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Review Article

THERAPEUTICALLY ACTIVE BIOMOLECULES FROM MARINE ACTINOMYCETES

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Abstract

For the past few centuries, the biological sources of terrestrial origin have been explored and exploited for bioactive metabolites. This has resulted in the stagnancy of discovering either novel compounds or compounds with novel bioactivities. Thus, researchers across the globe have started exploring our big Oceans, for the search of bioactive metabolites. During the past few decades, the research on bioactive metabolites from marine biological resources has geared up and among the sources marine actinomycetes are proved to be best. Marine actinomycetes, the filamentous bacteria from marine environment have been intensively studied for bioactive metabolites. The biological diversity of marine actinomycetes was found to be enormous, thanks to culture dependent and culture independent biodiversity approaches. This great diversity of marine actinomycetes has offered greater chemical diversity. The diverse chemical compounds of marine actinomycetes have been found to have various biological activities such as antimicrobial, anti-tumor, anti-malarial, anti-algal, antioxidant, anti-inflammatory etc. These various bioactive metabolites of marine actinomycetes are having scope for developing as potent therapeutic agents. The potential of marine actinomycetes is rightly realized though the current biological wealth of these organisms is relatively unexplored.

***Keywords*:** marine actinomycetes, bioactive metabolites, biological activities, biodiversity, therapeutic agents

INTRODUCTION

Actinomycetes, the filamentous, high G+C rich gram positive bacteria, are the most economically and biotechnologically valuable prokaryotic microorganisms. They were found to produce nearly half of the discovered bioactive secondary metabolites. These secondary metabolites include antibiotics, antitumor agents, immunosuppressive agents and enzymes (Berdy, 2005; Lam, 2006). Actinomycetes are proven resources for the search of novel bioactive metabolites. Hence, focus on the successful isolation of novel actinomycetes from terrestrial sources for drug screening programs in the past fifty years was given. However, the number of discovery of new metabolites from terrestrial actinomycetes has decreased, whereas the rate of re-isolation of known compounds has increased. Thus, it is crucial that new groups of actinomycetes from unexplored or underexploited habitats be pursued as sources of novel bioactive secondary metabolites (Fenical *et al*., 2009). The oceans cover 70% of the Earth's surface and harbor most of the planet's biodiversity. Although marine plants and invertebrates have received considerable attention as a resource for natural-product discovery, the microbiological component of this diversity remains relatively unexplored. Recent studies have concluded that selected groups of marine actinomycetes are found to offer a reliable source of new natural products (Fenical and Jensen, 2006). Hence, this paper would review the recent scenario about diverse marine actinomycetes and their bioactive metabolites.

BIODIVERSITY OF MARINE ACTINOMYCETES

During the last two decades, discoveries of new members of actinomycetes and novel metabolites from marine environments have drawn attention to such environments, such as sediment and sponge (Hameş-Kocabaş and Uzel, 2012). The marine environment has become a prime resource in search and discovery for novel natural products and biological diversity, and marine actinomycetes turn out to be important contributors (Ward and Bora, 2006). Many laboratories across the globe have isolated and identified many marine actinomycetes. A total collection of 26 marine endosymbiotic actinomycete strains, isolated from the Bay of Bengal (coast of India), were screened for antagonistic and antimicrobial activity against pathogenic bacteria and fungi (Gandhimathi *et al*., 2008). Nine selective culture media were used for isolation and enumeration of actinomycetes in marine water and sediments. Actinomycetes in water and sediment represented 3–4% and 5–6% of the total flora, respectively. 72.7% of the isolated strains were *Streptomyces*, 20.5% *Micromonospora* and 7% *Nocardia* (Barcina *et al*., 1987).

Dharmaraj (2010) has comprehensively reviewed the diverse marine actinomycetes genera and their bioactive potential. Representative genera of marine actinobacteria include *Actinomadura*, *Aeromicrobium*, *Dietzia*, *Gordonia*, *Marinophilus*, *Micromonospora*, *Nonomuraea*, *Rhodococcus*, *Saccharomonospora*, *Saccharopolyspora*, *Salinispora*, *Streptomyces*, *Solwaraspora*, *Williamsia*, *Verrucosispora* and several others. Among the genera of marine actinobacteria, the genus *Streptomyces* is represented in nature by the largest number of species and varieties, which differ greatly in their morphology, physiology, and biochemical activities (Dharmaraj, 2010). Thus, the diversity of marine actinomycetes is enormous and so having immense scope for the discovery of novel bioactive metabolites. However, the distribution of actinomycetes in the sea is largely unexplored and the presence of indigenous marine actinomycetes in the oceans remains elusive (Lam, 2006).

