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Review Article

Biomedical applications and therapeutic potential of marine natural products and marine algae

Sofia Khanam[1,*], Aman Prakash[2]

[1]*Dept. of Pharmacology, Calcutta Institute of Pharmaceutical Technology & Allied Health Sciences, Uluberia, Howrah, West Bengal, India*
[2]*Sam Higginbottom University of Agriculture, Technology and Sciences, Naini, Prayagraj, Uttar Pradesh, India*

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ABSTRACT

Recently there is an increase in the interest in the secondary or non-primary metabolites produced by the marine flora and fauna. It has become the center of attraction of chemists and pharmacologists in the previous decades. Stakeholders of the natural viewpoint emphasize that the examination of new and unusual organic molecules from marine organisms while the synthetic stakeholders' faiths in targeting these novel structures for the development of new analogs and new synthetic strategies and methodologies. The chemistry of marine organisms has changed dramatically in concern of investigating rationale. Analogous to the examination of terrestrial plants, many of the recent research and studies have concentrated on the potential application of marine extracted products in the treatment, curing of human diseases, and various other works. Marine products are the major components having biomedical-oriented natural products which can be used for various purposes. Marine natural products have enough potential to work prominently and also assisting in various kinds of human needs and works. In this review, we will be focusing on prominently their works, role in biomedical-related aspects.

1. Introduction

Nature is the best teacher and has the answers to all our questions. Natural resources and components have enough potential to tackle most of our problems. Marine Natural Products prominently represent the variety of novel chemotypes that serve as the template for the development and discovery of various therapeutic agents with their crucial role and distinct action mechanism. They are genetically encoded materials and compounds which is manufactured by evolutionary biosynthetic machinery which is quite a complex process and which is almost impossible to make or set up in our laboratories. There are limitations of isolation of desired materials from the source organisms but the advanced NMR technologies development and derestrict strategies have led us to the elucidation of the structure of those materials on a small scale. In the level of manifesting exploration and investigation of the therapeutic potential of marine natural products, the chemical characterization should be kept in parallel and at the same pace as the biological characterization. Majorly, the limited and restricted supply of marine natural products has become a serious problem and chief challenge in the investigation of biological targets. Numerous marine drugs are have reached the markets and numerous are under clinical trials.[1] However, the recognition of mechanisms of action of marine natural products in the early times of the discovery process is a major game-changing deed. As effectively connecting the marine natural products to their potential

* *Corresponding author*.
E-mail address: Sofiakhanam786@gmail.com (S. Khanam).

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biomedical therapeutic application enables the uplifting and conduction of the new energy wave of motivation to check out and tackle the challenge of synthesis and supply problem. During the tenure of the recent years, the increasing number of technologies and method development is being successfully applied to the marine natural products, ultimately leading the values of materials and compounds in concern with the biomedical utility. There is the requirement of the development of the advances in overcoming the bottlenecks in marine natural product research, emphasizing the development and advances of diverse target identification technologies applicable for the marine natural product.[2] From ancient times, natural products have served as the crucial and chief drugs that lead against a wide range of human problems and diseases. From 1981 till 2014, about 1211 small-molecule therapeutic agents are approved which account for 65% of the marketed drugs, which are used as their original or unaltered or manufactured on the naturally occurring structures.[1] The timeline of drugs from the ocean is summarized in Figure 1.[2]

