Vol 12, Issue 3, May – June 2024 DOI: https://doi.org/10.31426/ijrpb.2024.12.3.12301

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)

CrossRef DOI: https://doi.org/10.31426/ijrpb Indexed in CAS and CABI, Impact Factor: 0.64

BIODIVERSITY AND PHARMACEUTICALLY ACTIVE SECONDARY METABOLITES OF MARINE ACTINOMYCETES

Ponmadasamy M [1], Mohana Krishnan P [1], Sathiya Balan G *[2], Bhuvaneswari santharam [3], Vigneshwaran LV [4]

[1] PG Scholar, Department of Pharmacognosy, College of Pharmacy, Madurai Medical College, Madurai, Tamilnadu, India.
[2] Assistant Professor, Department of Pharmacognosy, College of Pharmacy, Madurai Medical College, Madurai, Tamilnadu, India.
[3] Assistant Professor, Department of Biochemistry, K.R. College of Arts and Science, Kovilpatti, Tuticorin, Tamilnadu, India.
[4] Professor and Head, Department of Pharmaceutics, Malik Deenar College of Pharmacy, Kasaragod, Kerala, India.
[*] **Corresponding Author** E-Mail ID: sathiyagbharathi@gmail.com

ABSTRACT

Keywords:

Actinomycetes, secondary metabolites, Marine environment, Pharmacological.

Actinomycetes (Actinobacteria) are gram-positive bacteria having a filamentous structure similar to that of fungi. They may thrive in many different environments. It is thought that marine actinomycetes may produce distinctive bioactive compounds due to the significant variations between terrestrial and marine settings. According to recent studies employing both culture-dependent and culture-independent approaches, native marine actinomycetes are discovered in the oceans and are widely distributed in many marine ecosystems. It has become easier to isolate new actinomycetes from samples collected in different marine environments. Numerous new types of secondary metabolites are produced by these marine actinomycetes. Many of these metabolites are physiologically active and could one day be applied to medicine. Marine actinomycetes are a rich and underutilized resource that can be used to identify novel secondary metabolites. 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.

Vol 12, Issue 3, May – June 2024 DOI: https://doi.org/10.31426/ijrpb.2024.12.3.12301

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)

CrossRef DOI: https://doi.org/10.31426/ijrpb Indexed in CAS and CABI, Impact Factor: 0.64

Introduction

Actinobacteria are the richest suppliers of secondary metabolites, as evidenced by previous research, and have been considered as possible sources of bioactive chemicals. Because of their diversity and demonstrated capacity to generate novel metabolites and other compounds of pharmacological significance, they are frequently used as targets in screening procedures [(1)]. Actinobacteria have been shown to generate a wide range of pharmaceutically useful substances, anticancer medicines, and industrially important enzymes since the discovery of actinomycin[(2)]. Growing evidence of the potential importance of marine sediments as sources of actinobacteria that generate beneficial bioactive metabolic products has surfaced in recent years [(3)].More than just invertebrates like sponges, corals, and echinoderms are associated with marine actinomycetes. Vertebrates like pufferfish are also associated with these organisms. Secondary metabolic pathway evolution may be influenced by these interactions, which may promote distinct chemical ecologies. Apart from interacting with other species, marine actinomycetes can inhabit planktonic and biofilm habitats; nonetheless, the bulk of strains have been identified from sediments [(4)].

The manufacture of antibiotics is largely derived from a wide group of free-living, saprophytic, filamentous, Gram-positive bacteria known as actinomycetes [(5)]. Their classification is Actinomycetales (Super kingdom: Bacteria, Phylum: Firmicutes, Class: Actinobacteria, Subclass: Actinobacteridae). They can be found in freshwater, marine, and soil habitats [(6)]. Their DNA has a high G+C content (>55%). They produce around two third of naturally occurring antibiotics, including those of medicinal value, making them the best common source of antibiotics [(7)]. Originally seen as a group in between bacteria and fungus, actinobacteria have since gained recognition for their own unique role [(8)]. The majority of secondary metabolites that have been found are produced by actinomycetes, which are the most valuable prokaryotes in terms of both biotechnology and economics. Their physiologically potential secondary metabolites have been successfully harnessed in recent decades. Actinomycins, tetracyclins, polyenes, polyketides, betalactams, glycopeptides, and aminoglycosides are among the many antimicrobial metabolites they create.