ANTIBIOTIC COMPOUNDS FROM MARINE ACTINOMYCETES

Approximately 23,000 biologically active secondary metabolites have been reported to be produced by microorganisms among which over 10,000 of these are produced by actinomycetes, representing 45% of all bioactive microbial metabolites discovered. Among actinomycetes, around 7,600 compounds are produced by *Streptomyces* species. Streptomycetes, being the chief producers of antibiotics were exploited enormously by the pharmaceutical industry (Berdy, 2005). A Pyridinium compound with antimicrobial activity was isolated from marine actinomycete, *Amycolatopsis alba* var. nov. DVR D4 (Dasari *et al*., 2012). Three new chlorinated dihydroquinones (1−3) and one previously reported analogue, 4 were isolated, purified and characterized for their antimicrobial activity from a new genus (tentatively called MAR4) within the family Streptomycetaceae strain CNQ-525, isolated from ocean sediments collected at a depth of 152 m near La Jolla, California (Soria-Mercado *et al*., 2005). The marine actinomycetes from the sponges are also proved to be potential sources of novel antibiotic leads (Gandhimathi *et al*., 2008). The cyclomarazines isolated from *Salinospora arenicola* demonstrate inhibitory properties against vancomycin-resistant *Entrococcus faecium* at 13 μg/mL and methicillin-resistant *Staphylococcus aureus* at 18 μg/mL (Renner *et al*., 1999). 208 isolates of marine actinomycetes were isolated from Bay of Bengal India and screened for various biological activities. Among 208 marine actinomycetes, 111 isolates exhibited antimicrobial activity against human pathogens, and 151 showed antifungal activity against two plant pathogens (Ramesh and Mathivanan, 2009). Numerous studies have proved that the actinomycetes isolated from coastal sand dune ecosystem are having potential antimicrobial activity against pathogenic bacteria and soil borne fungal phytopathogens (Hariharan *et al*., 2011; Sangeetha *et al*., 2011; Sangeetha *et al*., 2012)

Lam (2005) has extensively reviewed the novel metabolites from marine actinomycetes. Many antimicrobial compounds such as Abyssomicins, Aureoverticillactam, Bonactin, Caprolactones, Chandrananimycins, Chinikomycins, Chloro-dihydroquinones, Diazepinomicin, 3,6-disubstituted indoles, Frigocyclinone, Glaciapyrroles, Gutingimycin, Helquinoline, Himalomycins, Komodoquinone A, Lajollamycin, Marinomycins, Mechercharmycins,

Salinosporamide A, Sporolides, Trioxacarcins etc were obtained from marine actinomycetes mostly belong to genera like *Streptomyces, Salinispora* etc.

ANTITUMOUR COMPOUNDS FROM MARINE ACTINOMYCETES

Cancer, the King of Maladies is the most serious challenge encountered by biomedical scientists. The therapies and treatments vary with types of cancer. However, antitumor compounds are always preferred molecules by cancer biologists for therapy. Many cytotoxic compounds from natural resources were found to be having antitumor and anticancer activity. Many compounds with anticancer potential were isolated and developed from various biological resources like plants and microbes. Efforts are required to gain deeper knowledge regarding the various signal transduction pathways linked to cellular processes such as inflammation, cell differentiation and survival, carcinogenesis, and metastasis. Although it is very difficult to predict the final outcome of such a scheme of drug discovery, it can be assured that a focused approach and combined efforts would definitely accelerate the development of new marine antitumor drugs to be discovered with increased efficiency (Bhatnagar and Kim, 2010). Olano *et al*. (2009) have elaborately reviewed novel antitumor compounds identified from marine actinomycetes and classified them in terms of their chemical structure. Polyketides such as Griseorhodin A, Gutingimycin, Himalomycins etc, phenazines like Iodinin, Non-ribosomal peptides like Lucentamycins, Mechercharmycins etc., Isoprenoids like Marinones, Polypyrroles like Marineosins, Indolocarbazoles like Staurosporins and few other Methylpyridine, Tetrahydropyrrole, Prodigiosi, Butenolide, Pyrrolizidine and Benzoxazole compounds isolated from various marine actinomycetes were found to have antitumor activities (Olano *et al*., 2009). *S. arenicola* produces cyclomarin D, which has a slight toxic effect on human colon carcinoma cells, as well as the cyclomarin derivatives of cydomarazine A and cydomarazine B (Renner *et al*., 1999).

