PLANT SCIENCE TODAY
Vol 12(sp2): 01–09
https://doi.org/10.14719/pst.6492

eISSN 2348-1900

REVIEW ARTICLE

Pharmaceutically important bioactive natural products from marine microbes

Manali Singh[1*], Shivani Bhutani[2], Sumit Purohit[3], Satyajit Saurabh[4] & Nisha Dinkar[5]

[1]Department of Life Sciences, Parul Institute of Applied Sciences, Parul University, Post-Waghodia, Vadodara 391 760, India
[2]Department of Biotechnology, Invertis University, Bareilly- Lucknow National Highway, NH-24, Bareilly 243 123, India
[3]Regional Centre, Uttarakhand Council for Biotechnology, Patwadangar, Nainital 263 128, India
[4]DNA Fingerprinting Laboratory, Bihar State Seed and Organic Certification Agency, Patna 800 001, India
[5]Department of Biotechnology, Khandelwal College of Management Science and Technology, Kalapur, Bareilly 243 502, India

*Correspondence email - manalisingh15@gmail.com

Received: 03 December 2024; Accepted: 27 February 2025; Available online: Version 1.0: 17 May 2025

Cite this article: Manali S, Shivani B, Sumit P, Satyajit S, Nisha D. Pharmaceutically important bioactive natural products from marine microbes. Plant Science Today. 2025; 12(sp2):01–09. https:/doi.org/10.14719/pst.6492

Abstract

Secondary metabolites obtained from marine biodiversity have varied bioactive compounds that possess various properties of pharmaceutical relevance. The diversity in chemical and molecular forms imparts these metabolites tremendous pharmacological significance. So many diseases are still untreatable due to the non-availability of proper medicines. The novel drugs isolated from the marine microbes which are not yet explored will provide an extraordinary, advanced approach to drug discovery. The novelty in drug development owing to the presence of such bioactive compounds has led to exploring new horizons pertaining to diseases and their treatment. These metabolites also serve as an important tool in the field of agriculture as biocides for crop improvement. Nowadays, much of the research is being focused on alternative sources of energy, in which algae are contributing a great deal. Thus, these metabolites play a pivotal role in various industries in the production of commercial products that are beneficial for mankind. Much of the research still needs to be done in this field as most of the marine microbes are not easily accessible due to the ocean depths. If such microbes can be isolated from the deep ocean, then novel research will pave the drug discovery to treat those ailments which are not possible till date. Even a lot of study is needed in the area of bioprospecting for the advancements in isolation and characterization of potential compounds. If we can isolate the potent compound, we will not only be able to prevent the occurrence of such lethal diseases but also be able to save human lives. The present review focuses on the important metabolites extracted from the marine microbes and their pharmacological significance, which owe special significance to the medical community and drug development.

Keywords: drug discovery; marine environment; pharmacological significance; secondary metabolites

Introduction

Over millions of years, from marine to terrestrial, diverse life forms have evolved with contrast in their morphology and physiology. All life forms, eukaryotes and prokaryotes are involved in anabolism (biosynthesis) and catabolism (breakdown) of macromolecules or the primary metabolites in a similar way. The anabolism and catabolism are together known as metabolism or the primary metabolism, which serves as the vital force for the fulfilment of the necessities of all life forms, i.e. growth and development, reproduction and survival.

In addition to primary metabolites, living forms are involved in the synthesis of secondary metabolites, also known as natural products, through the process of secondary metabolism. As a survival strategy, microbes produce chemical constituents in the varied form of natural products known as secondary metabolites. These secondary metabolites are distributed in all the microbe kingdom under different taxonomic and chemotypic groups. Unlike primary metabolites such as amino acids, nucleotides, phytosterols, lipids, organic acids etc., the biosynthesis of these secondary metabolites was initially associated with inessentiality which was restricted to certain groups. These secondary metabolites as such do not participate primarily in the metabolic role in the plants. Moreover, their absence does not result in death, but after a certain period of time can cause danger to the microbe. The secondary metabolites are usually 100 to 1000 Da in molecular weight and are often different among different life forms (1-3). The secondary metabolites are not involved as a basic need for survival and reproduction of an organism but involved in expanding likelihood of its survival (1). Not only this but the secondary metabolites have also been reported to involve their role in various bioactivities and thus could be of importance for pharmaceuticals, therapeutics and others (Fig. 1).

More than 70% of the earth's surface is covered by oceans, having a marine ecosystem with diverse life forms such as coral reefs, sponges and microorganisms. The oceans are known to have significant origins of life on earth, including primitive and special life forms. The different zones in which oceans can be divided are:

Epipelagic zone

The epipelagic zone also called the euphotic zone with maximum sunlight. It is this zone where mainly the process of photosynthesis occurs. It is mainly occupied by the phytoplankton species on which the zooplankton feeds.

Mesopelagic zone

The mesopelagic zone (approximately 200-1000 m depth) is also called the twilight zone as it does not get enough sunlight for photosynthesis to occur. Thus, heterotrophs in this zone feed on the organic matter of the marine ecosystem for their survival.

Bathypelagic and abyssopelagic zones

The benthos inhabiting the depths of the oceans contribute at the global level in sequestering the carbon cycle. As these zones are nutrient deficient, they capture the photosynthetically synthesized food formed in the epipelagic zone.

The seabed

Till date, not much is known as far as research on ocean biodiversity is concerned. Due to the unavailability of proper implements, still a large portion of the ocean is inaccessible for exploration. Although a lot of efforts are being made by the researchers and deep water divers, not much could be achieved by them. Oceans serve as a huge reservoir of the minerals and organic matter and varied amounts of pharmaceutically active metabolites for the drug formulations.

Flora and fauna of marine environment

The marine biome could be characterized in three layers, viz., euphotic zone, disphotic zone and aphotic zone. The euphotic zone has enough sunlight and is overpopulated. The disphotic zone has insufficient sunlight (for photosynthesis), inhabiting the populations that survive in dark and gloomy environments. The aphotic zone has perpetual darkness inhabiting life forms that have adapted to the extreme conditions.

The marine fauna comprises both carnivores and herbivores. It is inhabited by vertebrates (such as sharks, fish, seals, dolphins, whales, turtles, parrotfish, otters and hermit crabs) and invertebrates (such as worms, sponges, ctenophores, cnidarians and crustaceans). The marine flora usually comprises algae, cyanobacteria, kemp, seagrasses, mangroves, etc. In addition to the flora and fauna, it has microorganisms like bacteria, fungi and viruses.