Role of Actinomycetes in Marine Environment

Beyond their ability to produce antibiotics, actinomycetes are important components of the marine ecosystem [(9, 10)]. Numerous bacteria play a mediated role in the ongoing breakdown and turnover of different materials [(11)]. There is conjecture that variations in the abundance or scarcity of a specific enzymatic microbe could reveal information about the amount of natural substrate present and the environmental circumstances. Actinomycete taxa have been found in significant numbers by a metagenomic study of the seawater column. Additionally, they are important for the mineralization of organic matter, the fixation of nitrogen, the solubilization of phosphate, the immobilization of mineral nutrients, the enhancement of physical parameters, and the preservation of the environment [(12)]. There

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)
CrossRef DOI: https://doi.org/10.31426/ijrpb **Indexed in CAS and CABI, Impact Factor: 0.64**

have been reports on the cellulolytic, proteolytic, amylolytic, lipolytic, chitinolytic, and phosphate-solubilizing properties of marine actinobacteria. Actinobacteria have also been shown to aid in the decomposition and recycling of organic substances [13].

Research Methods of Marine Actinomycetes

The diverse physiological traits and genetic metabolisms of marine actinomycetes are a result of the environment's novelty. It becomes vitally important to choose the right research techniques in order to examine their metabolites. These days, marine actinomycetes produce round half of the active compounds derived from marine microorganisms [14, 15, 16]. Research on secondary metabolites from marine actinomycetes involves a number of different areas of expertise and technology, including extraction and sampling, purification and separation, structural identification, and activity assessment. High-performance liquid chromatography and mass spectrometry are just two of the many techniques and technological instruments needed for this process. The examination of metabolite research procedures is extremely important since it serves as the basis and source for discovering lead compounds [17, 18].

Synthesis of Bioactive Secondary Metabolites

A group of prokaryotes that include Streptomyces, Actinomyces, Arthrobacter, Cornyebacterium, Frankia, Micrococcus, and several more, actinomycetes are the most economically viable and biologically useful prokaryotes. With a wide range of biological activities, actinomycetes are among the most potent and dynamic makers of secondary metabolites [19,20,21,22]. A large number of compounds with biological activity can be found in the species Streptomyces alone. Streptomyces produces a variety of secondary metabolites, each of which has a distinct biological activity, as illustrated in Figure 1. Many different secondary active metabolites could be obtained from this genus, which has enormous promise. As the likelihood of isolating new compounds from Streptomyces originating from terrestrial environments has gradually decreased, the resulting improved resistance to diseases has been seen[23,24]. Marine actinomycetes have the potential to serve as a platform for the manufacture of novel drugs, which could provide an exceptional weapon for battling a variety of resistant bacteria [25,26].