Very recently, the anticancer property of marine sediment actinomycetes against breast cancer cell lines MCF–7 and MDA–MB–231 was reported by Ravikumar *et al*. (2012). The cytotoxicity and antioxidant activity of 5-(2,4-dimethylbenzyl)pyrrolidin-2-one (DMBPO) extracted from marine *Streptomyces* VITSVK5 sp. which was isolated from sediment samples collected at the Marakkanam coast of Bay of Bengal, India (Saurav and Kannabiran, 2012). Two new anthracyclinones, 4,6,11-trihydroxy-9-propyltetracene-5,12-dione and 10β-carbomethoxy-7,8,9,10-tetrahydro-4,6,7α,9α,11-pentahydroxy-9-propyltetracene-5,12-dione with cytotoxic activity against the HCT-8 human colon adenocarcinoma cell line, were isolated from a strain of *Micromonospora* sp. associated with the tunicate *Eudistoma vannamei* (Sousa *et al*., 2012).

ANTI-INFLAMMATORY COMPOUNDS FROM MARINE ACTINOMYCETES

Inflammation, the defensive mechanism is a complex biological response of vascular tissues to harmful stimuli including pathogens, irritants or damaged cells. Untreated inflammation may lead to onset of diseases such as vasomotor rhinnorrhoea, rheumatoid arthritis, and atherosclerosis (Henson and Murphy, 1989). Currently available anti-inflammatory drugs like Opoids and NSAIDs drugs are not useful in all cases of inflammatory disorders, because of their side effects, economy and potency. As a result, a search for other alternatives is necessary (Sharma *et al*., 2010). Among the thirty bioactive compounds screened from marine actinomycetes, two compounds such as saphenic acid and lipomycin were found to have anti-inflammatory activity (Haridas *et al*., 2012). Charan *et al*. (2004) have identified Diazepinomicin (ECO-4601) from *Micromonosproa* sp with anti inflammatory activity along with antimicrobial activity. *S. arenicola* also produces the anti-inflammatory metabolites cyclomarin A and C. Swelling was reduced when cyclomarin A was administered topically or intraperitonially by 92% and 45% respectively (Renner *et al*., 1999).

THEREPEUTIC ENZYMES AND INHIBITORS FROM MARINE ACTINOMYCETES

Many enzymes from microbial sources are used as therapeutic agents of which thrombinase and L-asparaginase are of chief attraction. L-asparaginase, the enzyme which converts L-asparagine to L-aspartic acid and ammonia has been used as a chemotherapeutic agent. It has received increased attention in recent years

for its anticarcinogenic potential (Manna *et al*., 1995). A potent fibrinolytic protease (thrombinase) was isolated from marine actinomycetes *Streptomyces venezuelae* which can be used for the treatment of myocardial infarction. Effect of cultural and environmental parameter on the production of thrombinase by *S. venezuelae* was also optimized (Naveena *et al*., 2012). Saleem Basha *et al*. (2009) have reported the production, purification and characterization of extracellular anti-leukaemic enzyme L- asparaginase from marine actinomycetes by solid state and submerged fermentation. Dhevagi and Poorani (2006) have isolated and purified L-asparaginase from *Streptomyces* sp.PDK2 isolated from marine coastal sediments. The purified L-asparaginase showed cytostatic effects on JURKAT cells (Acute T cell leukemia) and K562 cells (Chronic myelogenous leukemia). Dharmaraj (2011) have reported the production of extra-cellular L-asparaginase using submerged fermentation from *Streptomyces noursei* MTCC 10469, a marine actinomycete associated with marine sponge *Callyspongia diffusa*. Several enzyme-inhibitor-producing actinomycetes were isolated from various samples collected from the marine environment and characterized. Most of them produced novel compounds that are useful in medicine and agriculture (Imada, 2005).