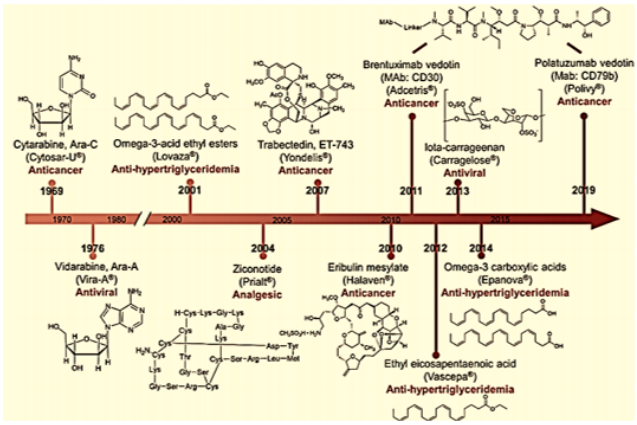

Fig. 1: Timeline for drugs from the ocean

In the current time, there is an increase in the interest and research of the marine sources because of the awareness of the great biodiversity in the marine water bodies which has the vision and enough capacity to ensure us for the new chemical compounds possessing a good biomedical potential. Due to the tremendous advancement in strategies and research address the key facts procuring to the marine natural product-based drug discovery and development.[3,4] Drug candidates from ocean to clinical trials are given in Figure 2.[5] Initial genome sequencing of marine natural product-producing microorganisms suggests that most marine natural products (MNPs) remain to be discovered.[6] The MNPs are well-considered powerful bio-weapons to compensate the drug leads to the pharmaceutical industry. Majorly, MNPs possess unique structural makeup covering a broad and wide chemical space, and consistently providing the base to inspire and promote natural drug development against various diseases. Along with their clinical utility, they are also applied as probes in improving the study of various biological pathways and exploring the unconventional and unexplored biological space for drug discovery.

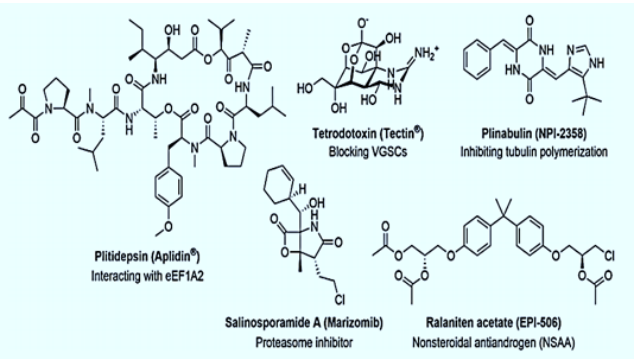

Fig. 2: Drug candidates from ocean to clinical trials

MNP drug discovery research requires addressing three major challenges:

1. How to identify novel molecules;
2. How to solve the supply issues and
3. How to correlate bioactivity with underlying target/MOA

Advances have been made in all these areas (Figure 3).[7] Some algae have biomedical properties. The functional components isolated and extracted from the algal biomass are majorly used as health, food, and dietary supplements having a list of applications in modern technology and food sciences. Algal products which have enough potential regarding skin tumor treatments, skin-whitening, anti-infection, anti-aging, and other dermal-related properties have got very much less attention. There is a need for a concentration of research focusing on the combined and integrating studies on algae relevant to human skincare, health, and therapy. The evolution of pharmacological evaluations of marine natural products has become a rise in the about jubilee years ago. The investigations began with the toxins which were then followed by the cytotoxic and antitumor activities to the forthcoming days.[2]

2. Natural Products from Marine Sources That Act on Membrane Receptors

From the viewpoint of cellular physiology and pharmacology, important molecules derived from marine sources are very much potent and Na^+ channel blockers are tetrodotoxin and saxitoxin. Pharmacological studies show that saxitoxin and tetrodotoxin played a crucial role in evaluating the concept of the Na^+channel in particular and general terms. These two compounds are small, structurally unrelated organic cations that act as Na+ channel which

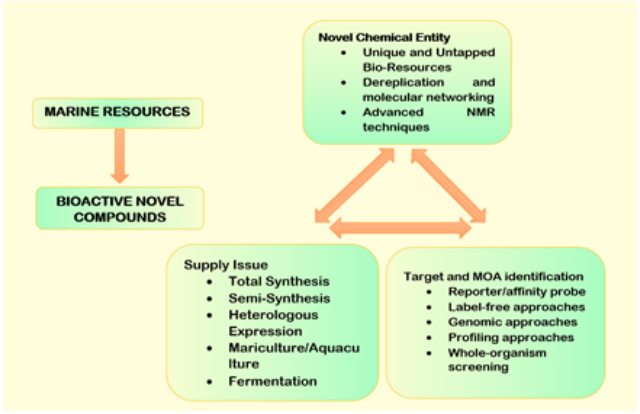

Fig. 3: Three bottlenecks and corresponding research highlights in marine natural product drug discovery

