces sp. VITMSS05	Marakkanam coast	Anti-oxidant and enzyme-inhibitory potential

Table 1 continued

Isolates	Location	Significance
Streptomyces violascens	Chorao Island, Goa	Phosphate-Solubilizing Efficiency
Streptomyces noboritoensis		
Streptomyces cinereorectus		
Streptomyces cinnabarinus		
Streptomyces parvulus SSNP11	Bay of Bengal coast near Visakhapatnam	Protein Encapsulated Silver Nanoparticles Production
Streptomyces sp. MAB36	Tuticorin harbor	Production of glycolipid biosurfactant
Streptomyces sp. VITSJK8	Cheyyur beach, Kanchipuram	Production of the cytotoxic compound, 1, 2- Benzene Dicarboxylic Acid, Mono 2- Ethylhexyl Ester
Streptomyces MS-26	Muttukadu estuary	Synthesis of Silver Nanoparticles
Streptomyces coelicoflavus	Visakhapatnam Coast	Production of Rhamnolipid Biosurfactant
Streptomyces sp. JRG-04	Karangadu mangrove forest	Antimicrobial Activity
Streptomyces radiopugnans	Ribandar saltern, Goa	Antibacterial Activity
Streptomyces sporocinereus		
Streptomyces griseus NIOT-VKMA29	Phoenix Bay, Port Blair	L-Asparaginase Production
Streptomyces sp. PM49	Parangipettai coastal area	Production of β-Lactamase Inhibitory Metabolite
Streptomyces sp. VITJS8	Ramanathapuram-SethuKarai Coast	Sesquiterpenes used as an anticancer agent
Streptomyces rubrolavendulae M56	Bay of Bengal Coast	Antagonistic activity against *Vibrio sp.*
Streptomyces violaceus VITYGM	Bay of Bengal Coast	Production of extracellular thrombolytic protease
Streptomyces cacaoi M20	Backwaters of Ariyankuppam, Puducherry	Larvicidal activity against *Aedes aegypti* and *Culex quinquefasciatus*
Streptomyces parvulus DOSMB-D105	Mangrove sediments of the South Andaman Islands	Antimicrobial activity
Streptomyces sp. VITMK1	Mangrove Soil of Pichavaram, Tamil Nadu	Antibacterial Activity
Streptomyces sp.	Kodiyakkarai Beach, Tamilnadu	Synthesis of Zinc Oxide nanoparticles and their anticancer and antibacterial activity
Streptomyces sp. VITBVK2	Kanyakumari salt pan	Antagonistic effect of protease inhibitor against *Leishmania donovani*
Streptomyces parvulus sankarensis-A10	Visakhapatnam coast	Production of bioactive metabolites

Table 1 continued

	Isolates	Location	Significance	
	Streptomyces sp. Ac1	The coastal region of Maharastra-Goa Border	Cellulase Production	
	Streptomyces sampsonii	Southern coastal regions of Tamil Nadu (Rameswaram, Kanniyakumari, Thirunelveli, and Chennai), and Kerala (Cochin)	Production of Antifungal Agent	
	Streptomyces tanashiensis			
	Streptomyces griseus			
	Streptomyces paradoxus sp. VITALK03	Rameswaram and Dhanushkodi coast	Production of antidiabetic compound GancidinW	
		Streptomyces laurentii VITMPS	Chennai Coastal region	Antimicrobial activity
	Streptomyces fungicidicus RPBS-A4	Chirala coast, Andhra Pradesh	Cellulase Production	
	Streptomyces sp. GS-1	Backwaters of Munanbam and Valapad, Kerala	Protease Production and its application as a dehairing agent	
	Streptomyces fradiae VITMK2	Pichavaram, Tamil Nadu	Antiviral activity of 9(10 H)-Acridanone against white spot syndrome virus in *Litopenaeus vannamei*	
Micromonospora	*Micromonospora sp. VITSDK3*	Marakkanam Coast	α-glucosidase and α-amylase inhibitory activity	
	Micromonospora sp BTS-108, BTS-205, BTS-713	Pudimadaka Coast	Production of Amylase and Protease	
	Micromonospora sp. VITSDK45 Micromonospora sp. VITSDK46	Puducherry coast	Production of Bioactive Compounds	
	Micromonospora sp	Kanyakumari, Nagercoil, Pallam, Thirunelveli, Madurai, and Chennai Coast	Degradation of Petroleum	
	Micromonospora sp	Karwar Mangroves, Karnataka	Antimicrobial Activity	
	Micromonospora species M104	Sediments of Pichavaram mangroves and Andaman Coast	Production of Antibacterial Metabolites	
	Micromonospora JAJ43	Saltpans, Tuticorin	Potential strains for bioactive compounds	
	Micromonospora JAJ01			
	Micromonospora sp BKM 26	Bhitherkanikka mangrove, Orissa	Potential strains for bioactive compounds	
	Micromonospora sp BKM 40			
	Micromonospora sp BKM 59			
	Micromonospora echinospora	Chilika brackish water lake, Orissa	Activity against fungal pathogens	
	Micromonospora rosaria			
	Micromonospora sp ICN36	Chinnamuttam Coast, Tamil Nadu	Production of phenolic compounds having anti-MRSA activity	

Table 1 continued

	Isolates	Location	Significance
	Micromonospora sp. KPMS10	Kayalpatnam Coast, Tamil Nadu	Synthesis of Silver Nanoparticles having resistance towards Multidrug-resistant Hospital-acquired Uropathogens
Nocardiopsis	*Nocardiopsis sp. VITSVK5*	Puducherry coast	Antimicrobial Activity
	Nocardiopsis lucentensis MSA04	Sponge *Dendrilla nigra*, southwest coast of India	Production of glycolipid biosurfactant
	Nocardiopsis sp. KE-1,	Anjuna Beach, Aguada Beach, Majorda Beach, Palolem Beach and Vagator Beach, Goa and Naval Academy Beach, Kannur District, Kerala	Activity against phytopathogens
	Nocardiopsis JAJ60	Saltpans, Tuticorin	Potential strains for bioactive compounds
	Nocardiopsis sp. BKM5	Bhitherkanikka mangrove, Orissa	Potential strains for bioactive compounds
	Nocardiopsis sp. BKM21		
	Nocardiopsis sp. BKM36		
	Nocardiopsis sp. BKM47		
	Nocardiopsis sp. BKM67		
	Nocardiopsis sp	Ribandar saltern, Goa	Production of anti-bacterial metabolites
	Nocardiopsis sp VITKSM06	Marakkanam, Tuticorin, Rameswaram, Pichavaram and Gulf of Mannar, Tamil Nadu and Cochin, Kerala	Production of histone deacetylase inhibitors
	Nocardiopsis sp. NCS1	Wasp Bay, Andaman and Nicobar Islands	Alkaloid compounds having antioxidant and cytotoxic activity
Saccaharopolyspora sp.	*Saccharopolyspora salina VITSDK4*	Marakkanam Coast, Tamil Nadu	Antimicrobial and cytotoxic activity
	Saccaharopolyspora sp. KA3-3	Anjuna Beach, Aguada Beach, Majorda Beach, Palolem Beach and Vagator Beach, Goa and Naval Academy Beach, Kannur District, Kerala	Activity against phytopathogens
	Saccharopolyspora JAJ12	Saltpans, Tuticorin	Potential strains for bioactive compounds
	Saccharopolyspora BKM11	Bhitherkanikka mangrove, Orissa	Potential strains for bioactive compounds
	Saccharopolyspora BKM15		
	Saccharopolyspora BKM19		
	Saccharopolyspora BKM31		
	Saccharopolyspora BKM62		
	Saccharomonospora oceani sp	Little Andaman Islands	Potential strains for bioactive compounds
	Saccharomonospora sp. JSA09	Seagrass *Cymodocea serrulata* collected from the Gulf of Mannar	Production of plant growth-promoting factors