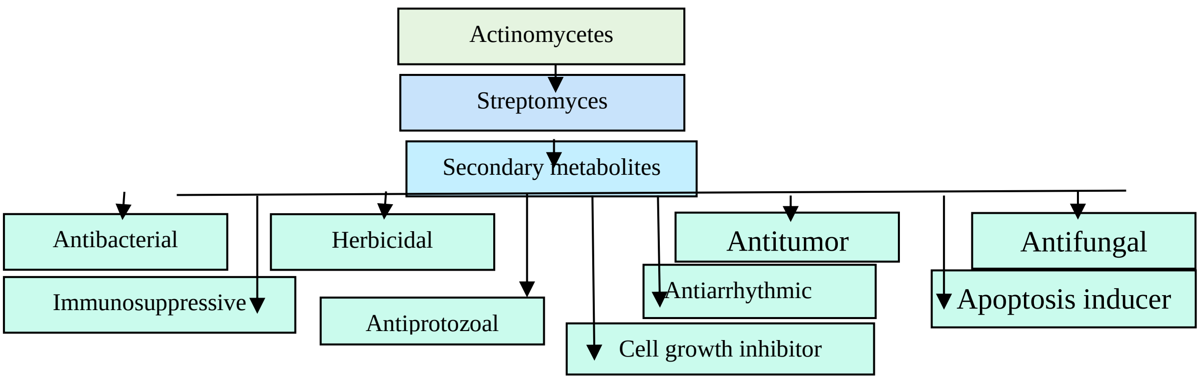

Figure 1: Different biological activities of secondary metabolites produced by the genus *Streptomyces*

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)
CrossRef DOI: https://doi.org/10.31426/ijrpb **Indexed in CAS and CABI, Impact Factor: 0.64**

Continuous research is being conducted in an effort to identify new marine actinomycetes that have not yet been isolated. Numerous marine actinomycetes species remain unidentified, undiscovered, and uncultivated despite ongoing advancements in the isolation and cultivation of these rare bacteria [27,28]. The ability of marine actinomycetes to produce unique bioactive secondary metabolites with a broad spectrum of biological activities, such as antibacterial, antifungal, anticancer, and antitumor properties, is well recognized. A variety of secondary metabolites produced by marine actinomycetes are shown in Fig. 2 [29].

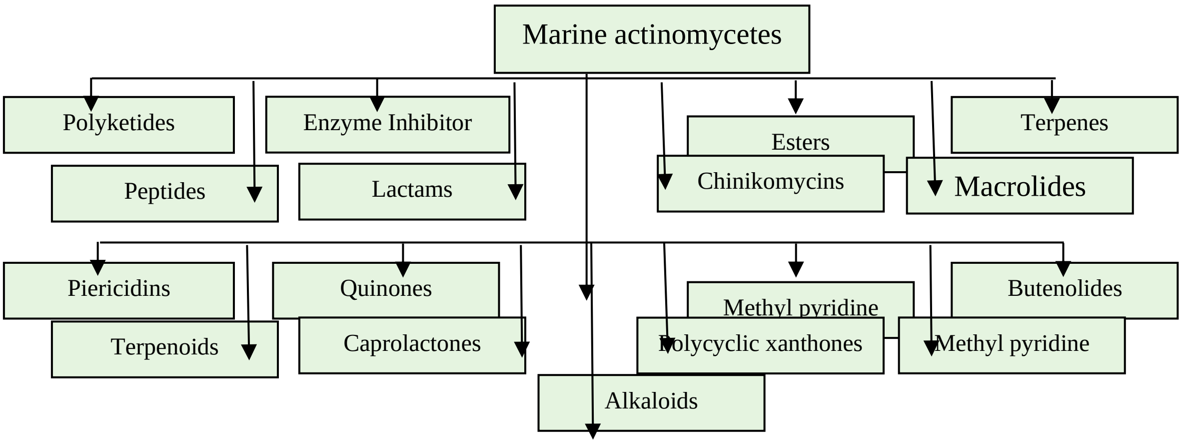

Figure 2: Different Secondary Metabolites Produced By Marine Actinomycetes

Pharmacological application of the actinomycetes: Production of antibiotics

The primary benefit of actinomycetes is their extensive variety of applications in various fields. Actinomycetes are the source of two-thirds of the antibiotics that are currently being researched. Among the antibiotics that are used are tetracyclines, anthracyclines, vancomycin, erythromycin, nucleosides, and chloramphenicol. Numerous human illnesses, such as leprosy, tuberculosis, respiratory conditions, and other fatal illnesses, are treated with these antibiotics [30]. Because of their remarkable capacity to synthesize both secondary metabolites and antibiotics, actinomycetes of the genus Streptomyces have the ability to manufacture a broad range of antibiotics [31]. Apart from this, the genus Streptomyces was the only source of antibiotics that were actinomycete-derived until 1974 [32].