works on the external surface of Na^+channels, which interrupts the influx of Na^+ ions. These compounds have been very much important in conceptualizing the occurrence of ion channels, the action mechanism by which that content works as the occluders. Two models are proposed which help in explaining the working and action of concerned toxins. This model can be understood in the simplest terms as the binding of the inhibiting to the pore blocking ion transport; the second model includes the binding of the toxin to a receptor on the exterior of the protein, causing a distinct change in channel permeability.[8]

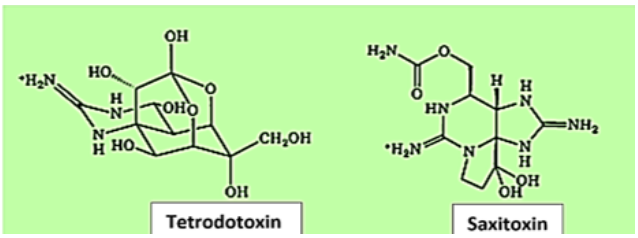

Fig. 4: Structure of tetrodotoxin and saxitoxin

Stoichiometry and binding studies suggest that tetrodotoxin and saxitoxin bind at or near the external mouth of the channel, and their blocking action is inhibited by a variety of monovalent and divalent cations. Recent evidence has put into question the simple "plug" model: the structural dependence for the activity of the toxins appears to be more complicated than necessary for simple pore blockage, and physiological behavior extends beyond simple occlusion.

These toxins have proven extremely useful and popular chemical tools for neurophysiology and neuropharmacology studies. Numerous experiments have been conducted using tetrodotoxin and saxitoxin to study the biophysics of Na^+ channel action, Na^+ channel expression and assembly during cellular development, and the potential antiarrhythmic properties of tetrodotoxin against occlusion-induced arrhythmias. Because of their potency and selectivity for Na^+ channels, tetrodotoxin and saxitoxin are often used in voltage-clamp studies where it is beneficial to distinguish the transient current (carried mostly by Na^+ ions) from the steady-state current (carried mostly by K^+ ions). Tetrodotoxin and saxitoxin will certainly remain valuable methods for studying Na^+ channels and excitatory phenomena in the future.[9] Pharmacologically active peptides found in the venoms of predatory cone snails (Conus spp.) are targeted on different ion channels and receptors. Conotoxins have become valuable tools for neuroscience studies because of their capacity to differentiate between closely associated receptor subtypes. The 22-residue polycyclic peptide μ-Conotoxin GIIIA (also known as geographutoxin II or GTX II), which was isolated from the piscivorous cone snail Conus geographus and contains three hydroxyprolines and three disulfide bridges, was shown to bind and thus occlude site 1 of the sodium channel in skeletal muscle.Since it has a little discernible impact on sodium channels in the cardiac, brain, or nervous tissue, μ-Conotoxin GIIIA is an effective tool for researching skeletal muscular neurotransmission. The neuron-specific antagonist -Conotoxin GVIA (w-CgTx), a 27-amino-acid peptide isolated from C. geographus, has a strong affinity for voltage-sensitive calcium channels (VSCC), which regulate neurotransmitter release in response to nerve termini depolarization. Depending on the tissue type, -Conotoxin GVIA interacted with N- and/or L-type channels, and was also useful in identifying these channel subtypes and their distribution in different tissues. The relative relevance of N- and L-type VSCCs to the release of different neurotransmitters have been measured in parallel studies using -conotoxin GVIA and nifedipine, nilvadipine, and PN 200-110 in combination with unique L-type calcium channel blocking ligands.To assess the distribution of calcium channels in rat brain tissue, the 1251-Labeled toxin was used and recognize N- and L-type VSCCs in bovine adrenomedullary plasma membranes, and envision toxin-binding sites in normal and cerebellar mutant mice's brain tissue.[10] Maitotoxin is a high-molecular-weight polyether neurotoxin developed by the marine dinoflagellate *Gambierdiscus toxicus* that induces death in mice (170 ng/kg) when injected intraperitoneally. It is one of the main toxins responsible for ingestive ciguatera fish poisoning. Maitotoxin elicits a variety of pharmacological responses in a dose-dependent manner, usually at concentrations in the pico- to nano-molar scale. Increased cellular calcium uptake, neurotransmitter/hormone release, phosphoinositide degradation, smooth and skeletal muscle relaxation, and stimulus effects on the heart are among these effects. The majority of maitotoxin's symptoms tend to be caused by either its contact with extracellular calcium or the