Natural products from the marine biodiversity

The marine ecosystem is not explored well, but it has more than a million species. This has shown the reason to search for natural products from marine environments. More species reflect more competition for survival and so the natural products produced for defense. The bioactive natural products from terrestrial life forms are extensively explored and studied (2). The researchers are attempting to explore the marine ecosystem for novel secondary metabolites (natural products). The simple, sessile and delicate sponges are known to produce bioactive substances in defense. In addition, the sponges have symbiotic association with surrounding micro-organisms to protect each other with production of bioactive compounds (3). Many novel bioactive natural products have been isolated and reported to have wider spectrum of bioactivities with potential to be promising in drug development. This review is an attempt to provide an overview on bioactive natural products from marine

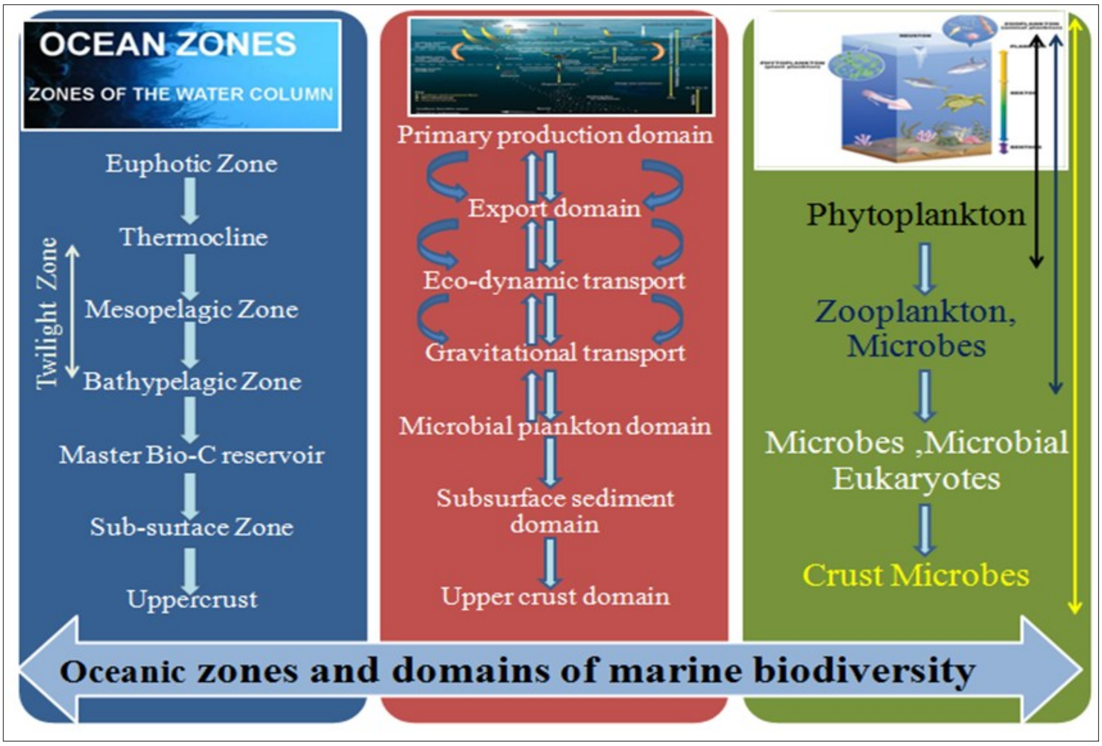

Fig. 1. Ocean zones and domains of marine biodiversity.

microbes and their potential use in pharmaceuticals. Marine microbes could adapt in marine habitats across the globe, from shallow to deep marine waters (4). In many cases, microbes are found associated with the marine organisms (like sponges, algae and corals) in symbiotic or mutualistic association with great microbial diversity. About 660 novel bioactive products of bacterial origin were reported, from 1997 to 2008, from actinobacteria, cyanobacteria, proteobacteria, bacteroidetes and firmicutes. In addition, 179 bioactive natural products of bacterial origin were identified in the year 2016 (2).

Even the marine microbes from marine ecosystems are reported to produce several parasites as pharmaceutically important bioactive natural products such as antimicrobial and anti-cancer. The ocean has an enormous proportion of diverse life forms on earth (3). The organisms are found in dense proportion and have competition for limiting factors termed as epibiosis. Thus, the organisms must go with the adaptations in such conditions for their survival and existence through tolerance, avoidance and defense (4). The defense mechanism is mostly based on the production of bioactive natural products by an organism. Some of the phytochemicals obtained from the marine biodiversity of pharmaceutical importance are as follows:

Phytochemicals

Various chemical compounds such as steroidal lactones, flavonoids, tannins, saponins etc., have been extracted, identified and isolated from marine microbes. Apart from these constituents they also contain starch, reducing sugar, hantreacotane, ducitol, chlorogenic acid, calystegines (nitrogen-containing polyhydroxylated heterocyclic compounds), a variety of amino acids including aspartic acid, proline, tyrosine, alanine, glycine, glutamic acid, cystine, tryptophan and a high amount of iron (5).

Phenols

The phenols act as antioxidants in a varied manner. Phenolic hydroxyls act as very good hydrogen donors: which react with reactive oxygen and nitrogen species in a termination reaction (6). The ability to chelate metal ions is attributed to the antioxidant capacity of phenolic compounds (7). However, by increasing their catalytic activity or by reducing metals, phenolics can act as pro-oxidants by chelating metals in a manner that forms free radicals (8). Due to their hydrophobic benzenoid rings and hydrogen-bonding potential of the phenolic hydroxyl groups, phenolics often have the potential to strongly interact with proteins. The phenolics inhibit some enzymes involved in radical generation, such as various cytochrome P450 isoforms, lipoxygenases, cyclooxygenase and xanthine oxidase (9). Phenols are secondary metabolites that are derivatives of the pentose phosphate, shikimate and phenylpropanoid pathways in plants. Phenols have immense pharmacological properties, such as anti-allergic, anti-inflammatory, anti-microbial, antioxidant, anti-thrombotic, cardioprotective and vasodilatory effects (10). These phytochemicals are not only of immense physiological and morphological importance for these marine microbes but also exploited for meeting the pharmacological demands (Fig. 2).

Flavonoids

Flavonoids, most of which are plant pigments, are abundantly found in nature (11). Flavonoids can be further divided into several subclasses as flavones, flavanones, flavonols, flavanols (also called flavan-3-ols or catechins), anthocyanidins and isoflavones (12). Flavonoids structurally comprise of C15 (C6-C3-C6) skeleton (13). Due to their high redox potential, flavonoids serve as important antioxidants, allowing them to act as reducing agents, hydrogen donors and singlet oxygen quenchers. In addition, they have a metal ion chelation potential. Flavonoids have been reported to have metal chelating properties.