Table 1 continued

	Isolates	Location	Significance
Kocuria	*Kocuria sediminis*	Kochi Beach	Pinkish-orange pigment production
	Kocuria palustris	Chorao Island, Goa	Phosphate-Solubilizing Efficiency
	Kocuria marina BS-15	Kovalam Beach	Biosurfactant Production
	Kocuria sp	Seagrass *Cymodocea serrulata* collected from the Gulf of Mannar	Production of plant growth-promoting factors
	Kocuria palustris	Ribandar saltern, Goa	Production of anti-bacterial metabolites
	Kocuria sp.		
Other Strains	*Nonomuraea JAJ18*	Saltpans, Tuticorin	Potential strains for bioactive compounds
	Nocardia JAJ31		
	Actinobispora yunnanensis	Manora coast, Thanjavur, Tamil Nadu	Phosphate Solubilisation
	Actinomadura sp.	Karwar Mangroves, Karnataka	Antimicrobial Activity
	Amycolatopsis alba var. nov. DVR D4	Visakhapatnam coast	Production of Novel Pyridinium compound and its antimicrobial and cytotoxic activities
	Actinopolyspora BKM4	Bhitherkanikka mangrove, Orissa	Potential strains for bioactive compounds
	Actinopolyspora BKM7		
	Actinopolyspora BKM10		
	Actinopolyspora BKM50		
	Actinopolyspora BKM53		
	Actinomadura BKM13		
	Actinomadura BKM23 Actinomadura BKM42 Actinomadura BKM56 Actinomadura BKM64		
	Streptoverticillium spp.	Eastern coast of Andaman island	Potential bioactive compounds
	Actinoplanes sp.		
	Actinomadura spp.		
	Nocardia spp.		
	Streptosporangium spp.		
	Actinoalloteichus sp. MA-32	Tuticorin coastal region	Keratinase Production

the abundant growth of various life forms. Hence, recent actinomycetes isolation is focused on unexplored and extreme environments like hypersaline marine environments, extreme inland saline zones, volcanic zones, hyperarid, and glaciers. Solar salterns of India provide an extreme halophilic environment for the marine actinomycetes where the salinity varies from 35 to 50 ppt. It has been observed that different actinomycetes genera are found along the solar salterns of Tuticorin, India. *Streptomycetes* records the majority of the isolated actinomycetes population (48%) as well as rare actinomycetes genus *Nonomuraea* was also reported [6]. The potent isolates were further studied for their antimicrobial activity and production of bioactive compounds. *Streptomyces* spp. AJ8 was isolated from the Kovalam solar salt pans and studied against both bacterial and fungal pathogens. The crude ethyl acetate extract obtained from the culture successfully inhibited the white spot syndrome virus (WSSV) by 85% [7]. Actinobacterial diversity has been studied from a tropical marine hot spot near Andaman and Nicobar Islands that have an extreme environment for some rare genera like *Saccharopolyspora, Streptomyces, Streptoverticillium, Microtetraspora, Actinopolyspora, Actinokineospora, Dactylosporangium*, and *Nocardiopsis.* Many isolates produced industrially important enzymes such as amylases, proteases, gelatinases, lipases, DNases, cellulases, ureases, and phosphatases. Reports also explain the presence of relatively rare genera like *Agromyces* and *Amycolatopsis*. *Agromyces indicus* has been isolated from Chorao Island, Goa whereas *Amycolatopsis alba* var. nov DVR D4, from the Bay of Bengal, Visakhapatnam.

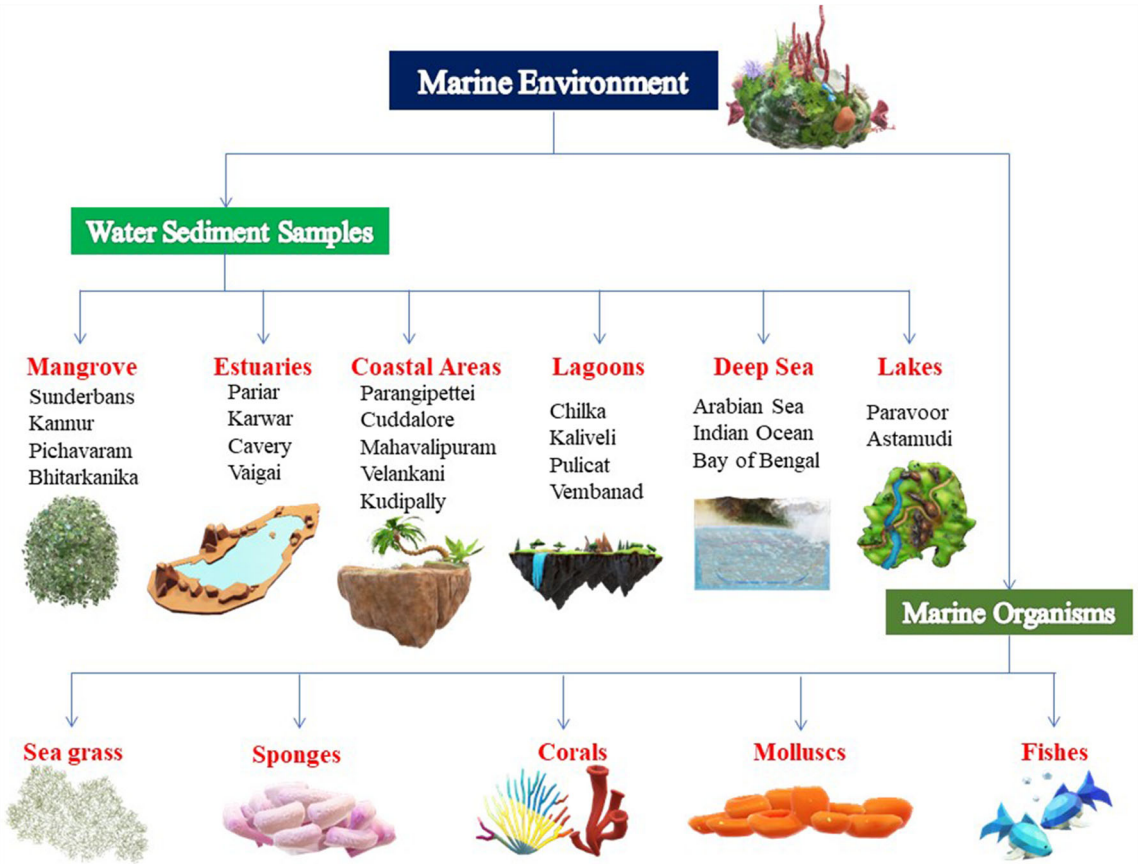

Fig. 2 Different sources for the isolation of marine actinomycetes

Actinomycetes Isolated from the Different Marine Environment

Marine environments possess many unique features different from other aquatic environments. It contains various dissolved salts and minerals that formulate about 85% of the solids in seawater. The remaining 15% includes different elements like sulfate, calcium, potassium, magnesium, bicarbonate, borate, strontium, bromide, fluoride, and others. The average salinity of the water varies between 33 and 37 ppt. along with extreme environments like high temperature, pressure, and pH variation from acidic to alkaline. Most marine life cannot adapt to significant changes in the salinity of its environment. This feature allows microorganisms to produce different bioactive compounds than their terrestrial counterparts. They adapt themselves to grow in these challenging adverse environments by producing compatible solutes (e.g., polyols, amino acids) and increasing the concentration of cytoplasmic ions. Out of 9 maritime states in India, only four states namely Maharashtra, Tamil Nadu, Kerala, and Andhra Pradesh have been studied extensively for actinobacterial diversity whereas other states, Gujarat, Goa, Karnataka, Orissa, West Bengal, and Andaman and the Nicobar Islands remains unexplored. Marine sediments, surface waters, mangroves, brackish lagoons, estuaries as well as bodies of marine animals as sponges, corals, mollusks, and fishes provide an important source for the isolation of novel actinomycetes strains to produce their unique metabolites (Fig. 2).