increased calcium influx. Calcium-ion entry blockers and polyvalent cations were found to significantly reduce or eliminate any of maitotoxin's muscle-contracting effects, according to a recent report. Maitotoxin's promise as a one-of-a-kind pharmacological tool for researching calcium transport has yet to be realized.[11] The α-conotoxins isolated from cone shells have a consensus sequence of 13 to 15 amino acids that probably retains some structural and hence functional homology. α-conotoxins (so-called because of their pharmacological resemblance to snake a-toxins) have been shown to inhibit neuromuscular transmission by acting as antagonists of the nAChR at the endplate area of neuromuscular junctions. Preincubation with other nAChR antagonists, such as a-bungarotoxin, blocked this binding, which was reversible. Whole-animal experiments revealed that α-conotoxins were selective for nACh receptors at neuromuscular junctions; at concentrations that caused paralysis, the α-conotoxins-GI and -MI had little effect on blood pressure, heart rate, or responses to vagal and preganglionic stimulation. More surprisingly, α-conotoxin-SI, which has a proline instead of a positively charged residue at position nine, showed phylogenetic selectivity for nACh receptors, signifying that these receptors are structurally nonhomogeneous.The composition of the agonist receptor sites on the α-subunits has been investigated using α-conotoxins in combination with monoclonal antibodies and other agonists and antagonists of the nAChR. The findings of this study backed up a model of two ACh binding sites on the receptor, and they showed that these sites are structurally distinct. Because of their high selectivity for nACh receptors at neuromuscular junctions, α-conotoxins are likely to remain effective probes of this mechanism.[12]

2.1. *Anti-tumors compounds*

The Caribbean sponge Tethya crypta was used to isolate spongothymidine (arabinosyl thymine; araT) and spongouridine (arabinosyl uracil; araU) in the early 1950s. This finding led to the creation of a new class of arabinosyl nucleoside analogs. One of these analogs, arabinosyl cytosine (ara-C), showed antileukemic action in vivo. Ara-C resulting its activity by conversion to arabinosyl cytosine triphosphate, incorporation into cellular DNA, and subsequent inhibition of DNA polymerase. It is currently being used to treat acute myelocytic leukemia and non-lymphoma Hodgkin's in clinical trials. The arabinosyl nucleosides aided in the hunt for antitumor compounds from marine sources by acting as a catalyst. Several development efforts have centered on this goal over the next four decades. While several marine-derived compounds with in vitro activity have been isolated, only didemnin B has been tested in a clinical trial.[13]

Didemnins, a novel class of depsipeptides isolated from the ascidian *Tridemnum solidum,* have been shown to have promising cytotoxic, antitumor, antiviral, and immunosuppressive properties. At a dose of 0.001 μg/ml, didemnin B, the most potent which showed cytotoxicity against L1210 murine leukemia cells in vitro. Didemnin B has also been shown to be effective in stem-cell assays against several human tumors, including mesothelioma, sarcoma, hairy cell leukemia, and breast, ovarian, and kidney carcinomas. In mice, didemnin B demonstrated strong in vivo activity against intraperitoneally implanted B16 melanoma and P388 leukemia cells. Didemnin B caused a 45 percent survival rate and a 2.7-fold life extension in rats challenged with Yoshida ascites tumor cells at the highest nontoxic dosage. These positive in vivo outcomes led to preclinical toxicology tests and, eventually, phase I clinical trials in the United States to test didemnin B as an anticancer agent. The lymphatics, gastrointestinal tract, liver, and kidney were shown to be the most dangerous organs in preclinical toxicological tests. Hepatic toxicity was caused by Didemnin B, which resulted in a reduction in clotting factors. Based on these outcomes, it was predicted that gastrointestinal or hepatotoxicity will determine the maximal acceptable dose in humans. Didemnin B has completed phase I clinical trials, which identified maximum tolerable clinical doses. It will be tested in phase II trials, to observe objective tumor response.[14]