OTHER BIOACTIVE COMPOUNDS OF THERAPEUTIC VALUE FROM MARINE ACTINOMYCETES

The comprehensive review by Lam (2005) has listed many compounds from marine actinomycetes with novel bioactivities such as antialgal activity of Chandrananimycins from *Actinomadura* sp., Neuritogenic activity of Komodoquinone A from *Streptomyces* sp., and antimalarial activity of Trioxacarcins from *Streptomyces* sp. A total of 600 actinomycetes strains were isolated from marine sediments from various sites in the Pacific and Atlantic oceans and screened for the production of bioactive secondary metabolites. Marine streptomycete strains and some new marine members of the rare genus *Verrucosispora* seem to be promising sources for novel bioactive secondary metabolites (Fiedler *et al*., 2005). Amongst prokaryotes, actinomycetes, notably marine streptomycetes, remain a rich source of new natural products though it has become increasingly difficult to find such metabolites from common actinomycetes as screening 'old friends' leads to the costly rediscovery of known compounds (Goodfellow and Fiedler, 2010). A literature survey covering more than twenty-three thousand bioactive microbial products including eight thousand antiinfectives demonstrated the increasing relevance of the so called 'rare' actinomycetes as a source of new antibiotics (Lazzarini *et al*., 2001). A unique selective enrichment procedure has resulted in the isolation and identification of two new genera of marine-derived actinobacteria. Biological activity testing of fermentation products from the 102 actinomycetes isolated from subtidal marine sediments collected from the Bismarck Sea and the Solomon Sea off the coast of Papua New Guinea revealed that several had activities against multidrug-resistant gram-positive pathogens, malignant cells, and vaccinia virus replication (Magarvey *et al*., 2004). The production of tetrodotoxin (TTX), known otherwise as puffer fish toxin, was investigated in various actinomycetes collected from the marine environment. Of 10 isolates from various sea areas, 9 produced TTX as judged by their retention times on high-performance liquid chromatography (HPLC) and this was reported for the first time by Imada (2005). The fermenting sponge-associated *Streptomyces* isolate (AQBMM35) produced carotenoids namely phytoene which has antioxidant activity and also can be used as a food additive (Dharmaraj *et al*., 2009). A study by Prudhomme *et al.* (2008) underline the potential of secondary metabolites, derived from marine microorganisms, to inhibit *Plasmodium* growth. More specifically, it has highlighted the effect of proteasome inhibitors such as salinosporamide A on *in vitro* and *in vivo* parasite development. According to Prudhomme *et al.* (2008) Salinosporamide A (NPI-0052) now being advanced to phase I trials for the treatment of refractory multiple myeloma will need to be further explored to evaluate the safety profile for its use against malaria.

CHALLENGES IN MARINE ACTINOMYCETES RESEARCH

Actinomycetes, being the single most productive source of naturally occurring antibiotics, are a logical component of many research studies, and success with this group will be enhanced by the inclusion of

previously unknown taxa. Recent studies of marine-derived actinomycetes have revealed the widespread distribution of unique marine taxa residing in ocean sediments (Jensen and Fenical, 2005.). A review by Hameş-Kocabaş, and Uzel (2012) comprehensively evaluates the traditional and innovative techniques and strategies used for the isolation of actinomycetes from marine sponge and sediment samples. Most of the studies conducted in tropical countries like India, pertain to isolation, identification and maintenance of these organisms in different culture media. Further, antimicrobial activities of these actinobacteria were also concentrated. Their biotechnological and therapeutic potentials are yet to be fully explored (Sivakumar *et al*., 2007). Continued efforts to characterize marine actinomycete diversity and how adaptations to the marine environment affect secondary metabolite production will create a better understanding of the potential utility of these bacteria as a source of useful products for biotechnology (Jensen *et al*., 2005). Thus, culturing and screening for various bioactivities of marine actinomycetes are two major challenges in marine actinomycetes research. Culture independent studies and new high throughput screening methods would enhance the pace of research in this area.

CONCLUSION

The immense scope of marine actinomycetes for the exploration of therapeutically active biomolecules has been realized recently. Many studies world over have paved the way for intensification of research on marine actinomycetes for the search of new drugs or drug leads. However, the exact potential of marine actinomycetes in drug discovery is yet to be concentrated.

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REFERENCES

Barcina I, Iriberri J and Egea L. 1987. Enumeration, isolation and some physiological properties of actinomycetes from sea water and sediment. *Systematic and Applied Microbiology* 10:85–91.

Berdy J. 2005. Bioactive microbial metabolites. *Journal of Antibiotics (Tokyo)* 58:1–26.