Tannins

Tannins are produced by plants as secondary metabolites with a molecular mass of up to 30,000 Da (14). Tannins are divided into two classes of macromolecules, termed as condensed tannins formed by the condensation of monomers of flavan-3-ol units (15) and hydrolysable tannins (polymers of ellagic acid, or gallic acids with glucose) with molecular masses of 500 and 5000 Da. They possess astringent character (16) and antioxidant activity (17).

Tannins in combination with proteins of animal hide convert them into leather, thus preventing their putrefaction. This ability comprises all kinds of proteins and, therefore, enzymes are included. They possess antioxidant activity by scavenging free radicals, chelating trace metals and binding to proteins, as a result suppressing their enzymatic activity, like phenols and flavonoids (18). Oxidative stress plays a role in neurodegenerative diseases and aging processes and is also involved in the pathology of cancer, arteriosclerosis, malaria and rheumatoid arthritis.

Pharmaceutical significance of marine bioactive compounds

For the last 15 years, marine microbes have been gaining attention and are being investigated exponentially in search of bioactive pharmaceutical natural products produced by them, as part of sustainable chemistry or green chemistry, with reduced side effects and minimal environmental impact. Additionally, these compounds are considered safe and cheap and could be more effective with slight modifications (Table S1, Fig. 2).

The microbes are known to have a counter-action mechanism as a defense for their survival and existence. The natural products produced by these microbes for defense have been screened for their potential to advance the drug development program to produce advanced drugs and formulations. The marine microorganisms are being investigated for significance of natural products in pharmaceuticals, food, cosmetics and textiles (Table S2, Fig. 3 & 4). The products from marine microbes with pharmaceutical significance are: (i) anticancerous (ii) antiviral; (iii) antifungal; (iv) antiparasitic; (v) antitumour; (vi) antiinflammatory; (vii) antioxidant; (viii) anticarcinogenic; (ix) anticoagulant; (x) antimetagenic; (xi) antihypoglycemic; (xii) immunomodulator; (xiii) photoprotection; (xiv) emulsifier; (xv) gelling agent; (xvi) task astringent; (xvii) enzyme inhibitor; (xviii) antimicrotubule; (xix) stimulator etc.

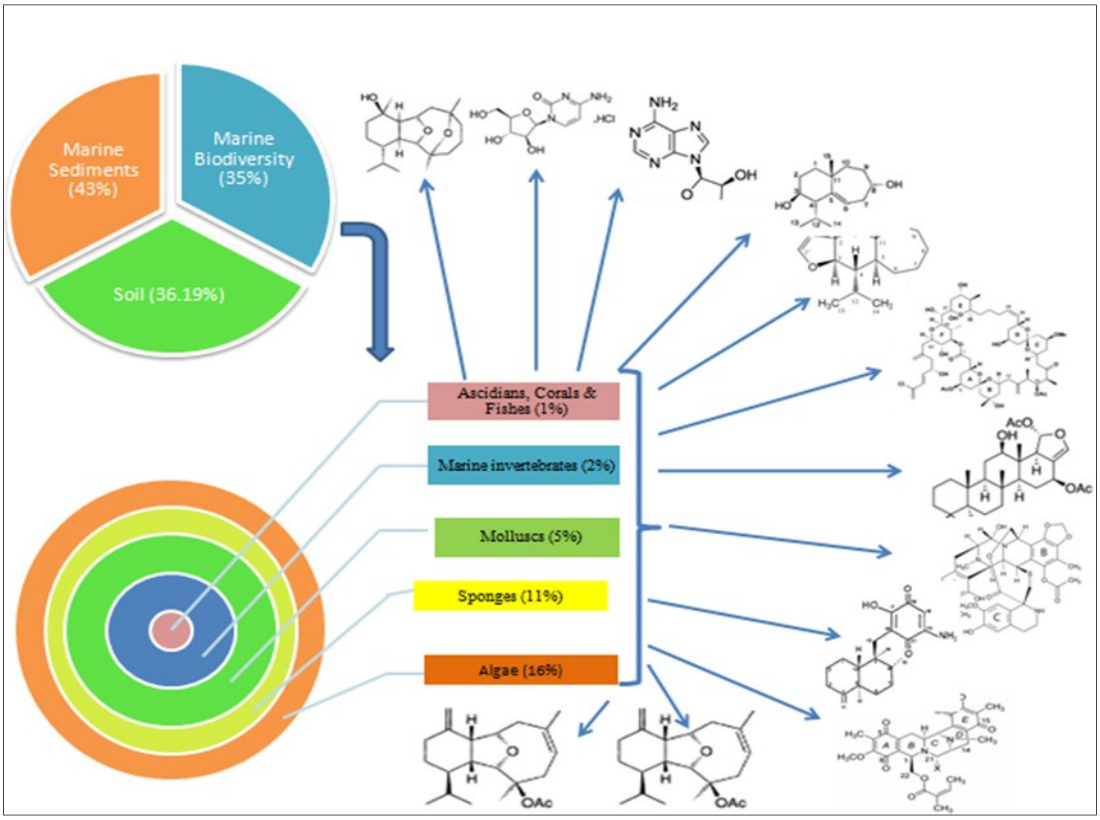

Fig. 2. Percentage distribution of marine biodiversity and their potential application in the extraction of pharmaceutically active metabolites.

Advancements in technology and their limitation of isolation and extraction of these bioactive metabolites

The search, isolation and investigations for novel bioactive natural products from marine microbes are being carried out to discover more effective formulations for the treatment of cancer and infections caused by bacteria, fungi, viruses, etc. However, detailed and extensive studies are ongoing in search of more compounds, their functions and their commercial applications in future. As it has proven its potential and vitality in suitability to green sustainable chemistry. The bioactive compounds have been obtained from a diverse range of microbes since antiquity. However, the microbes are not exploited to produce those compounds but have been used as a whole culture. As evidenced from past and ongoing research nowadays, the microbial consortium is considered an excellent plethora of bioactivities.

Over the last three decades, the marine organisms have been accepted as sources for many novel bioactive compounds with pharmaceutical importance (20). Although marine microbes have proven their potential in the production of several pharmaceutically relevant compounds such as antibiotics, anti-tumor, anti-inflammatory, etc., extensive research and studies are still ongoing in search of their potential in producing compounds for the treatment or therapy of immune-, neuro -and other fatal diseases. About 75% of total antibiotics are discovered and isolated from terrestrial microbes and have revolutionized medicine. But the antibiotics are now being challenged by serious consequences of drug resistance. This could be addressed by searching for novel antibiotics (with their potent activities against bacteria, fungi, viruses, etc.) isolated from deep-sea microorganisms.