Water and Sediment Samples

Mangrove

According to ISFR 2017 report, the deltas of the Ganges, Mahanadi, Krishna, Godavari, and Kaveri rivers constitute the major part of the mangrove ecosystem in India. Apart from these regions, parts of the Andaman and Nicobar Islands, Karnataka, and Kerala also have mangrove ecosystems. These are coastal environments with varying salinity, water levels, and nutrient availability. It constitutes tidal swamps that occur in intertidal zones of tropical and subtropical sheltered coastlines mainly dominated by mangrove forests. These ecosystems are characterized by fine sediments with high organic content and salinity and hence serve as a great source for undiscovered microbes

having the rich potential to produce important bioactive secondary metabolites.

Extensive research has been carried out to explore the different mangrove ecosystems in India for the actinomycetes population [4]. Arifuzzaman et al. [8] reported rare actinomycetes species like *Actinomyces, Nocardia*, and *Micromonospora* from the Karanjal region of the Sundarbans [8]. *Streptomyces sundarbansensis*, a novel strain, was isolated from the Sundarbans which produced an anti-microbial compound, 2-allyloxyphenol [9]. Sediment samples collected from mangroves of the Andaman island and Manakkudi, Tamilnadu were mainly populated with actinomycetes genus *Streptomyces*. Samples collected from the mangrove sediments of Bhitharkanika, Orissa were comprised of various rare actinomycetes genera like *Saccharopolyspora, Nocardiopsis, Micromonospora, Actinomadura, Actinomyces*, and *Actinopolyspora* [10]. Mangrove sediments collected from Ennoor and Palaverkadu, Tamil Nadu showed the prevalence of uncommon actinomycetes genera namely *Actinokineospora, Actinopolyspora, Amycolata, Glycomyces, Microbispora, Microtetraspora, Micropolyspora, Nocardia, Nocardiopsis, Promicromonospora, Saccharothrix, Saccharopolyspora, Streptomyces, Streptoverticillium, Spirillospora*, and *Thermomonospora*. *Streptomyces albogriseolus* NRRL B-1305 and *Streptomyces himastatinicus* BSA11, isolated from the mangroves of Sunderbans, West Bengal, and Bhitarkanika, Orissa respectively, were responsible for producing anti-microbial bioactive compounds [11]. *Pseudonocardia sp*. VUK-10, a novel strain having antimicrobial properties was isolated from the mangrove sediments of Nizampatnam, Andhra Pradesh [12]. 2 actinomycetes strains, PMA2 and PMA6 isolated from the sediment samples of Thandavarayan, Tamil Nadu were extracted for secondary metabolites using ethyl acetate. 45 and 40 compounds were detected after GC-MS analysis; among these compounds, cinnamic acid was obtained which was a notable anti-microbial agent [13].

Different reports state that majority of the actinomycetes isolated from different mangroves mostly belong to the genera *Streptomycetes* followed by genera *Nocardia* and *Micromonospora*. Very few rare actinomycetes have been reported to date. Mangroves from the southern region of Tamil Nadu and Kerala are extensively exploited whereas mangroves from the eastern belt of Sunderbans showed minimal results. The mangroves of Sundarbans were last explored by 2010, since then higher scope has been developed for investigating the actinomycetes community. The actinomycetes isolated from the different mangroves such as Sunderbans of West Bengal, Bhitarkanika of Orissa, Coringa of Andhra Pradesh, Pichavaram of Tamil Nadu, and some areas of Kerala have a notable antagonistic effect towards different pathogenic organisms. These qualities can be further investigated to obtain the targeted compound and further drug discovery studies.

Lagoons and Brackish Water Lakes

Lagoons are small water bodies separated from the ocean or sea by dunes or coral reefs and have a distinct marine ecosystem. Similarly, brackish water lakes are a mixture of salty seawater mixing with fresh water. Both of these water bodies possess a salinity of 5–30 ppt and are a rich source of different microorganisms. The most important lagoons in India include Chilika Lake (Orissa), Kaliveli Lake (Tamil Nadu), Kerala backwaters, Pulicat Lake (Tamil Nadu), and Vembanad Lake (Kerala). Despite having a favorable environment for the survival of different genera of actinomycetes, the search for novel strains is very much limited. More investigations for novel actinomycetes are encouraged in these unexplored regions. Chilka backwaters in Odisha also record several novel actinomycetes strains due to its distinct ecosystem which is slightly different from the deep seawater bodies. A halophilic novel strain, *Streptomyces chilikensis sp. nov*. has been isolated which produces a metal tolerant chitinase enzyme [14]. Another study reported a new strain *Streptomyces vinaceusdrappus* strain S5MW2 which possesses strong antifungal properties against different phytopathogens like *Rhizoctonia solani, Fusarium udum*, and *Fusarium oxysporum f. sp. ciceri*. Actinomycetes strains having anti-microbial activity were obtained from the sediment samples collected from Pulicat Lake.

The extreme condition of the lagoons helps the actinomycetes strains to develop different industrially important enzymes which are more robust than other enzymes obtained from normal microorganisms. These enzymes are tolerant to extensive heat, pH, and metal concentrations. Other than enzymes, different studies showed actinomycetes strains having anti-microbial activity Reports from different lagoons from the southern region of India showed clear dominance of the *Streptomyces* genera over the other actinomycetes genus. Future scope prevails in the investigation of these lagoons and backwaters for any novel and distinctive actinomycetes strain.

Estuaries

An estuary is a partially enclosed coastal body of brackish water with one or more rivers or streams flowing into it, and with a free connection to the open sea. It forms a transition zone between river environments and maritime environments. Most of India's major estuaries occur on the east coast; in contrast, the estuaries on the west coast are smaller. The estuaries on the eastern coast cover a vast area of the states including Tamil Nadu, Andhra Pradesh, West

Bengal, and Orissa. The notable estuaries on the west coast are the Mandovi (Karnataka), Periyar (Kerala), and Zuari (Goa) estuaries. *Streptomyces bikiniensis* isolated from the Vellar estuary is noted for showing resistance towards bacterial pathogens. Ennore backwaters possess halophilic conditions and hence is the source for various extremophilic actinomycetes. *Streptomyces spp*. VITDDK3, isolated from Ennore saltpans, showed biosurfactant production and heavy metal resistance. The strain was also reported for significant antimicrobial activities. A total of 304 actinomycetes colonies were isolated from marine soil sediments of Pulicat, Muttukadu, and Ennore estuaries, Tamil Nadu. The majority of the isolates (60%) belonged to the genus *Streptomyces*, 35% of the isolates were assigned to the genus *Actinopolyspora* while only 5% of isolates belonged to the genus *Nocardiodes* [15]. Another isolate, *Streptomyces* MS-60 isolated from marine sediments of Ennore and Muttukadu estuaries, has a cytotoxic effect on colon cancer cell line HT-29 [16]. 12 different isolates, reported from Manakudy, Tamil Nadu, were found to exhibit significant antibacterial and antifungal activities. Ramarajan and Senthilkumar isolated 10 different actinobacterial strains from Tharangambadi, Tamil Nadu, however only T9 showed antagonistic activity towards different pathogenic bacteria.