The potential of marine actinomycetes as new antibiotic manufacturers has been extensively researched. Marine actinomycetes are producing a variety of new antibiotics. The marine Verrucosispora strain that produces the novel antibiotic abyssomicin C has the capacity to function as a potent antibacterial agent against gram-positive bacteria when combined with clinical isolates of vancomycin-resistant and multi-resistant Staphylococcus aureus.It has been demonstrated that a unique species of marine Streptomyces is capable of producing new antibiotics called chlorinated

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)

CrossRef **DOI:** https://doi.org/10.31426/ijrpb **Indexed in CAS and CABI, Impact Factor: 0.64**

dihydroquinones. Essramycin is a new antibiotic that has been discovered in Streptomyces sp. and is effective against both gram-positive and gram-negative bacteria. Other novel antibiotics with antibacterial action against different bacterial species include caboxamycin, bisanthraquinone, gliciapyrroles, Himalomycins A and B, and others [(33–36)].

In addition to producing a range of new antibiotics with antibacterial properties, research is being done on marine actinomycetes to find out if they can also produce antibiotics that work against pathogenic fungi. In addition to possessing antialgal action against Chlorella vulgaris and Chlorella sorokiniana, chandanin A, a new antibiotic isolated from Actinomadura species, possesses the potent property of functioning as an antifungal agent against Mucor michei. Bacillus subtilis and Staphylococcus aureus have both shown antibacterial activity against chandananimycin A. There is evidence that this new antibiotic has anti-cancer properties as well [(37)].

Production of Enzyme Inhibitors:

Actinomycetes are able to produce inhibitors of low molecular weight enzymes. Up to 60 enzyme inhibitors have been reported since Umezawa's discovery of the first enzyme inhibitor from a Streptomyces strain. Leupreptines, for instance, block the actions of plasmin, papain, and trypsin. A further inhibitor that inhibits papain, chymotrypsin, trypsin, and cathepsin B is antipain. These actinomycete inhibitors play a role in the therapy of cancer because they have the capacity to block a wide range of enzymes. As an illustration, it has been reported that a strain of Streptomyces produces the enzyme inhibitor revistin, which inhibits reverse transcriptase. Another illustration is the inhibitor alistragin, which is found in Streptomyces roseoviridis culture filtrates [(38)].

Actinomycetes and Cancer:

Cancer is still regarded as the deadliest illness and a major health issue. Furthermore, breast cancer ranks as the second most common cause of cancer-related deaths among women. Today's cancer treatments include surgical procedures, chemotherapy, radiation therapy, and immunotherapy. These treatments, either alone or in combination, can be beneficial, depending on the patient's circumstances. While in-depth research on anti-cancer chemicals produced from marine actinomycetes is lacking, several compounds from these microorganisms have been found to exhibit anti-cancer activity [(39-42)].

The marine actinomycetes Salinispora tropica have been used as a source of purified bioactive chemicals that showed minimal inhibitory effects in different types of cancer cells. It has been reported that Salinosporamide A, a unique bicyclic beta-lactone gamma-lactam, can be isolated from the obligate marine actinomycetes Streptomyces tropica. This substance has been implicated in multiple myeloma cell apoptosis induction. Unlike the currently marketed anticancer medication bortezomib, this molecule is an oral active proteasome inhibitor [(43-46)]. Recently, Streptomyces sp. has been used to

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)
CrossRef DOI: https://doi.org/10.31426/ijrpb Indexed in CAS and CABI, Impact Factor: 0.64

identify antibiotics known as caprolactones, which have demonstrated some phytotoxic and anticancer activity [47].