Bioprospecting for potential drugs

Use of marine organisms does not show a significant role in developing traditional medicines but there is use of seaweeds as a fertilizer and the production of purple dye from marine mollusks as used in woolen cloth. Marine environment consists of many bioactive compounds, some of which are considered novel chemicals as they are not yet found in terrestrial sources (19).

Drug discovery and development face many challenges when taken from natural environment. The paths involved in marine drug discovery are sample extraction, strategies for determining the structure and methods for identifying the target. Sample collection required specific techniques because some compounds were easy to collect as they were present near shore while other compounds were hard to collect as they can be unidentified macro and microorganisms. Structural identification of nanomolecular scale can be done by mass spectrometry, circular dichroism and NMR spectroscopy. After the phenotypic screening, the compound has been discovered and is further taken to identify its site of action and target. To detect the drug target, many steps were taken like affinity chromatography; an example is didemnin b. A research identified the mechanism of action of theonellamides a-f, which were isolated from *theonella* sp (21). Another study has potentially identified cytotoxin apratoxin a by phenotypic cell viability assay (22). The large-scale production of trabectedin by fermentation required a parallel process of paclitaxel. From the needle of *Taxus baccata* the precursor 10-desacetylbaccatin iii is obtained which is a large-scale supply of paclitaxel. Natural product chemistry with genome guide discovery is a new

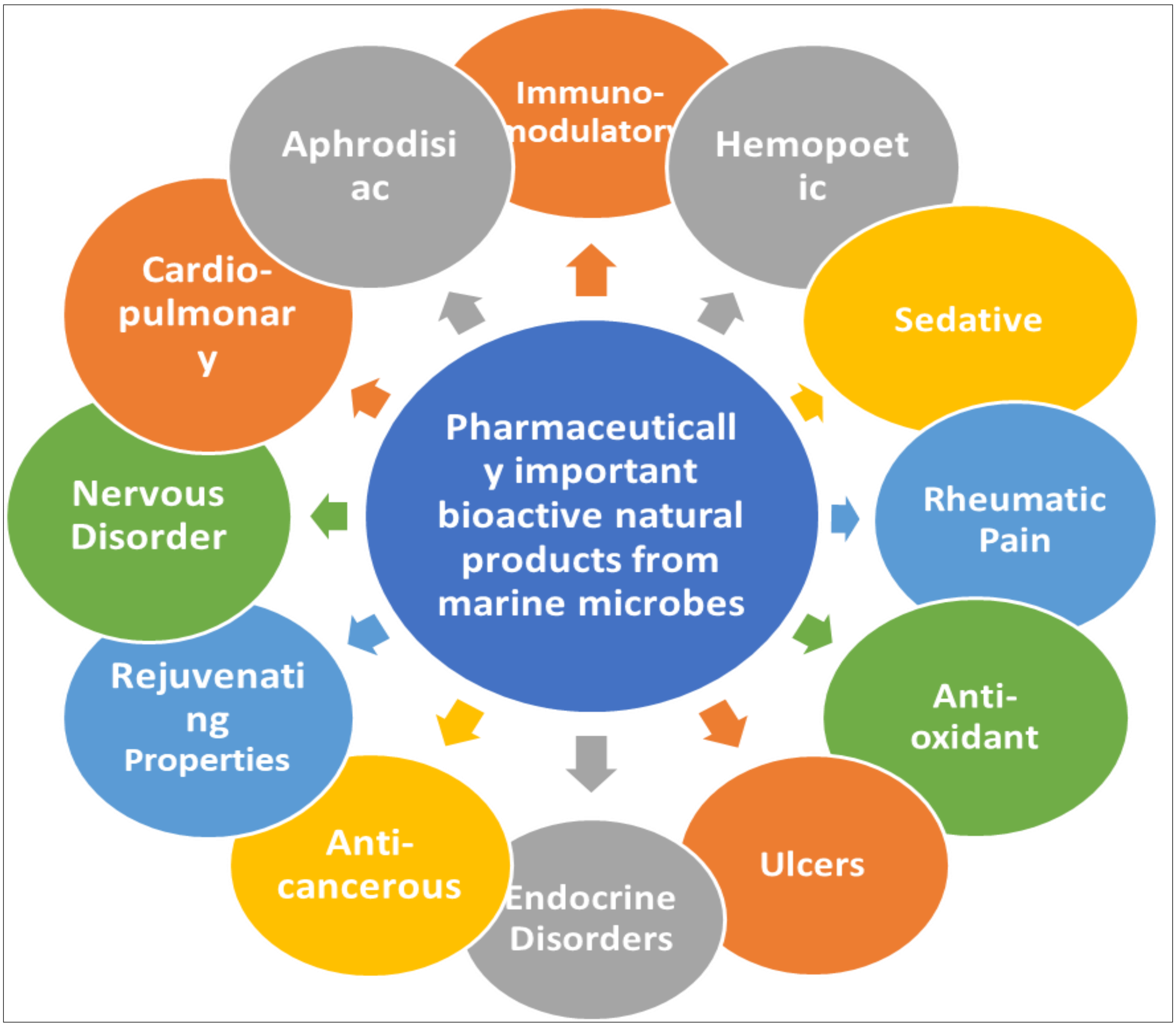

Fig. 3. Pharmaceutical significance of the secondary metabolites obtained from marine microbes.