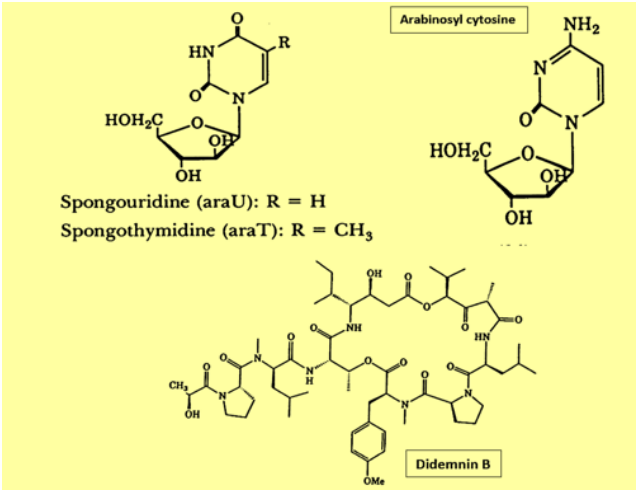

Fig. 5: Structure of antitumor agents

2.2. *Anti-inflammatory/analgesic compounds*

Several anti-inflammatory and analgesic marine natural products have been used to investigate the functions of arachidonic acid synthesis and calcium mobilization in inflammation. Calcium ions (Ca^{2+}) are mobilized/released from intracellular or extracellular supplies as proinflammatory stimuli are induced. Calcium mobilization is assumed, to begin with, the binding of an agonist to the receptor. A guanine nucleotide-binding

protein (G-protein) transmits a signal to a phospholipase (e.g., PLA_2, PLC) that hydrolyzes membrane phospholipids to release a sequence of second messengers (e.g., inositol triphosphate, and arachidonic acid).Ca^{2+} is released from intracellular stores as inositol triphosphate binds to its receptor on the rough endoplasmic reticulum. The release of arachidonic acid is assumed to influence extracellular calcium release. Either cyclooxygenase pathway to prostaglandins, prostacyclins, and thromboxanes, or the lipoxygenase pathway to tetraenoic acids, leukotrienes, and lipoxins, this fatty acid is metabolized. Ca^{2+} is mobilized from extracellular outlets as these metabolites bind to their receptors on hormone-activated Ca^{2+} channels. The physiological effects of several agents that mediate inflammation (accompanied by pain) and proliferation are mediated by the regulation of phospholipid metabolism and Ca^{2+} mobilization. As a result, anti-inflammatory and analgesic compounds inhibit phospholipase and/or Ca^{2+} mobilization.[15]