Reports from Cochin estuary showed the isolation of 42 different actinomycetes out of which only 2 isolates (ER2 and ER7) were considered for their anti-microbial properties. These isolates were most used against different human and fish pathogens [17]. Similarly, Mesta and Onkarappa successfully obtained 43 isolates from Aghanashini, Sharavathi, and Kali estuaries, Karnataka which was able to successfully inhibit various pathogenic bacteria and fungi [18]. The isolates obtained from different estuary samples from all over the country were mostly noted for anti-microbial properties. Purification, chemical explanation, and profiling of these antimicrobials are indeed required to determine their quality, uniqueness, and economic worth.

Coastal Areas and Beaches

India has a long coastline along both eastern and western margins. This vast coastal area has a diverse environment with varied environmental conditions. Various actinobacterial genera have been reported from these coastal areas but the majority of the isolates belong to the genus *Streptomyces* establishing it as a predominant one. *Streptomyces sp*. DPTB16, isolated from the Cuddalore coast, showed broad-spectrum resistance towards the pathogenic fungal strains like *Candida albicans, Aspergillus niger, A. fumigatus, A. flavus.* The compound is identified as 4' phenyl-1-naphthyl-phenyl acetamide as a potent antifungal agent [19]. *Streptomyces sp*. D1 isolated from the western coasts produced highly stable amylase which can be used commercially [20]. *Streptomyces olivochromogenes* obtained from sediment samples of the Parangipettai coast produced L-glutamine for therapeutic purposes. Similarly, sediment samples collected from Thiruvanmayyur, Rameshwaram, and Pichavaram beaches also showed actinomycetes diversity. Sirisha et al. reported actinomycetes diversity along the eastern coast of the Bay of Bengal. Samples were collected along with different locations in Andhra Pradesh (Visakhapatnam, Kakinada, Divipoint, Singarayakonda) and Tamil Nadu (Chennai, Cuddalore, Nagapatnam) [21]. The majority of the isolates from these coastal areas belong to the genus *Streptomyces* (85%), while the other genera include *Micromonospora* (7%), *Nocardia* (4%), *Streptosporangium* (3%). Coastal regions of Tamil Nadu are extensively explored whereas the coastal region of western and eastern India are minimally investigated for actinomycetes isolates. Studies on actinomycetes diversity in Kachhighadi Coast, Gujrat was one of the pioneer studies from the western coast of India [22].

Different isolates were noted for their production of bioactive compounds which have anti-microbial and anti-tumor properties. Further purification of these compounds is essential for their commercialization. *Streptomyces* sp. VITSJK8, isolated from the samples of Cheyyur beach, produced a compound 1, 2- benzene dicarboxylic acid, mono 2- Ethylhexyl ester (DMEHE). The compound showed cytotoxic effects for different cell lines viz. mouse embryonic fibroblast (NIH 3T3), human keratinocyte (HaCaT) normal cell lines, human hepatocellular liver carcinoma (HepG 2), and human breast adenocarcinoma (MCF-7) [23]. The further report also states that sediments collected from Marina and Thiruvanmaiyur beaches showed a significant actinomycetes population having potential for bioactive compounds. *Streptomyces globosus* VITR004 was isolated from the sediment samples collected from the coastal areas of Rameshwaram and Dhanushkodi. The strain showed antagonistic activity towards pathogenic bacteria like *Escherichia coli, Proteus mirabilis, Bacillus cereus*, and *Staphylococcus aureus.* Two bioactive compounds, N-Isopropyluredo Acetic Acid and Benzene Propanamine, N-(1, 1-Dimethyl Ethyl) - Alpha Methyl - Gamma Phosphate can also be obtained from this isolate that has significant antibacterial activity [24]. Kavitha and Sabitri reported 73 actinobacterial strains from different beach locations in Andhra Pradesh (Suryalanka, Chirala, Peddapalem). A pigment-producing strain, *Streptomyces bellus* MSA1 was isolated from Kovalam Beach. Another strain *Streptomyces bacillaris* RAM25C4 successfully showed antibacterial activity against human pathogens such as *Staphylococcus aureus*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa.* Several potential antimicrobial compounds were also extracted from the isolate viz.

1,4-benzenediol, 2,6-di-*tert*-butylphenol and 1 H, 5 H, pyrrolo (1′ 2′:3, 4) imidazo [25]. 37 actinomycetes strains were isolated from the sediment sample of Kovalam coast, out of which 10 isolates possessed antagonistic activities against all the five test organisms (*Escherichia coli, Klebsiella sp., Pseudomonas sp., Enterococcus sp., Proteus sp.*) [26].

Marine Organisms

Marine organisms reside in a significantly distinct habitat from the terrestrial one, and their secondary metabolite will vary significantly. The symbiotic relationship between microorganisms and marine organisms is abundant and widespread in the sea. Diverse and widespread symbiotic microorganisms are hosted by different marine creatures and crops such as sponges, sea squirts, corals, worms, and algae. Marine microbial symbionts, isolated from their host organisms, are the substantial producers of some bioactive marine natural products. These metabolites may be useful for understanding the biosynthesis mechanisms of related natural products and solving the current problem of limited supply in drug development. Most marine invertebrates and algae shelter varied microbial symbionts including prokaryotic bacteria, actinomycetes, cyanobacteria, and fungi. Current studies implicate that microbial symbiont is the real source for many marine organism-derived compounds. Marine microbial symbionts are proved to be a hotspot in the field of marine microbiology because of their potential for producing important secondary metabolites.

Corals collected from the Gulf of Mannar (*Acropora digitifera*) were proved to be a rich source for actinomycetes diversity. The isolated strains showed significant inhibition against all the biofilm-forming pathogens [27]. Many sponges contain furthermore symbiotic microbial consortia within their mesohyl matrix that may amount up to nearly half of their biomass. Sponge *Callyspongia diffusa* collected from the Bay of Bengal was the source for actinomycetes possessing antimicrobial compounds. *Streptomycetes sp*. AQBWWS1, isolated from this sponge produced carotenoid pigment when fermented under fluorescent white light [28]. Another isolate, *Nocardiopsis alba* MSA10 was isolated from *Fasciospongia cavernosa* which produced a lipopeptide biosurfactant [29]. Sponge *Dendrilla nigra*, was the source for the strain *Nocardiopsis dassonvillei* MAD08, which showed significant antibacterial and anticandidal activity [30]. *Spongia officinalis* also proved to be a potent source for antibacterial compound-producing actinomycetes. Isolate MAPS08, MAPS10 and MAPS15 produced an active fraction, 2-pyrrolidone which acts as an anti-bacterial agent [31]. Sea grass-like *Cymodaceae sp., Enhalus sp., Halophila sp., Halodule sp., Syringodium sp*., and *Thalassia sp* showed the presence of 30 different isolates. These strains were analyzed for antibacterial compounds [32]. *Cymodocea serrulata* and *Syrgodium isoetifolium* were the sources for 10 actinomycetes strains, which showed resistance against both human and fish pathogens [33]. Fishes like *Mugil cephalus*, *Chaetodon collare*, and *Archamia fucata* produce various actinomycetes strains. These isolated strains were extremely beneficial for different industries. *Streptomyces actuosus* produces cellulase that is stable in various environmental conditions. 7 different *Streptomycetes* strains, isolated from these sources, successfully inhibited the growth of *Vibrio chorelae* (Murugan produced bioactive compounds that inhibit both bacterial and fungal pathogens [34].