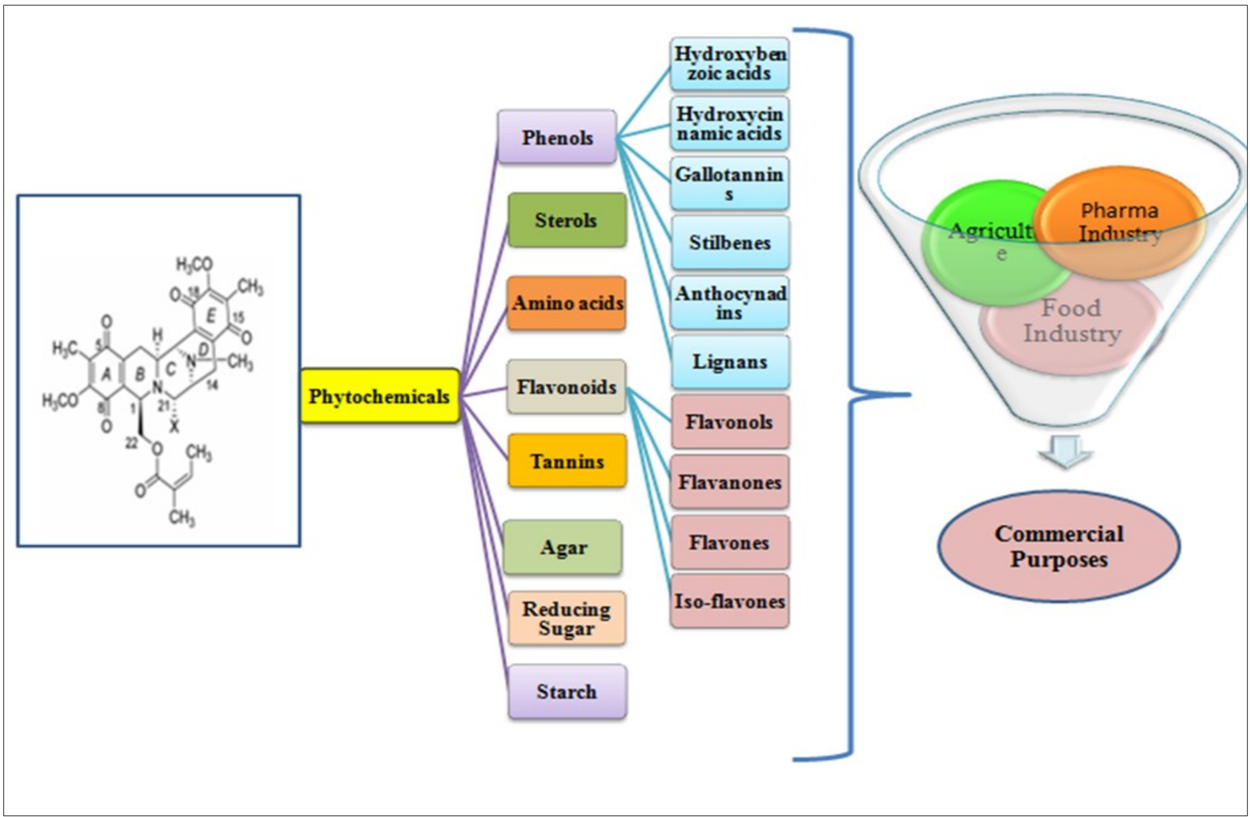

Fig. 4. Applications of bioactive compounds of marine microbes.

drug discovery approach that is used to identify the macrolactam salinilactam a. Fluorosalinosporaminide derivatives are produced by genetic engineering, while bromine and iodine substitute derivatives are produced by precursor-directed biosynthesis and semi-synthesis. Production of cryptophycins (from okinawan marine sponge) was carried out by precursor-directed biosynthesis after the identification of enzymes involved in biosynthesis. Novel depsipeptide natural products are released by structurally diverse starter units, which are accepted by biosynthetic enzymes and can be identified (20).

In vitro culture of isolated marine micro-organisms

The bioprospecting for potential bioactive compounds involves growing microbes in the laboratory. The broth culture of the specific microbe has to be segregated for cells and supernatant.

Isolation, identification and characterization of potential bioactive compounds

It is necessary to develop methods for the estimation of active constituents or marker compounds as the qualitative and quantitative targets to assess the authenticity and inherent quality of the phytochemicals isolated from marine microbes.

The supernatant has to be filtered and the crude extract is then allowed for TLC. TLC is reported as the primary tool for identification as part of monographs on all medicinal plants (23). TLC profiling of the plant extracts gives an idea about the presence of various phytochemicals. Different Rf (retention factor) values of various phytochemicals provide valuable clues regarding their polarity and selection of solvents for the separation of phytochemicals (24).

After TLC, HPLC analysis of the extract is done, which involves running through the HPLC columns. The compounds present in crude extracts could be separated on the basis of their polarity. as the compounds are either polar or non-polar. Each compound, with different Rf values, is subjected to screening for bioactivities.

Molecular techniques are used to study the active metabolites pathway and gain the information with the help of genome sequencing. Specific inducers and elicitors can be used to stimulate or upregulate metabolite production. Manipulating the clusters of genes responsible for the biosynthesis can help in the induction of metabolites (20). Bacteria can perform the biosynthesis of fatty acids, which is essential to form a phospholipids membrane. This pathway occurs in γ *Proteobacteria* which include the species of *Vibrio, Colwellia, Moritella, Photobacterium, Shewanella* genera. Secondary metabolites of marine bacteria can be synthesized with the help of gene clusters. For example, *Alcanivorax borkumensis* SK2 is responsible for degrading hydrocarbons. Its four domains within NRPS gene can incorporate and activate the amino acid into the increasing peptide chain. Bioengineering of microbes causes a significant impact on improving the biological activity. Regulatory genes in the secondary metabolite can control the structural biosynthetic gene expression. To increase the cluster-specified compound production the manipulation in specific regulators pathway can be done. To optimize the production of metabolites the cellular mechanism or expression of genes can be modified at specific aspects like by strong promoter insertion and alteration of precursors level. For the production of thiocoraline, about 53 kbp region in *S. lividans* and *S. albus* is expressed heterologously. Several novel biosynthetic gene clusters and cloning can be identified by bioinformatic and metagenome sequencing. A new biosynthetic pathway can be created with the help of direct DNA synthesis or PCR from a small DNA fragment to whole genome (25) (Table S3, Fig. 4 & 5).

Metabolic pathway for the production of marine secondary metabolites with special reference to the marine microbes

The structural databases are available for prediction of the atomic arrangements of different compounds such as PubChem, ChEMBL, ZINC, Reaxsys, TCM, NAPRALERT etc. These databases could be used to perform cheminformatic analysis to predict the physico-chemical and structural properties for defining the bioactive characteristics of the given compound. Many undiscovered and appealing alternatives from bioinformatics perspective require enormous amount of data from distinct sources, i.e. sequence, biology and physiology of protein (enzymes), comparative genomics, chemical structure, reactivity of organic compounds, environmental biology etc. CADD (Computer Aided Drug Designing) gives a better understanding of cell functioning by analyzing sequence data because of the central dogma of biology in which genetic information is transcribed from DNA to RNA and from RNA to proteins.

Omics-based tools like genomics, transcriptomics, interactomics, proteomics and metabolomics can help in studying the structure and functional characterization of the potential compound. This technology assists in correlating DNA sequences with mRNA, protein and metabolite abundance thereby giving a clear and truer picture of their interaction with each other and environment. It is also used to study the genes responsible for the production of bioactive metabolites present in marine microorganisms (26). Post-genomics techniques such as interactomics, transcriptomics and proteomics, along with metagenomics, which are less restrictive in comparison to gene microarrays, can also be considered for their detailed study.