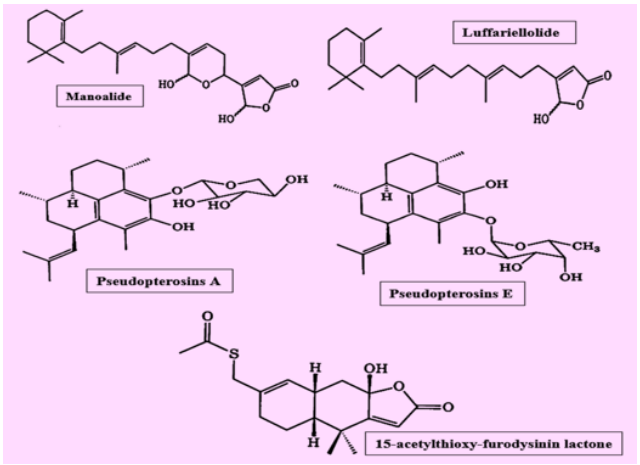

Fig. 6: Structure of anti-inflammatory agents

Manoalide, a nonsteroidal sesterterpene isolated from the sponge Luffariella variabilis, has proven to be a useful tool in the study of inflammation, as it inhibited PLA_2 irreversibly. Luffariellolide, a PLA_2 inhibitor that was partly reversible and was an analog of manoalide isolated from the same organism, had anti-inflammatory efficacy but was significantly less active than manoalide. and E, diterpene ribosides isolated from the gorgonians Pseudopterogorgia bipinata and P. elisabethae, have potent anti-inflammatory and analgesic properties and serve as reversible regulators of lipoxygenase and PLA_2. Although the previous compounds all had anti-inflammatory properties, the Dysidea sp.-derived 15-acetylthioxy-furodysinin lactone had the opposite effect.[16]

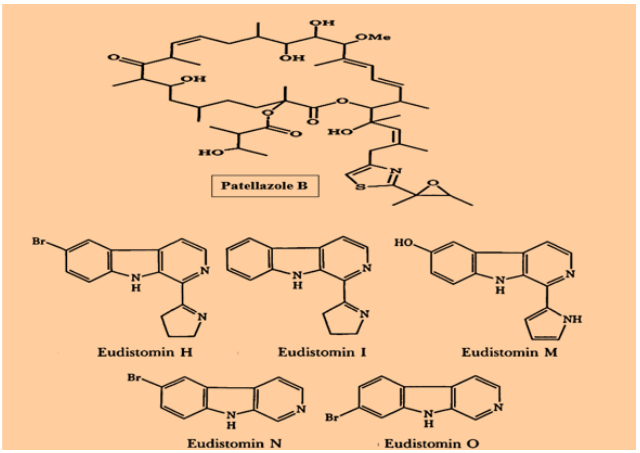

Fig. 7: Structure of antiviral agents

2.3. Antiviral agents

The search for viral chemotherapeutic agents derived from marine sources has proven fruitless. Ara-A, a semisynthetic dependent on arabinosyl nucleosides isolated from the sponge *Tethya crypta,* is the only compound that has shown substantial therapeutic efficacy so far. In vitro, a variety of marine metabolites have shown potentiality; however, only the didemnins have shown in vivo activity. In the antitumor section, didemnins, depsipeptides isolated from the Caribbean ascidian *Trididemnum solidum,*were discussed. They had antiviral effects in vitro and in vivo, in addition to antitumor activity. Patellazole B, an antiviral compound isolated from the ascidian *Lissoclinum patella* **,** was found to be very effective against herpes simplex viruses. In shipboard antiviral assays, the eudistomins, a class of β-carbolines isolated from the Caribbean ascidian Eudistoma olivacea, were stable. After activation with UV-A light, five of the eudistomins showed increased activity in subsequent experiments.[17]

3. Marine Algae

Marine algae also referred to as macroalgae or seaweed, are photosynthetic eukaryotic species that thrive in coastal environments. Rhodophyta (red algae), Chlorophyta (green algae), and Phaeophyceae (brown algae) are the three main macroalgae taxa based on their morphological pigmentations. Temperature, sunlight, pH, salinity, physiological state, and CO_2 supply can all affect the chemical composition of marine algae. Because of various adaptation strategies, macroalgae can survive in harsh environmental conditions.[18] Due to the requisite mechanisms of adaptation, macroalgae's metabolism varies, and as a consequence, macroalgae develop various secondary metabolites to overcome different conditions. In a variety of environments, such as the desert and the arctic, macroalgae can withstand very high or very

low light intensities. Macroalgae contain a range of natural bioactive compounds and metabolites, such as polysaccharides, polyunsaturated fatty acids, and phlorotannins, to function in such complex and severe conditions. Bioactivities of the constituent components of marine algae have been extensively researched, as macroalgae are one of the most highly studied and used marine resources.[19] Polyphenols are bioactive molecules that have anticancer, antidiabetic, antioxidant, and anti-inflammatory properties. Polysaccharides are known to have significant antioxidant and immunomodulatory properties. Because of the growing demand for natural and environmentally sustainable products, especially in the nutraceutical and cosmetics industries, a lot of work has gone into determining the potential of using bioactive compounds extracted from macroalgae in functional foods, pharmaceuticals, and cosmeceuticals. Bioactive compounds from macroalgae, in particular, have further potential uses in dermatology disorders or disorders such as acne, skin aging, pigmentation, and melanoma.[20]