Secondary Metabolites and Bioactivity by Actinomycetes

Actinomycetes are noted for their ability to produce several metabolites used in the diverse sector (Fig. 3).

Antimicrobial Activity

Antibacterial

Many reports show that various pathogenic bacteria are gaining rapid resistance towards the standard antibiotics present in the market. This increases the need of finding a

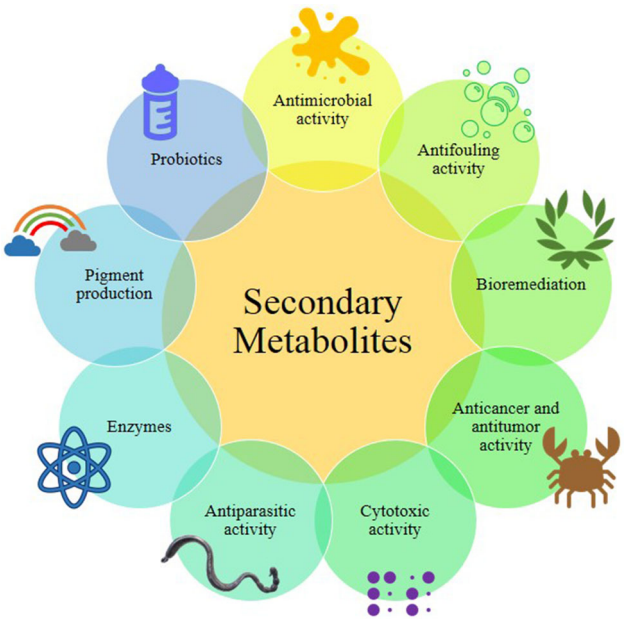

Fig. 3 Importance of different secondary metabolites produced by marine actinomycetes

new alternative for inhibiting these strains. Marine actinobacteria are studied for their capability of producing bioactive compounds having antagonistic effects towards both gram-positive and gram-negative bacterial as well as fungal pathogens. The antibacterial compound has been obtained from marine actinomycetes *Streptomyces* sp. strainVITSVK9 isolated from samples collected from Puducherry and Marakkanam coast of Bay of Bengal. The crude extract showed a zone of inhibition against different bacterial and fungal pathogens. The strain can be further exploited for lead compound isolation. Studies were also carried out with the sediment samples from South Andaman Island along the Bay of Bengal Coast and Andaman Sea Coast. A total of 42 different cultures were isolated and 13 among them showed significant antibacterial activity against different bacterial pathogens. Secondary metabolite produced from actinomycetes strains A107 was also tested for antimicrobial activity and thus can be further tested for other novel metabolites. Anti-bacterial fraction extracted from *Nocardiopsis dassonvillei* strain MAD08 (isolated from a marine sponge *Dendrilla nigra*) successful resistance towards 13 gram-positive and 9 gram-negative multidrug-resistant bacteria [30]. *Streptomyces sannanensis* strain SU118 isolated from phoomdi in Loktak Lake of Manipur can successfully inhibit the growth of gram-positive bacterial pathogens like *Mycobacterium smegmatis* (MTCC 6) and *Bacillus circulans* (MTCC 8074) [35]. Although terrestrial actinomycetes strain SCA 7 was isolated from Thiruvannamalai, Tamil Nadu produced an active fraction of 2,4-bis (1,1-dimethyl ethyl) phenol. It showed significant antagonistic activity towards *Staphylococcus epidermidis* (31.25 µg/mL) and *Malassezia pachydermatis* (500 µg/mL). It could be used in the development of new substances for industrial applications [36]. Different antibacterial compounds such as 1,4-benzenediol, 2,6-ditert-butylphenol, and 1 H, 5 H, pyrrolo (1′ 2′:3, 4) imidazo were obtained from *Streptomyces bacillaris* RAM25C4 [25]. *Kocuria* sp. rsk4 showed prominent antibacterial properties against bacterial pathogens including multidrug-resistant bacteria *S.aureus*. Purification followed by characterization of the produced antibiotic reveals that it is unique from other known antibiotics [37]. *Streptomyces parvulus* isolated from Muthupet mangrove samples also shows significant anti-microbial properties [38]. Another bioactive compound, a derivative of Diketopiperazine was isolated from *Nocardiopsis sp.* SCA30 with antagonistic activity against MRSA [39].

Antifungal Activity

Studies are carried out to detect different antifungal antibiotics from actinomycetes, especially from the marine source due to their distinct habitat and different mode of adaptation. Out of 208 actinomycetes strains, isolated from Pulicat lake to Kanyakumari, 151 showed antifungal activities against 2 plant pathogens [40]. Actinomycetes strains isolated from the soil also show significant antifungal activity. As recorded by Valanarasu et al., *Streptomyces* spp. ERI-04, isolated from the Western Ghats in Tamil Nadu, produced some antifungal metabolite which successfully inhibited the growth of various pathogenic fungal strains like *Trichophyton rubum, Trichophyton simii, Epidermophyton floccosum, Magnaporthe grisea, Trichophyton mentagrophytes, Scopulariopsis sp., Botyritis cinere Aspergillus niger*, and *Candida albicans* [41]. Actinomycetes strain *Streptomycetes VITSVK5* spp., isolated from the Marakkanam coast, was reported to have significant antifungal activities against eleven multidrug-resistant *Aspergillus* strains. Ethyl acetate extract of the isolate showed a zone of inhibition from 22 to 28 mm with MIC of 0.125-4 µg/ml and hence proved to be a potent antifungal agent [42]. Another drug, Caerulomycin A was obtained from an actinomycetes strain PM0525875, phylogenetically similar to *Actinoalloateichus cyanogriseus.* It has been isolated from marine invertebrates collected from Arjuna beach, Goa. Caerulomycin A showed a MIC within the range of 0.39–1.56 µg/ml against *Candida sp.* and hence, can be used as a potentially broad-spectrum antifungal agent [43]. Haloalkaline actinomycetes strains, *Streptomyces sampsonii, Streptomyces tanashiensis, Actinoalloteichus cyanogriseus*, and *Streptomyces griseus* were isolated from the mangrove sediments of Tamil Nadu and Kerala. The bioactive compounds from these strains were extracted using acetone and it showed significant potential against fungal pathogens such as *Trichophyton rubrum, Aspergillus clavatus, Aspergillus niger, Candida albicans*. Hence, the bioactive compounds were of pharmaceutical importance due to the presence of good antioxidant properties analyzed by DPPH and reducing power assay [44].