Antiviral Activity

Actinomycetes are also used to extract antiviral compounds, and numerous reports on antiviral agents derived from marine actinomycetes have been documented. Fish nodavirus (FNV) is antagonistically affected by the metabolite furan-2-yl acetate (C6H6O3), which was produced by Streptomyces sp. VITSDK1. Furan-2-yl acetate, at a concentration of at least 20 lg/ml, was found to effectively inhibit the replication of the virus in studies conducted on SIGE (Sahul Indian Grouper Eye) cells infected with the aforementioned virus [48]. According to another study, a protease inhibitor that was isolated from Streptomyces chromop fuscus 341 exhibits antiviral properties against influenza viruses. The virus-induced cytopathic effect, the expression of the viral haemagglutinin on the surface of infected cells, and the infectious virus yield were all decreased to non-toxic concentrations depending on the dosage. The identical outcome was obtained when the experiment was conducted in vivo. Thus, this protease inhibitor demonstrated potential in a variety of pharmacological and medical fields [49]. White spot syndrome virus in shrimps can be efficiently inhibited at a level of 85% by Streptomyces spp. AJ8, which was isolated from Kovalam salt pans [50]. Many antiviral drugs derived from actinomycetes are still being studied, and many of these compounds are currently undergoing clinical trials.

Antiparasitic Activity

The compounds known as antiparasitic compounds are the ones that stop the growth of the parasites or their larvae. Anopheles stephensi, Hippobosca maculate, Haemaphysalis bispinosa, Rhipicephalus microplus, and Culex tritaeniorhynchus are all susceptible to the antiparasitic effects of Actinomycetes strain LK1 [51]. In order to determine their larvicidal effectiveness against the three different mosquito genera Culex quinquefasciatus, Aedes aegypti, and Anopheles stephensi, various actinomycetes strains from the salt pan of the Tuticorin coast were tested. Regarding Anopheles stephensi, ISO2 showed the lowest activity, whereas ISO7 showed the highest activity [52].

Pigment Production

The creation of pigment is mostly dependent on marine actinomycetes, which have unique structures with extra antibacterial, antioxidant, anticancer, and anti-inflammatory qualities. F1, F2, and F3 of Streptomycetes sp. were isolated from a sample of sea sand and were found to produce melanin. Additionally, an antagonistic activity of the pigment on pathogenic strains was discovered [53]. Streptomyces bellus MSA1, isolated from Kovalam Beach, Chennai, developed an intercellular pigment with antioxidant properties [54].

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)

CrossRef **DOI:** https://doi.org/10.31426/ijrpb **Indexed in CAS and CABI, Impact Factor: 0.64**

Cardiac Arrhythmia

Cardiac arrhythmias are a major cause of morbidity and mortality worldwide, contributing between 10% and 15% of fatalities (55). The marine substance known as tetrodotoxin (TTX), which is beneficial for cardiac arrhythmia, is produced by actinomycetes of maritime sediments. It is commonly known as the puffer fish toxin in excitable neurons [56].

Anti-Inflammatory

The marine actinomycetes produce two anti-inflammatory compounds: lipomycin and saphenic acid. It's also been demonstrated that Micromonospora sp. produces bioactive compounds with antibacterial and anti-inflammatory properties. Another Streptomyces species produces the anti-inflammatory metabolites cyclomarin A and C, the latter of which have anti-tuberculosis and anti-malarial properties. Furthermore, topical or intraperitoneal administration of cyclomarin A reduces inflammation [57].