Bhatnagar I and Kim S. 2010. Marine antitumor drugs: status, shortfalls and strategies. *Marine Drugs* 8:2702–2720.

Charan RD, Schlingmann G, Janso J, Bernan V, Feng X and Carter GT. 2004. Diazepinomicin, a new antimicrobial alkaloid from marine *Micromonospora* sp. *Journal of Natural Products* 67:1431–1433.

Dasari VR, Muthyala MK, Nikku MY and Donthireddy SR. 2012. Novel Pyridinium compound from marine actinomycete, *Amycolatopsis alba* var. nov. DVR D4 showing antimicrobial and cytotoxic activities *in vitro*. *Microbiological Research* 167:346–351.

Dharmaraj S. 2011. Study of L-asparaginase production by *Streptomyces noursei* MTCC 10469, isolated from marine sponge *Callyspongia diffusa*. *Iranian Journal of Biotechnology* 9:102–108.

Dharmaraj S, Ashokkumar B and Dhevendaran K. 2009. Fermentative production of carotenoids from marine actinomycetes. *Iranian Journal of Microbiology* 1:36–41.

Dhevagi Pand Poorani E. 2006. Isolation and characterization of L- asparaginase from marine actinomycetes. Indian Journal of Biotechnology 5:514–520.

Fenical W, Baden D, Burg M, de Goyet CV, Grimes JD, Katz M, Marcus NH, Pomponi S, Rhines P, Tester P and Vena J. 1999. Marine derived pharmaceuticals and related bioactive compounds. In: *From monsoons to microbes: Understanding the ocean's role in human health*. Fenical W, Editor. The National Academies Press: Washington; pp 71–86.

Fenical W and Jensen PR. 2006. Developing a new resource for drug discovery: marine actinomycete bacteria. *Nature Chemical Biology* 2, 666 – 673.

Fiedler HP, Bruntner C, Bull AT, Ward AC, Goodfellow M, Potterat O, Puder C and Mihm G. 2005. Marine actinomycetes as a source of novel secondary metabolites. *Antonie Van Leeuwenhoek* 87:37–42.

Gandhimathi R, Arunkumar M, Selvin J, Thangavelu T, Sivaramakrishnan S, Kiran GS, Shanmughapriya S and Natarajaseenivasan K. 2008. Antimicrobial

potential of sponge associated marine actinomycetes. *Journal of Medical Mycology* 18:16–22.

Goodfellow M and Fiedler HP. 2010. A guide to successful bioprospecting: informed by actinobacterial systematics. *Antonie Van Leeuwenhoek* 98:119–42.

Hameş-Kocabaş EE and Uzel A. 2012. Isolation strategies of marine-derived actinomycetes from sponge and sediment samples. *Journal of Microbiological Methods* 88:342–347.

Haridas M, Joseph A and Sunil Kumar N. 2012. Discovery of new anti-inflammatory drug-leads from marine microorganisms: bioinformatics' way. *Biobytes* 4:1

Hariharan S, Karthigeyan CP, Sangeetha S, Jaffar Hussain A and Jayaprakashvel M. 2011. Potential of marine actinomycetes as biocontrol agents against fungal pathogens of ground nut seedling. In: Proceedings of National Seminar on Current Trends in Biotechnological Strategies for Eco-friendly Crop Protection. Mathivanan N, Editor. University of Madras Press; Chennai, India; p–11.

Henson PM and Murphy RC. 1989. Mediators of the inflammatory process. 6th Ed. Elsevier. Amsterdam; p–404.

Imada C. 2005. Enzyme inhibitors and other bioactive compounds from marine actinomycetes. *Antonie van Leeuwenhoek* 87:59–63.

Jensen PR and Fenical W. 2005. New natural-product diversity from marine actinomycetes. *Natural Products Part V,* Zhang L and Demain AL, Editors. Humana Press: New York; pp 315–328.

Jensen PR, Mincer TJ, Williams PG and Fenical W. 2005. Marine actinomycete diversity and natural product discovery. *Antonie van Leeuwenhoek* 87:43–48.

Lam KS. 2006. Discovery of novel metabolites from marine actinomycetes. *Current Opinion in Microbiology* 9:245–251.

Lazzarini A, Cavaletti L, Toppo G and Marinelli F. 2001. Rare genera of actinomycetes as potential producers of new antibiotics. *Antonie Van Leeuwenhoek* 79:399–405.