Antiviral Activity

Antiviral compounds are also being extracted from actinomycetes and various reports on antiviral agents are recorded from marine actinomycetes. *Streptomyces* sp. VITSDK1 produced the metabolite furan-2-yl acetate ($C_6H_6O_3$), which has an antagonistic effect against fish nodavirus (FNV). It has been studied over SIGE (Sahul Indian Grouper Eye) cells infected with the said virus where furan-2-yl acetate (at a minimum concentration of 20 µg/ml) effectively inhibited the replication of the virus [45]. Another report by Serkedjieva et al. describes that a protease inhibitor, isolated from *Streptomyces chromofuscus* 34–1 shows the antiviral effect towards the influenza virus. Different measures of virus growth like an expression of the viral haemagglutinin on the surface of infected

cells, the virus-induced cytopathic effect, and the infectious virus yield were all reduced to non—toxic concentration based on the dosage. The experiment was carried out in vivo where the same result was replicated. Hence this protease inhibitor showed a promising effect in different medical and pharmaceutical industries [46]. *Streptomyces* spp. AJ8, isolated from Kovalam salt pans, can effectively inhibit the white spot syndrome virus in shrimps at the level of 85% [7]. Research is still going on regarding different antiviral compounds obtained from actinomycetes and many compounds are undergoing clinical trials.

Anticancer and Antitumor Activity

Marine actinobacteria are known for producing structurally different and biologically active secondary metabolites that can act as potent drugs, which cannot be produced by any terrestrial organisms. The majority of the anticancer compounds come from marine sources, especially actinomycetes, and these metabolites serve as an important source for pharmaceutical industries. It has been reported that actinomycetes strains, ACT01, and ACT02 showed toxicity towards breast cancer cell lines, MCF-7, and MDA-MB-231. The IC_{50}value of ACT01 and ACT02 is determined to be (10.13 ± 0.92) and (22.34 ± 5.82) µg/mL concentrations, respectively for MCF–7 cell line at 48 h. ACT01 showed the minimum (18.54 ± 2.49 µg/mL) level of IC_{50} value with the MDA-MB-231 cell line and hence both strains can be used as anticancer agents against breast cancer cell lines [47]. Another report explains that the crude antibiotic obtained from *Streptomyces cavouresis* KUV39 was treated with Hela cells and the IC_{50} value is determined to be 63.9 µg/mL. The cytotoxic activity of this strain could be clinically important and needed to be investigated for further anticancer properties [48]. Similar reports were also obtained from their terrestrial counterparts. The ethyl acetate extract of *Streptomyces galbus* ERINLG-127, isolated from Marapalam forest, Nilgiris, showed prominent cytotoxic activity in vitro against the A549 lung adenocarcinoma cancer cell line. It has been detected that the maximum dosage of 100 µg/mL showed 75.1% activity with an IC_{50} value of 60 µg/mL [49]. Similarly, protease-producing strains (ERIA − 31 and ERIA-33), isolated from the northern Himalayas, showed cytotoxic effect against the same cell line where the IC_{50} value was detected to be 57.04 and 55.07 µg/mL respectively [50]. It has been reported by Naine et al., that the ethyl acetate extract of *Streptomyces* sp. VITJS8 showed cytotoxicity against HepG2 cells at IC_{50} of 250 µg/mL. The progression of apoptosis was observed by morphological changes after nuclear staining. The active compound successfully inhibited the sub-G0/G1 phase of the cell cycle of the HepG2 cells and thus can be used as a potent anti-cancer agent [51]. Recently, Nalli et al. isolated a *Streptomyces* sp, from marine ascidian *Synoicum indicum*, from which 10 purified compounds (pyrazine-1,4-dione substituted cyclic dipeptide) were obtained. Out of these 10 compounds, 3, 4, 5, 7 and 8 showed significant results against tumor necrosis factor-α (TNF - α) and interleukin-6 (IL−6) [52]. These reports show that marine ecosystems in India are a pristine source of different antitumor compounds and are very minimally explored. Proper investigation, profiling, and characterization of the compounds are required before commercial uses.

Antiparasitic Activity

Antiparasitic compounds are responsible for either inhibiting the growth of the parasites or their larva. Actinomycetes strain LK1 acts as an antiparasitic agent for *Anopheles stephensi*, *Hippobosca maculate, Haemaphysalis bispinosa*, *Rhipicephalus microplus*, and *Culex tritaeniorhynchus* [53]. Recent studies showed that compounds extracted from the marine actinomycetes could inhibit the growth of *Leptospira interogans* serovar Autumnalis strain N2. Strains isolated from Palk Strait, Gulf of Mannar, and Lakshadweep showed significant anti leptospiral activity with the most potent strain MSU5 showed a MIC of 125 µg/ml which is better than the standard drug doxycycline [54]. Different actinomycetes strains, from the salt pan of the Tuticorin coast, were screened for larvicidal activity against 3 kinds of mosquito genera *Culex quinquefasciatus, Aedes aegypti*, and *Anopheles stephensi*. The minimum activity was observed for ISO2 while the maximum activity was observed for ISO7 against *Anopheles stephensi* [55]. Recently, *Streptomyces* sp. VITBVK2 detected an inhibitory effect towards *Leishmania donovani*, the causative agent of visceral leishmaniasis [56]. The results obtained suggest that the marine actinobacterial extract which has novel metabolites can be considered as a potential source for the development of drugs.

Cytotoxic Activity

Marine *Streptomyces* are significant producers of most of the bioactive compounds that are used in the medical and pharmaceutical industries as effective drugs against different diseases. The cytotoxic activity of the pure compound 1, 2-benzene dicarboxylic acid, mono 2-Ethylhexyl ester (DMEHE) obtained from marine-derived actinomycete *Streptomyces* sp. VITSJK8 was tested against mouse embryonic fibroblast (NIH 3T3), human keratinocyte (HaCaT) normal cell lines, human hepatocellular liver carcinoma (HepG 2), and human breast adenocarcinoma (MCF-7) cell lines which detected IC_{50} value of 42,

Table 2 Different enzymes obtained from different marine actinomycetes isolated from different marine sources in India