REFERANCES

1) Ellaiah P, Ramana T, Raju KV, Sujatha P, Sankar AU. Investigations on marine actinomycetes from bay of Bengal near Kakinada coast of Andhra Pradesh. Asian Journal of Microbiology Biotechnology and Environmental Sciences. 2004;6:53-6.
2) Tanaka Y, Omura S. Metabolism and products of actinomycetes-an introduction. Actinomycetologica. 1990 Jun 25;4(1):13-4.
3) Goodfellow M, Haynes JA. Actinomycetes in marine sediments. Biological, biochemical and biomedical aspects of actinomycetes. 1984 Jan 1:453-72.
4) Jagannathan SV, Manemann EM, Rowe SE, Callender MC, Soto W. Marine actinomycetes, new sources of biotechnological products. Marine Drugs. 2021 Jun 25;19(7):365.
5) Valli S, Suvathi SS, Aysha OS, Nirmala P, Vinoth KP, Reena A. Antimicrobial potential of Actinomycetes species isolated from marine environment. Asian Pacific journal of tropical biomedicine. 2012 Jun 1;2(6):469-73.
6) Gebreselema Gebreyohannes GG, Feleke Moges FM, Samuel Sahile SS, Nagappan Raja NR. Isolation and characterization of potential antibiotic producing actinomycetes from water and sediments of Lake Tana, Ethiopia.
7) OLAMI Y. Search and discovery of new antibiotics. Actinomycetes in biotechnology.. 1988:33-67.
8) Pandey B, Ghimire P, Agrawal VP. Studies on the antibacterial activity of the Actinomycetes isolated from the Khumbu Region of Nepal. Journal Biology Science. 2004 May; 23:44-53.
9) Donadio S, Maffioli S, Monciardini P, Sosio M, Jabes D. Antibiotic discovery in the twenty-first century: current trends and future perspectives. The Journal of antibiotics. 2010 Aug;63(8):423-30.
10) Meena B, Rajan LA, Vinithkumar NV, Kirubagaran R. Novel marine actinobacteria from emerald Andaman & Nicobar Islands: a prospective source for industrial and pharmaceutical byproducts. BMC microbiology. 2013 Dec;13:1-7.

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)

CrossRef DOI: https://doi.org/10.31426/ijrpb **Indexed in CAS and CABI, Impact Factor: 0.64**

11) Jensen PR, Moore BS, Fenical W. The marine actinomycete genus Salinispora: a model organism for secondary metabolite discovery. Natural product reports. 2015;32(5):738-51.
12) Dastager SG, Damare S. Marine actinobacteria showing phosphate-solubilizing efficiency in Chorao Island, Goa, India. Current microbiology. 2013 May;66:421-7.
13) Sivakumar K, Sahu MK, Thangaradjou T, Kannan L. Research on marine actinobacteria in India. Indian Journal of Microbiology. 2007 Sep;47:186-96.
14) Williams PG. Panning for chemical gold: marine bacteria as a source of new therapeutics. Trends in biotechnology. 2009 Jan 1;27(1):45-52.
15) Mincer TJ, Jensen PR, Kauffman CA, Fenical W. Widespread and persistent populations of a major new marine actinomycete taxon in ocean sediments. Applied and environmental microbiology. 2002 Oct;68(10):5005-11.
16) Prieto-Davó A, Villarreal-Gómez LJ, Forschner-Dancause S, Bull AT, Stach JE, Smith DC, Rowley DC, Jensen PR. Targeted search for actinomycetes from nearshore and deep-sea marine sediments. FEMS microbiology ecology. 2013 Jun 1;84(3):510-8.
17) Hameedat F, Hawamdeh S, Alnabulsi S, Zayed A. High performance liquid chromatography (HPLC) with fluorescence detection for quantification of steroids in clinical, pharmaceutical, and environmental samples: a review. Molecules. 2022 Mar 10;27(6):1807.
18) Loos G, Van Schepdael A, Cabooter D. Quantitative mass spectrometry methods for pharmaceutical analysis. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences. 2016 Oct 28;374(2079):20150366.
19) Bull AT. Microbial diversity and bioprospecting. 2004.
20) Berdy J. Bioactive microbial metabolites. The Journal of antibiotics. 2005 Jan;58(1):1-26.
21) Mann J. Natural products as immunosuppressive agents. Natural product reports. 2001;18(4):417-30.
22) W. Pecznska, M. Mordaski, Academic Press London (1988) 219-283.
23) Rasool U, Hemalatha S. Diversified role and applications of marine actinomycetes in the field of biology. World Scientific News. 2017(74):1-4.
24) Ekwenye UN, Kazi ER. Investigation of plasmid DNA and antibiotic resistance in some pathogenic organisms. African Journal of Biotechnology. 2007 Apr 2;6(7):877.
25) Lam KS. Discovery of novel metabolites from marine actinomycetes. Current opinion in microbiology. 2006 Jun 1;9(3):245-51.
26) Fenical W, Jensen PR. Developing a new resource for drug discovery: marine actinomycete bacteria. Nature chemical biology. 2006 Dec;2(12):666-73.
27) Stach JE, Maldonado LA, Ward AC, Goodfellow M, Bull AT. New primers for the class Actinobacteria: application to marine and terrestrial environments. Environmental microbiology. 2003 Oct;5(10):828-41.
28) Mincer TJ, Fenical W, Jensen PR. Culture-dependent and culture-independent diversity within the obligate marine actinomycete genus Salinispora. Applied and environmental microbiology. 2005 Nov;71(11):7019-28.
29) Solanki R, Khanna M, Lal R. Bioactive compounds from marine actinomycetes. Indian journal of microbiology. 2008 Dec;48:410-31.
30) S. Mukesh, Int. J. Curr. Microbiol. App. Sci 3 (2) (2014) 801-832.