The set of genes transcribed in a given condition and time is known as the transcriptome, which is an important link between cellular phenotype, interactome, genome and proteome. Commonly, under stress conditions, many genes may be up and down-regulated. The control of gene expression is a major key process for adapting to changes in environmental conditions and thus for survival. Transcriptomics interpret this process in a genome wide range. For determination of mRNA expression level, DNA microassay analysis is an immensely powerful tool in transcriptomics. The detection of these potential bioactive compounds is known as interactomics. The various steps involved in drug design are as follows:

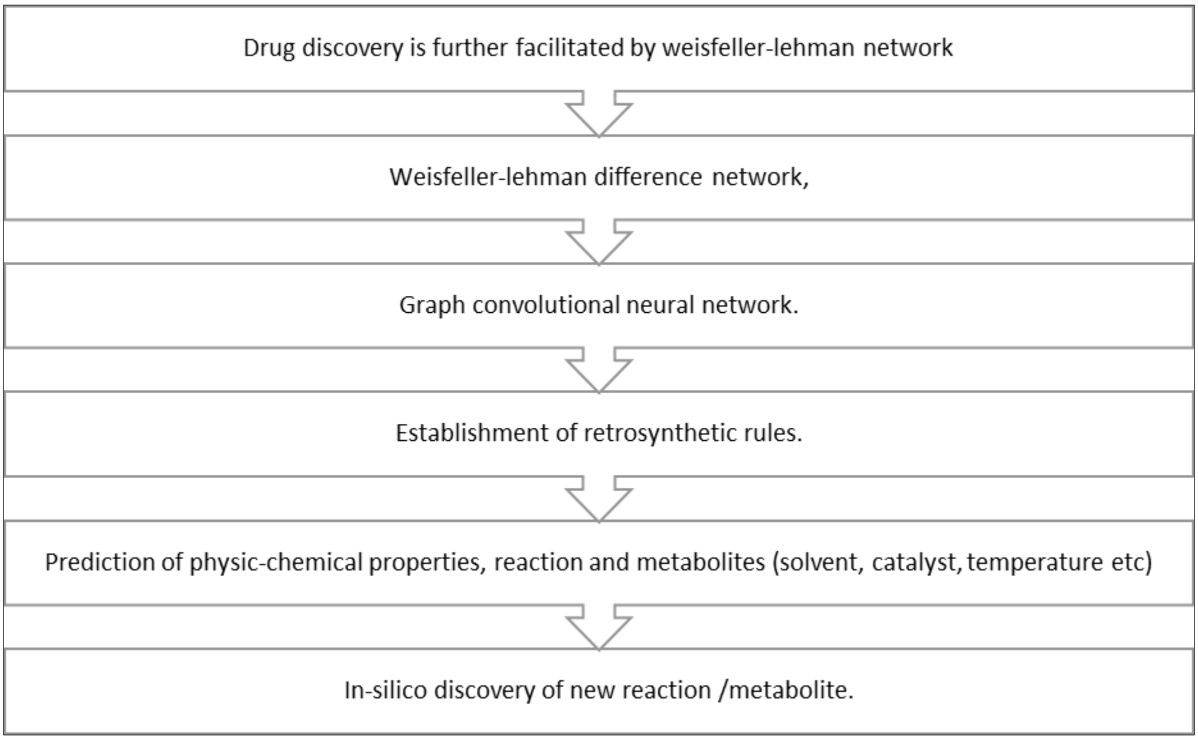

Fig. 5. Flowchart showing the steps involved in drug designing.

Conclusion

Approval of pharmaceuticals is being carried out prominently by the USFDA, EMEA (European Medicines Agency), Japanese Ministry of Health and Australia's therapeutic goods administration. About 30 compounds are in the clinical pipeline as candidates for drug development under phase 1, phase 2, phase 3 and approved categories. Natural compounds obtained from the marine microbes are under research interest due to the presence of compounds being exploited in the formulation of novel drugs. These metabolites also help the marine microbes during the defense mechanism. The natural compounds have immense properties which make them of research interest. These metabolites are capable of curing ailments like cancer, wound healing, antimicrobial activity, antiseptic, antiviral, antifungal, antiparasitic; anti-inflammatory; antioxidant; anticoagulant; antimetagenic; antihypoglycemic; immunomodulator; photoprotection; emulsifier; gelling agent; task astringent; enzyme inhibitor; antimicrotubule; stimulator. A plentiful and mainly unexplored source of bioactive natural compounds with substantial therapeutic potential is marine microorganisms. Numerous chemicals with promise antibacterial, anticancer, anti-inflammatory and other therapeutic properties are produced by these microbes. Discovering new bioactive compounds that could be the basis for creating new medications is made possible by the investigation of marine microbial biodiversity. To fully achieve the therapeutic promise of marine-derived natural compounds, however, obstacles like sustainable collection, elucidating the biosynthetic route and resolving resistance concerns must be addressed. It is anticipated that marine microbes will become more and more important in the creation of next-generation medications as research progresses, advancing global health.

Acknowledgements

We gratefully acknowledge Centre for Research and Development and PIAS of Parul University, for providing the financial support in carrying out this work.

Authors' contributions

MS conceptualized the study and wrote the manuscript, SB and SP edited the manuscript, SS and ND finalized the manuscript.

Compliance with ethical standards

Conflict of interest: The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this research article.

Ethical issues: None

References

1. Dias DA, Urban S, Roessner U. A historical overview of natural products in drug discovery. Metabolites. 2012;2:303–36. https://doi.org/10.3390/metabo2020303
2. Blunt JW, Carroll AR, Copp BR. Marine natural products. Nat Prod Rep. 2018;35:8–53. https://doi.org/10.1039/C7NP00052A
3. Mora C, Tittensor DP, Adl S, Simpson AGB, Worm B. How many species are there on earth and in the ocean? PLoS Biol. 2011;9(8):e1001127. https://doi.org/10.1371/journal.pbio.1001127
4. Wahl M, Goecke F, Labes A, Dobretsov S, Weinberger F. The second skin: ecological role of epibiotic biofilms on marine organisms. Front Microbiol. 2012;3:292. https://doi.org/10.3389/fmicb.2012.00292
5. Ganzera, M, Choudhary MI, Khan IA. Quantitative HPLC analysis of

withanolides in *Withania somnifera*. Fitoterapia. 2003;74:68–76. https://doi.org/10.1016/S0367-326X(02)00325-8