Magarvey NA, Keller JM, Bernan V, Dworkin M and Sherman DH. 2004. Isolation and characterization of novel marine-derived actinomycete taxa rich in bioactive metabolites. *Applied and Environmental Microbiology* 70:7520–7529.

Manna S, Sinha A, Sadhukan R and Chakrabarty SL. 1995. Purification, characterization and antitumor activity of L-asparaginase isolated from *Pseudomonas stutzeri* MB-405. *Current Microbiology* 30:291–298.

Naveena P, Sakthiselvan P, Elaiyaraju P and Partha P. 2012. Ultrasound induced production of thrombinase by marine actinomycetes: Kinetic and optimization studies. *Biochemical Engineering Journal* 61:34–42.

Prudhomme J, McDaniel E, Ponts N, Bertani S, Fenical W, Jensen P and Le Roch K. 2008. Marine actinomycetes: a new source of compounds against the human malaria parasite. *PLoS One* 3:e2335.

Ramesh S and Mathivanan N. 2009. Screening of marine actinomycetes isolated from the Bay of Bengal, India for antimicrobial activity and industrial enzymes. *World Journal of Microbiology and Biotechnology* 25:2103–2111.

Ravikumar S, Fredimoses M and Dnanadesigan M. 2012. Anticancer property of sediment actinomycetes against MCF–7 and MDA–MB–231 cell lines. *Asian Pacific Journal of Tropical Biomedicine* 2:92–96.

Renner MK, Shen YC, Cheng XC, Jensen PR, Frankmoelle W, Kauffman CA, Fenical W, Lobkovsky E and Clardy J. 1999. Cyclomarins A-C, new antiflammatory cyclic peptides produced by a marine bacterium (*Streptomyces* sp.). *Journal of the American Chemical Society* 121: 11273–11276.

Dharmaraj S. 2010. Marine *Streptomyces* as a novel source of bioactive substances. *World Journal of Microbiology and Biotechnology* 26:2123–2139.

Saleem Basha N, Rekha R, Komala M and Ruby S. 2009. Production of extracellular anti-leukaemic enzyme L-asparaginase from marine actinomycetes by solidstate and submerged fermentation: purification and characterisation. *Tropical Journal of Pharmaceutical Research* 8:353–360.

Sangeetha S, Jaffar Hussain A and Jayaprakashvel M. 2011. Antagonistic activity of actinobacteria against soil borne fungal phytopathogens. In:

Proceedings of National Seminar on Current Trends in Biotechnological Strategies for Eco-friendly Crop Protection. Mathivanan N, Editor. University of Madras Press; Chennai, India; p–15.

Sangeetha S, Jaffar Hussain A and Jayaprakashvel M. 2012. Antagonistic activity of salt tolerant actinobacteria against phytopathogens. In: Abstracts of National Conference on Marine Environmental Challenges and coastal zone management strategy. Manoharan V, Editor. Bharathidasan University Press: Trichirappalli, India; p–12.

Saurav K and Kannabiran K. 2012. Cytotoxicity and antioxidant activity of 5-(2,4-dimethylbenzyl) pyrrolidin-2-one extracted from marine *Streptomyces* VITSVK5 spp. *Saudi Journal of Biological Sciences* 19:81–86.

Sharma US, Sharma UK, Sutar N, Singh A. and Shukla DK. 2010. Anti-inflammatory activity of *Cordia dichotoma forst f.* seeds extracts. *International Journal of Pharmaceuticals Analysis* 2:1–4.

Sivakumar K, Sahu MK, Thangaradjou T and Kannan L. 2007. Research on marine actinobacteria in India. *Indian Journal of Microbiology* 47:186–196.

Soria-Mercado IE, Prieto-Davo A, Jensen PR and Fenical W. 2005. Antibiotic terpenoid chloro-dihydroquinones from a new marine actinomycete. *Journal of Natural Products* 68:904–910.

Sousa TS, Jimenez PC, Ferreira EG, Silveira ER, Braz-Filho R, Pessoa ODL and Costa-Lotufo LV. 2012. Anthracyclinones from *Micromonospora* sp. *Journal of Natural Products* 75:489–493.

Ward AC and Bora N. 2006. Diversity and biogeography of marine actinobacteria. *Current Opinion in Microbiology* 9:279–286.