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)

CrossRef **DOI:** https://doi.org/10.31426/ijrpb **Indexed in CAS and CABI, Impact Factor: 0.64**

31) Berdy J. Bioactive microbial metabolites. The Journal of antibiotics. 2005 Jan;58(1):1-26.
32) Dilip CV, Mulaje SS, Mohalkar RY. A review on actinomycetes and their biotechnological application. International Journal of pharmaceutical sciences and research. 2013 May 1;4(5):1730.
33) Riedlinger J, Reicke A, Zähner HA, Krismer B, Bull AT, Maldonado LA, Ward AC, Goodfellow M, Bister B, Bischoff D, SüSSMUTH RD. Abyssomicins, inhibitors of the para-aminobenzoic acid pathway produced by the marine Verrucosispora strain AB-18-032. The Journal of antibiotics. 2004 Apr 25;57(4):271-9.
34) Manivasagan P, Venkatesan J, Sivakumar K, Kim SK. Pharmaceutically active secondary metabolites of marine actinobacteria. Microbiological research. 2014 Apr 1;169(4):262-78.
35) Soria-Mercado IE, Prieto-Davo A, Jensen PR, Fenical W. Antibiotic terpenoid chloro-dihydroquinones from a new marine actinomycete. Journal of natural products. 2005 Jun 24;68(6):904-10.
36) El-Gendy M, Shaaban M, Shaaban KA, El-Bondkly AM, Laatsch H. Essramycin: a first triazolopyrimidine antibiotic isolated from nature. The Journal of antibiotics. 2008 Mar;61(3):149-57.
37) Maskey RP, Li FC, Qin S, Fiebig HH, Laatsch H. Chandrananimycins AC: production of novel anticancer antibiotics from a marine Actinomadura sp. isolate M048 by variation of medium composition and growth conditions. The Journal of antibiotics. 2003 Jul 25;56(7):622-9.
38) Peczynska-Czoch W, Mordarski M, Goodfellow M, Williams ST, Mordarski M. Actinomycetes in biotechnology. Eds. Goodfellow, M., ST Williams & M. Mordarski, Aacademic Press, London. 1988:219-83.
39) Ravikumar S, Gnanadesigan M, Thajuddin N, Chakkaravarthi V, Banerjee B. Anticancer property of sponge associated actinomycetes along Palk Strait. J Pharm Res. 2010 Oct;3(10):2415-7.
40) J-P Gillet, T. Efferth, J. Remacle, Biochim Biophys Acta (BBA)-Rev Cancer 1775 (2) (2007) 237-262.
41) Ravikumar S, Fredimoses M, Gnanadesigan M. Anticancer property of sediment actinomycetes against MCF–7 and MDA–MB–231 cell lines. Asian Pacific journal of tropical biomedicine. 2012 Feb 1;2(2):92-6.
42) Prudhomme, E. McDaniel, N. Ponts, S. Bertani, W. Fenical, P. Jensen, L. R. Karine, PLoS ONE 3 (6) (2008) e2335.
43) Feling RH, Buchanan GO, Mincer TJ, Kauffman CA, Jensen PR, Fenical W. Salinosporamide A: a highly cytotoxic proteasome inhibitor from a novel microbial source, a marine bacterium of the new genus Salinospora. Angewandte Chemie International Edition. 2003 Jan 20;42(3):355-7.
44) Jensen PR, Williams PG, Oh DC, Zeigler L, Fenical W. Species-specific secondary metabolite production in marine actinomycetes of the genus Salinispora. Applied and environmental microbiology. 2007 Feb 15;73(4):1146-52.
45) Chauhan D, Catley L, Li G, Podar K, Hideshima T, Velankar M, Mitsiades C, Mitsiades N, Yasui H, Letai A, Ovaa H. A novel orally active proteasome inhibitor induces apoptosis in multiple myeloma cells with mechanisms distinct from Bortezomib. Cancer cell. 2005 Nov 1;8(5):407-19.
46) Stritzke K, Schulz S, Laatsch H, Helmke E, Beil W. Novel caprolactones from a marine streptomycete. Journal of natural products. 2004 Mar 26;67(3):395-401.
47) Suthindhiran K, Kannabiran K. Hemolytic activity of Streptomyces VITSDK1 spp. isolated from marine sediments in Southern India. Journal de mycologie médicale. 2009 Jun 1;19(2):77-86.