6. Valentao, P, Fernandes E, Carvalho F, Andrade PB, Seabra RM, Bastos ML. Hydroxyl radical and hypochlorous acid scavenging activity of small centaury (*Centaurium erythraea*) infusion. A comparative study with green tea (*Camellia sinensis*). Phytomedicine. 2003;10 (6-7):517–22. https://doi.org/10.1078/094471103322331485
7. Yang, CS, Landau JM, Huang MT, Newmark HL. Inhibition of carcinogenesis by dietary polyphenolic compounds. Annu Rev Nutr. 2001;21(1):381–406. https://doi.org/10.1146/annurev.nutr.21.1.381
8. Croft KD. The chemistry and biological effects of flavonoids and phenolic acids. Ann NY Acad Sci. 1998;854(1):435–42. https://doi.org/10.1111/j.1749-6632.1998.tb09922.x
9. Parr AJ, Bolwell GP. Phenols in the plant and in man. The potential for possible nutritional enhancement of the diet by modifying the phenols content or profile. J Sci Food Agric. 2000;80 (7):985–1012. https://doi.org/10.1002/(SICI)1097-0010(20000515)80:7<985::AID-JSFA572>3.3.CO;2-Z
10. Manach C, Mazur A, Scalbert A. Polyphenols and prevention of cardiovascular diseases. Curr Opin Lipidol. 2005;16(1):77–84. https://doi.org/10.1097/00041433-200502000-00013
11. Majer P, Neugart S, Krumbein A, Schreiner M, Hideg E. Singlet oxygen scavenging by leaf flavonoids contributes to sunlight acclimation in *Tilia platyphyllos*. Environ Exp Bot. 2014;100:1–9. https://doi.org/10.1016/j.envexpbot.2013.12.001
12. Ziberna L, Fornasaro S, Cvorovic J, Tramer F, Passamonti S. Bioavailability of flavonoids: the role of cell membrane transporters. In: Watson RR, Preedy VR,Zibadi S, editors. Polyphenols in Human Health and Disease. Vol 1.San Diego: Academic Press; 2014.489–511. https://doi.org/10.1016/B978-0-12-398456-2.00037-2
13. Andersen OM, Jordheim M. Chemistry of flavonoid-based colors in plants. In: Mander L, Liu HW, editors. Comprehensive Natural Products II: Chemistry and Biology, Elsevier Science; 2010. p. 547–614. https://doi.org/10.1016/B978-008045382-8.00086-1
14. Saric T, Rogosic J, Zupan I, Beck R, Bosnic S, Sikic Z, et al. Anthelmintic effect of three tannin-rich Mediterranean shrubs in naturally infected sheep. Small Rumin Res. 2015;123(1):179–82. https://doi.org/10.1016/j.smallrumres.2014.11.012
15. Waterhouse A. Wine phenolics. Ann N Y Anad Sci. 2002;957(1):21–36. https://doi.org/10.1111/j.1749-6632.2002.tb02903.x
16. Shahat AA, Marzouk MS. Tannins and related compounds from medicinal plants of Africa. Med Plant Res Africa. 2013;13:479–555. https://doi.org/10.1016/B978-0-12-405927-6.00013-8
17. Figueroa-Espinoza MC, Zafimahova A, Alvarado PGM, Dubreucq E, Poncet-Legrand C. Grape seed and apple tannins: emulsifying and antioxidant properties. Food Chem. 2015;178:38–44. https://doi.org/10.1016/j.foodchem.2015.01.056
18. Seabra RM, Andrade PB, Valentão P, Fernandes E, Carvalho F, Bastos ML. In: Fingerman M, Nagabhushanam R, editors. Biomaterials from aquatic and terrestrial organisms. Science Publishers: Enfield, NH, USA; 2006. p. 115–74.
19. Gordon M, Cragg DJ. Newman natural products: a continuing source of novel drug leads. Biochem Biophys Acta. 2013;1830:3670–95. https://doi.org/10.1016/j.bbagen.2013.02.008
20. Chauhan A, Basniwal RK, Narwadia SC. Cyanobacteria: an emerging source for antibacterial, antimycobacterial and antifungal properties. Sci Arch. 2020;1 (1):35–41. https://doi.org/10.47587/SA.2020.1104
21. Nishimura S, Arita Y, Honda M, Iwamoto K, Matsuyama A, Shirai A. Marine antifungal theonellamides target 3β-hydroxysterol to activate Rho1 signalling. Nat Chem Biol. 2010;6:519–26. https://doi.org/10.1038/nchembio.387.
22. Luesch H, Yoshida WY, Moore RE, Paul VJ, Corbett TH. Total structure determination of apratoxin A, a potent novel cytotoxin from the marine cyanobacterium *Lyngbya majuscula*. J Am Chem Soc. 2001;123(23):5418–23. https://doi.org/10.1021/ja010453j
23. Reich E, Blatter A, Meier B. TLC for the analysis of herbal drugs - A critical review of the status and proposal for improvement of monographs. Pharmeuropa. 2003;15(3):424–30.
24. Talukdar AD, Choudhury MD, Chakraborty M, Dutta K. Phytochemical screening and TLC profiling of plant extracts of *Cyathea gigantea* (Wall. ex. Hook.) Haltt. and *Cyathea brunoniana*. Wall.ex. Hook (Cl. & Bak.). Assam Univ J Sci Technol. 2010;5(1):70–74.
25. Giordano D, Coppola D, Russo R, Denaro R, Giuliano L, Lauro FM, et al. Marine microbial secondary metabolites: Pathways, evolution and physiology. Adv Microb Physiol. 2015;66:357–428. https://doi.org/10.1016/bs.ampbs.2015.04.001
26. El-Shafei R, Hegazy H, Acharya B. A review of antiviral and antioxidant activity of bioactive metabolites of macroalgae within an optimized extraction method. Energies. 2021;14:3092. https://doi.org/10.3390/en14113092
27. Singh M, Shrivastava JN, Bhutani S, Bhasin S, Mehra A, Suyal DC. Industrial Importance of Marine Algae. In: Soni R, Suyal DC, Morales-Oyervides L, Fouillaud M, editors. Current Status of Marine Water Microbiology. Springer, Singapore; 2023. p. 367–80. https://doi.org/10.1007/978-981-99-5022-5_16
28. Ata A, Ackerman J, Radhika P. Cladixazole: a novel sesquiterpene from a marine soft coral of genus *Cladiella*. Tetrahedron Lett. 2003;44:6951–53. https://doi.org/10.1016/S0040-4039(03)01712-X
29. Lee Y, Jang KH, Jeon JE, Yang YW, Sim CJ. Cyclic Bis- 1,3-dialkylpyridiniums from the Sponge *Haliclona* sp. Mar Drugs. 2012;10:2126–37. https://doi.org/10.3390/md10092126
30. Mona S, Malyan SK, Saini N, Deepak B, Pugazhendhi A, Kumar SS. Towards sustainable agriculture with carbon sequestration and greenhouse gas mitigation using algal biochar. Chemosphere. 2021;275:129. https://doi.org/10.1016/j.chemosphere.2021.129856
31. Jimenez PC, Ferreira EG, Araujo LA, Guimaraes LA, Sousa TS, Pessoa OD. Cytotoxicity of actinomycetes associated with the ascidian Eudistomavannamei (Millar, 1977), endemic of the northeastern coast of Brazil. Lat Am J Aquat Res. 2018;41(S2):335–43. https://doi.org/10.3856/vol41-issue2-fulltext-12
32. Carter NJ, Susan JK. Trabectedin: a review of its use in the management of soft tissue sarcoma and ovarian cancer. Drugs. 2007;67(15):2257–76. https://doi.org/10.2165/00003495-200767150-00009
33. Khoo KS, Chew KW, Yew GY, Leong WH, Chai YH, Show PL, et al. Recent advances in the downstream processing of microalgae lipid recovery for biofuel production. Bioresour Technol. 2020;304:122996. https://doi.org/10.1016/j.biortech.2020.122996
34. Nunes MC, Graca C, Vlaisavljevic S, Tenreiro A, Sousa I, Raymundo A. Microalgal cell disruption: effect on the bioactivity and rheology of wheat bread. Algal Res. 2020;45:101749. https://doi.org/10.1016/j.algal.2019.101749
35. Sansone C, Brunet C, Noonan DM, Albini A. Marine algal antioxidants as potential vectors for controlling viral diseases. Antioxidants. 2020;9:392. https://doi.org/10.3390/antiox9050392
36. Sagar S, Mandeep K, Kenneth PM. Antiviral lead compounds from marine sponges. Mar. Drug. 2010;8:2619–38. https://doi.org/10.3390/md8102619
37. Mioso R, Francisco JTM, Ranilson de SB, Flavio VPB, De V, Barbara OS, et al. Cytotoxic compounds derived from marine sponges. A review (2010–2012). Molecules. 2017;22:208. https://doi.org/10.3390/molecules22020208
38. Matz C, Webb JS, Schupp PJ, Phang SY, Penesyan A, Egan S, et al. Marine biofilm bacteria evade eukaryotic predation by targeted chemical defense. PLoS one. 2008;3:e2744. https://doi.org/10.1371/journal.pone.0002744