Enzymes	Sample Location	Isolates
Cellulases	Southwest Ghats, Tamil Nadu	*Streptomyces noboritoensis*
	Sponge (*Dendrilla nigra*)	*Marinobacter sp MS 1032*
	Kodiyakarai coast (India)	*Streptomyces alboniger*
	Vedharanyam (India)	*Streptomyces albus*
		Streptomyces cyaneus
	Tiruchendhur coast (Tamil Nadu, India)	*Streptomyces clavuligerus*
	Visakhapatnam coast	*Streptomyces parvulus strain sankarensis*-A10
	Havelock island	*Actinoalloteichus sp.* MHA15
	Mangrove forest of South India	*Brevibacillus brevis* EGS 9
	Kanyakumari	*Actinomycetales bacterium*-PV7
	Chirala coast, Andhra Pradesh	*Streptomyces fungicidicus RPBS-A4*
Amylase	Goa, Alibagh, and Mumbai coastal region	*Nocardiopsis sp.* strain B2
	Marine sponge *Ircinia* sp. from Cape Comorin coast	*Streptomyces* sp. – SBU3
	Andaman & Nicobar, St. Mary's Island-Udupi, Kannur, Kerala, and Mangalore	AcAn53
	Lonar Lake, Maharashtra	*Georgenia satyanarayanai*
	Visakhapatnam coast	*Streptomyces parvulus* strain *sankarensis*-A10
	South coastal areas of Tamil Nadu	*Streptomyces gancidicus*-ASD_KT852565
	Pichavaram (Tamil Nadu, India)	*Streptomyces sp. VITMK1*
	Muthupet (Tamil Nadu, India)	*Streptomyces sp. S6*
	Seaweed *Sargassum myriocystum* (India)	*Streptomyces sp. SNAJSM6*
	Kachhighadi (Hyderabad, India)	*Nocardiopsis dassonvillei KaS11*
	Kachhighadi (Hydrabad, India)	*Streptomyces lopnurensis KaM5*
Xylanase	Tiruchendur coast, Tamil Nadu	*Streptomyces albus*
	Tiruchendur coast, Tamil Nadu	*Streptomyces clavuligerus*
	Mangrove Sediment	*Streptomyces olivaceus MSU3*
Lipase	Bay of Bengal, Visakhapatnam	ABT – 206
	Visakhapatnam coast	*Streptomyces parvulus* strain sankarensis-A10
	Kanyakumari	*Actinomycetales* bacterium-PV7
	Tiruchendur coast, Tamil Nadu	*Streptomyces hygroscopicus*
Protease	Pulicat Lake and Pichavaram	*Streptomyces fungicidicus* MML1614
	Mud crab, *Scylla serrate*	7 isolates (LK 1–7)
	Pudimadaka	*Streptomyces sp. BTS 205*
	Kakinada, Andhra Pradesh	*Streptomyces carpaticus*
	Okka port, Gujrat Coast	*Nocardiopsis. alba* OK-5
	Salterns in Southern India	*Actinopolyspora* sp. VITSDK2
	Kanyakumari	*Actinomycetales* bacterium-PV7
	Visakhapatnam coast	*Streptomyces parvulus* strain sankarensis-A10
	Kachhighadi, Hyderabad	*Streptomyces lopnurensis KaM5*
	Backwaters of Munanbam and Valapad, Kerala	*Streptomyces sp. GS-1*
	Okka port, Gujrat Coast	*Nocardiopsis dassonvillei albirubida (strain OK-14)*
L-Asparaginase	Tamil Nadu and Kerala	*Streptomyces spp. S3*
		Streptomyces spp S4
		Streptomyces spp K8
	Phoenix Bay in Port Blair	*Streptomyces griseus* NIOT-VKMA29
	Thoothukudi coast	*Streptomyces* DS8
	Sponge *Callyspongia diffusa*	*Streptomyces noursei*
	Bay of Bengal Coast	*Streptomyces sp. SS7*

Table 2 continued

Enzymes	Sample Location	Isolates
L-glutaminase	Parangipettai	*Streptomyces olivochromogenes*
	Kothapattanam, Andhra Pradesh	BSAIP5
	West Coast, Kerala	*Streptomyces* sp.
	Cape Comorin coast (India)	*Streptomyces sp.-SBU1*
Keratinase	Tuticorin	*Actinoalloteichus sp.* MA-32
Chitinase	Manakudy estuary (India)	*Streptomyces sp. ESM7, ESM9, and ESM10*
	East Coast (Tamilnadu, India)	*Streptomyces sp. ACT7*
	Mumbai marine water sample (India)	*Streptomyces sp M1*

100, 250, and 500 µg/ ml respectively. Cell viability was determined as it showed cytotoxic activity against HepG2 and MCF-7 cancer cell lines and low toxicity against normal HaCaT and NIH 3T3 cell lines [23]. Similarly, a terrestrial strain, *Streptomyces scabrisporus* isolated from soil of Kashmir Himalayas, exhibited cytotoxicity for a broad spectrum of cell lines including N2a, MCF-7, Mia-Paca-2, PC-3, HCT-116, MDA-MB-231, HL-60, and A-549 cells. The active compound, alborixin showed the maximum cytotoxic activity against HCT-116 cells inducing apoptotic cell death, and can be further evaluated for its potential as an anticancer agent [57]. Another strain, *Streptomyces paradoxus* VITALK03 produced secondary metabolites that can be identified as (3R,8aR)-3-(2-methyl propyl)-octahydropyrrolo[1,2-a] piperazine-1,4-dione (gancidin W). It showed cytotoxicity for breast cancer cells (MCF-7) with an IC_{50} value of 1.56 µg/mL, whereas the value was 12.5 µg/mL, in the case of VERO cells (control). Hence, the compound, gancidin W, can be used to develop as a breast cancer drug [58]. Another report by Varghese et al. showed that *Nocardiopsis* sp VITKSM06 showed significant cytotoxicity against HeLa cells with an IC_{50} value of 5·9 μg/ml. The cells showed condensed chromatin which may be due to HDAC inhibition [59]. Thus, in recent years, we can get various evidence that signifies that major research is going on to explore the marine actinobacterial resources to get different novel anti-cancer compounds. These compounds can be further formalized as potent drugs for clinical trials.

Enzymes

Marine actinomycetes are capable of producing a wide range of enzymes that have diverse industrial applications. These enzymes act as a catalyst for different biochemical reactions. Recently, enzymes like cellulase, amylase, protease, lipase, L-Asparaginase, L-glutaminase obtained from different marine sources are used commercially and are of immense economic importance. Out of 90 actinomycetes strains isolated from the Konkan Coast of Maharashtra, 76 strains successfully produced protease enzyme followed by 70 strains producing gelatinase enzymes. 65, 39, 34, and 15 strains were noted to produce amylase, lecithinase, cellulose, and urease enzymes respectively [60]. Different isolates from Chennai, Tuticorin, Kerala, and Pooombukar showed the production of enzymes like amylase, cellulose, and lipase. 5 halophilic actinomycetes isolated from the Arabian Sea and salt pan of Charwada successfully produced enzymes like amylase, gelatinase, caseinase, lipase, and urease. It has been reported that the isolates NIOT-VKKMA02, NIOT-VKKMA22, and NIOT-VKKMA26, from various sites of Port Blair Bay, synthesized 13.27 U/ml, 9.85 U/ml, and 8.03 U/ml amylase; 7.75 U/ml, 5.01 U/ml, and 2.08 U/ml of cellulase and 11.34 U/ml, 6.89 U/ml and 3.51 U/ml of protease enzyme, respectively. A record of different enzymes is given in Table 2.

Bioremediation

Marine actinomycetes developed a unique way of surviving in extreme conditions. They are significant for their production of a wide range of secondary metabolites. These organisms also produce different enzymes that can catalyze different reactions. These organisms react with different sources of environmental pollution and eventually result in degradation and denaturation of the pollutants into harmless compounds. Hence, these organisms can be employed as potential bioremediation agents [61]. These organisms also produce biosurfactants that are applied to enhance oil removal from the polluted water surface and are also applied in food, cosmetics, and pharmaceutical industries. *Streptomyces gedanensis* strain LK-3 was isolated from marine sediments of the Nicobar Islands and examined for

biosurfactants production. The strain was evaluated by the E24 emulsification index and is a potent organism for biosurfactant production. This organism was also able to degrade tributyrin [62]. Similarly, *Streptomycetes* sp. strains VITDDK1, VITDDK2, and VITDDK3, isolated from Ennore saltpan soil, were reported for significant biosurfactant activity and heavy metal (mercury, cadmium, lead, zinc, and copper) resistance. Another potential isolate from saltpan soil in Andhra Pradesh, *Streptomyces* strain VITSSB2 showed biosurfactant activity in oil recovery at room temperature. This strain also can degrade tributyrin [63]. Desale et al. reported the role of nearly 200 morphologically different actinomycetes strains isolated from different ecological niches like freshwater, geothermal springs, acid soils, etc. from different locations in India. These strains were screened for their resistance towards heavy metals such as cadmium, mercury, lead, nickel, strontium, iron, molybdenum, zinc, and manganese. *Nocardiopsis B4* produced a biosurfactant that can withstand high temperatures, a wide range of pH and salt concentrations.