Indian Journal of Research in Pharmacy and Biotechnology (IJRPB)
www.ijrpb.com ISSN: 2321-5674 (Print), 2320-3471 (Online)
CrossRef DOI: https://doi.org/10.31426/ijrpb **Indexed in CAS and CABI, Impact Factor: 0.64**

48) Serkedjieva J, Dalgalarrondo M, Angelova-Duleva L, Ivanova I. Antiviral potential of a proteolytic inhibitor from streptomyces chromofuscus 34–1. Biotechnology & Biotechnological Equipment. 2012 Jan 1;26(1):2786-93.
49) Jenifer JS, Donio MB, Michaelbabu M, Vincent SG, Citarasu T. Haloalkaliphilic Streptomyces spp. AJ8 isolated from solar salt works and its’ pharmacological potential. AMB Express. 2015 Dec;5:1-2.
50) Loganathan K, Kumar G, Kirthi AV, Rao KV, Rahuman AA. Entomopathogenic marine actinomycetes as potential and low-cost biocontrol agents against bloodsucking arthropods. Parasitology research. 2013 Nov;112:3951-9.
51) Vinodhkumar T, Subhapriya M, Ramanathan G, Suresh JI. Kalpana, 2015. Screening of bioactive potential for larvicidal activity of marine actinomycetes. Int. J. Curr. Microbiol. appl. Sci.;4:972-80.
52) Vasanthabharathi V, Lakshminarayanan R, Jayalakshmi S. Melanin production from marine Streptomyces. African journal of biotechnology. 2011 Sep 19;10(54):11224.
53) Srinivasan M, Keziah SM, Hemalatha M, Devi CS. Pigment from Streptomyces bellus MSA1 isolated from marine sediments. InIOP conference series: Materials science and engineering 2017 Nov 1 (Vol. 263, No. 2, p. 022049). IOP Publishing.
54) Blackwell DJ, Schmeckpeper J, Knollmann BC. Animal models to study cardiac arrhythmias. Circulation research. 2022 Jun 10;130(12):1926-64.
55) Do HK, Kogure K, Imada C, Noguchi T, Ohwada K, Simidu U. Tetrodotoxin production of actinomycetes isolated from marine sediment. Journal of Applied Microbiology. 1991 Jun 1;70(6):464-8.
56) Pandey A. Pharmacological significance of marine microbial bioactive compounds. Environmental Chemistry Letters. 2019 Dec;17(4):1741-51.