39. Zheng, L, Chen H, Han X, Lin W, Yan X. Antimicrobial screening and active compound isolation from marine bacterium nj6-3-1 associated with the *sponge Hymeniacidon perleve*. World J Microbiol Biotechnol. 2005;21:201–06. https://doi.org/10.1007/s11274-004-3318-6

40. Nicolaou, KC, Lim YH, Becker J. Total synthesis and absolute configuration of the bisanthraquinone antibiotic be-43472b. Angew Chem Int Ed. 2009;48:3444–48. https://doi.org/10.1002/anie.200900058

41. Kamei Y, Isnansetyo A. Lysis of methicillin-resistant *Staphylococcus aureus* by 2,4-diacetylphloroglucinol produced by *Pseudomonas* sp. AMSN isolated from a marine alga. Int J Antimicrob Agents. 2003;21:71–74. https://doi.org/10.1016/S0924-8579(02)00251-0

42. Kim MY, Sohn JH, Ahn JS, OH H. Alternaramide, a cyclic depsipeptide from the marine-derived fungus *Alternaria* sp. Sf-5016. J Nat Prod. 2009;72:2065–68. https://doi.org/10.1021/np900464p

43. Maya SP, Kong F, Jeffrey JE, Daniel AA, Paola SA, Valerie BS. Novel alpha-pyrones produced by a marine *Pseudomonas* sp. F92s91: taxonomy and biological activities. J Antibiot. 2003;56:1033–44. https://doi.org/10.7164/antibiotics.56.1033

44. Isnansetyo A, Kamei Y. B. Anti-methicillin-resistant *Staphylococcus aureus* (MRSA) activity of mc21-b, an antibacterial compound produced by the marine bacterium *Pseudoalteromonas phenolica* O-BC30T. Int J Antimicrob Agents. 2009;34:131–35. https://doi.org/10.1016/j.ijantimicag.2009.02.009

45. Gao C, Tian HXP, Qi SH, Luo XM, Wang P, Zhang S. Antibacterial and antilarval compounds from marine gorgonian-associated bacterium *Bacillus amyloliquefaciens* SCSIO 00856. J Antibiot. 2010;63:191–93. https://doi.org/10.1038/ja.2010.7

46. Gorajana A, Venkatesan M, Vinjamuri S, Kurada VVSNB, Peela S, Jangam P, et al. Resistoflavine, a cytotoxic compound from a marine actinomycete, *Streptomyces chibaensis* AUBN1/7. Microbiol Res. 2007;162:322–27. https://doi.org/10.1016/j.micres.2006.01.012

47. Rickards RW, Rothschild JM, Willis AC, Chazal NM de, Kirk J, Kirk K, et al. Calothrixins a and b, novel pentacyclic metabolites from calothrix cyanobacteria with potent activity against malaria parasites and human cancer cells. Tetrahedron. 1999;55:13513. https://doi.org/10.1016/S0040-4020(99)00833-9

48. Burja AM, Banaigs B, Abou-mansour E, Burgess JG, Wright PC. Marine cyanobacteriaa- the prolific source of natural products. Tetrahedron. 2001;57:9347–77. https://doi.org/10.1016/S0040-4020(01)00931-0

49. Xie LW, Jiang SM, Zhu HH, Sun W, Ouyang YC, Dai SK, et al. Potential inhibitors against *Sclerotinia sclerotiorum,* produced by the fungus *Myrothecium* sp. Associated with the marine sponge *Axinella* sp. Eur J Plant Pathol. 2008;122:571–78. https://doi.org/10.1007/s10658-008-9326-x

50. Zhang Y, Li XM, Wang CY, Wang BG. A new naphthoquinoneimine derivative from the marine algal-derived endophytic fungus *Aspergillus niger* EN-13. Chin Chem Lett. 2007;18:951–53. https://doi.org/10.1016/j.cclet.2007.05.054

51. Wang F, Fang Y, Zhu T, Zhang M, Lin A, Gu Q, et al. Seven new prenylated indole diketopiperazine alkaloids from holothurian-derived fungus *Aspergillus fumigatus*. Tetrahedron. 2008;64:7986–91. https://doi.org/10.1016/j.tet.2008.06.013

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https://horizonepublishing.com/journals/index.php/PST/open_access_policy

Publisher's Note: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS, UGC Care, etc
See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

Publisher information: Plant Science Today is published by HORIZON e-Publishing Group with support from Empirion Publishers Private Limited, Thiruvananthapuram, India.