Antifouling Activity

Marine biofouling can be defined as the undesirable growth of marine organisms on different immersed surfaces like jetty pilings, ship hulls, navigational instruments, and pipelines. Biofouling on ships reduces their speed resulting in increased fuel and maintenance costs. Biofouling also accelerates corrosion and increases the risk of mechanical failure on static structures such as piers, buoys, and jetties. It also causes blockage of seawater intake pipes. Antifouling agents are synthetic in nature that causes additional environmental hazards. Hence, research is going on for new antifouling agents from natural sources and several marine actinomycetes were screened that inhibit the biofouling causing organisms to adhere to these water logging surfaces. *Streptomyces filamentosus* (R1) has been reported to inhibit the growth of 3 different strains, *Bacillus* sp. (BB11), *Serratia* sp. (BB13), and *Alteromonas* sp. (BB14) [64]. Actinomycetes strains were used for synthesizing nanoparticles that were proved to be potential antifouling agents. *Streptomyces* sp. VITSDSB was used for the synthesis of zirconium oxide nanoparticles and *Streptomyces* sp SV2 and SV3, for titanium dioxide nanoparticles. These nanoparticles showed significant results in inhibiting biofouling-producing organisms. The growth of biofouling microorganisms on surfaces of poultry is also a major issue. 10 isolates from coastal areas of Tamil Nadu proved to be beneficial in inhibiting these organisms and inhibiting their growth. *Streptomyces fradiae* PE7 isolated from Vellar estuarine was reported to produce antifouling agent PE7-C which was later identified as quercetin. The purified quercetin was active against 18 biofouling bacteria with MIC range between 1.6 and 25 µg/ml, algal spore germination, and mollusk foot adherence found at 100 µg/ml and 306 ± 19.6 µg ml^{-1} respectively [65].

Pigment Production

Various industries like textile, food, cosmetics, and pharmaceutical utilize synthetic pigments for coloration as they are economically feasible. But, different studies have proved that excessive use of such synthetic compounds leads to carcinogenicity, genotoxicity, and neurotoxicity. Hence these synthetic colors are highly replaced with natural pigments from various herbal and microbial sources. Microorganisms are considered a better source for biopigment over plants due to their easy availability, consistent stability, cost efficiency, yield, and easy downstream processing. Marine actinomycetes play a lead role in pigment production with novel structures with additional antimicrobial, antioxidant, anticancer, and anti-inflammatory properties. Melanin was produced by *Streptomycetes sp.* F1, F2, and F3 were isolated from a marine sediment sample. The pigment was also found to have an antagonistic effect against pathogenic strains [66]. Intercellular pigment with antioxidant activity was produced by *Streptomyces bellus* MSA1 isolated from Kovalam beach, Chennai [67]. *Streptomyces* sp. MVCS13, isolated from Versova Coast, produced dark brown melanin pigment antagonistic towards different fish pathogens.

Probiotics

The actinomycetes strains having adhesion for the inner mucus of the gastrointestinal tract are considered as potential candidates for probiotic strains. The potential probiotic strain should be non-toxic, antagonistic effect towards various pathogenic organisms, the high survival rate in variable pH, decomposing macromolecular substrates in the host and the environment, and beneficial towards the host. The actinomycetes strains that have antimicrobial and non-hemolytic properties were further screened for bacterial adhesion for hydrocarbons (BATH) test. Cultures having $> 50\%$ in the BATH test are considered positive and able to absorb xylene when mixed with the cell pellet. Hydrophobic interactions are one of the most important mechanisms responsible for the attachment of microorganisms to the gastrointestinal tract of the host. The potential probiotic strains interact to attach with the inner lying of the gut and should not be expelled from the body with excretion. Marine *Streptomyces* strains CLS-28, CLS-39, and CLS-45 were used to detect its antagonistic effect towards *Vibrio harveyi* and *Vibrio proteolyticus* in

Artemia nauplii and adult *Artemia*. A significant reduction was observed for the mortality of nauplii and adult *Artemia* against both the pathogens as well as an increase in length, weight, and survival rate was observed for black tiger shrimp *Penaeus monodon*. Hence these *Streptomyces* strains are of immense importance as probiotic agents in mariculture [68]. Marine sponges like *Callyspongia diffusa, Mycale mytilorum, Tedania anhelans*, and *Dysidea fragilis* are a rich source of actinomycetes population having potential probiotic qualities. 7 *Streptomycetes* strains isolated from sponges collected from Vizhinjam port, Trivandram were examined as feed for ornamental fish *Xiphophorus helleri.* These strains were successful in increasing the growth and length of *X. helleri* [69].

Conclusion and Future Perspective

Actinomycetes play a leading role in the generation of different novel metabolites that have pharmaceutical and other industrial applications. Different actinomycetes isolate from terrestrial sources are also capable of producing different secondary metabolites; in fact, the majority of antibiotics come from these sources. But different pathogens are gaining resistance towards the antibiotics that are commonly used. Hence, there is an emergency in drug development to inhibit the growth of these pathogens. A broad range of antibiotics in the market was obtained from actinomycetes which can effectively degrade a vast range of xenobiotic compounds and can also transform them into organic compounds of high commercial value. Considering the enormous ecological variety of the sea, it is becoming increasingly clear that the seas include a substantial number of unique chemical substances. Different actinomycetes are surviving in extreme marine conditions by maintaining a symbiotic relationship with different marine organisms like sponges, corals, fishes, etc. Because marine actinomycetes have developed with the highest genetic and metabolic diversity, research into them as a source of new secondary metabolites should be prioritized. Researchers have been going on to discover more novel molecules with ample therapeutic applications, especially from actinomycetes. Different pharmaceutical companies used microbial natural bioproducts as one of the potential sources of unique drugs. Studies were carried out to explore the different marine ecosystems present in India. Still, many unexplored water bodies are rich sources for novel actinobacterial strains. Different zones of the Indian Ocean have diverse environmental conditions. The main focus should be on the selection of sampling sites and further research is required for retrieving both cultivable and uncultivable novel actinobacterial strains from it. The genera of *Streptomyces* have been focused on in different previous reports regarding the diversity of the actinobacterial population in different locations. More strains from other genera like *Actinopolyspora, Micromonospora* are yet to be reported. Various novel compounds having remarkable activity towards different pathogens as well as diseases have been reported in the past decade. Marine actinomycetes were also noted for their production of a huge range of different enzymes that were stable at a wide range of temperatures and pH. These enzymes have a wide application in different sectors like food, brewery, leather, textiles, paper, and detergent. Around 25,000 biologically active compounds have been recorded, out of which ~ 12,000 compounds are obtained from marine actinomycetes. Different compounds obtained from the marine actinomycetes have a huge impact on aquaculture industries where they are used as either antifungal or anti larvicidal agents. Thus the secondary metabolites reported to date are of immense importance for different industries and have prospects for mass production and commercialization.

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Declarations

Conflict of interest The authors declare that there is no conflict of interest.

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