Acne vulgaris, also known as acne, is a widespread skin disorder that affects a lot of teenagers and young adults. Blackheads or whiteheads, pimples, greasy skin, and possible scarring are all symptoms. Acne will last for years, leaving lifelong scars, disfigurement, and have negative physiological effects. Acne is a multifactorial disease with complex pathogenesis. Acne is generally believed to be an inflammatory condition, but other factors such as hair follicle keratinization, sebum secretion, and bacteria can also play a role. Acne is commonly caused by *Staphylococcus epidermidis, Staphylococcus aureus,* and *Pseudomonas aeruginosa* **.** Acne vulgaris is often associated with P. acnes, a gram-positive anaerobic bacteria. Antibiotics such as clindamycin and erythromycin have historically been used to treat acne vulgaris caused by bacterial development. Antibiotic extensive application, on the other hand, has resulted in bacterial resistance. Antibiotics can also cause skin allergies and irritation. As a result, extracting bioactive compounds from marine algae may be a healthy, safe, and natural solution. Antibacterial and antifungal properties have been identified in macroalgae extracts. The antibacterial efficacy of extracts from various marine algae was tested against skin bacteria. Furthermore, extracts from certain macroalgae have anti-inflammatory properties and can modulate the levels of growth factors and collagen, which may help to strengthen acne skin and speed up skin repair.[21]

Skin cancer is one of the most common malignant tumors. Basal cell carcinoma, squamous cell carcinoma, and melanoma are the three major types of skin cancer. Non-melanoma skin cancers include basal cell carcinoma and squamous cell carcinoma. Melanoma, which is caused by melanocytes, is the most dangerous and widespread form of skin cancer. Melanoma appears in a variety of shades, ranging from brown to purple, and may also have a pink, red, or fleshy look, and is more aggressive and can cause itching or bleeding. Skin cancer is caused by both genetic and environmental causes, such as white skin, sun radiation, and numerous benign naevi.[22] The most significant risk factor for skin cancer is excessive UV radiation. Repeated exposure to UV radiation has been found to cause skin cancer in many laboratory animal experiments.[23] As a result, using sunscreen and limiting UV exposure are good ways to avoid skin cancer. Other therapies are also needed, such as surgery, chemotherapy, radiation therapy, and targeted therapy. Chemotherapy medications that are widely used have greater cytotoxicity and side effects, which may damage other body organs, impair quality of life, and worsen disease conditions. In the treatment of metastatic melanoma with CTLA-4 antibody therapy, autoimmune-mediated side effects such as colitis, hypophysitis, hepatitis, and iridocyclitis have been recorded.[24] Facial palsy is a side effect of the drug vemurafenib, which is used to treat metastatic melanoma.[25] More safe and reliable skin cancer medications are desperately needed.

Polysaccharides, phlorotannins, carotenoids, sterol, fatty acids, as well as minerals and vitamins, have also been found in marine algae. Algae have long been used in food diets and herbal therapies due to their immune-regulating and disease-fighting properties. The promise of marine algae as a medicinal and cosmeceutical product has recently received a lot of interest. Because of their anti-acne, antioxidant, anti-aging, anti-inflammatory, melanogenesis suppression, UV photoprotective, and anti-melanoma properties, marine algae have a lot of interest in dermatology care. Scientists have discovered that compounds obtained from marine algae have a variety of beneficial effects on skin wellbeing and treatment.[26] When compared to terrestrial plants, which also include bioactive components, marine algae has obvious advantages as a source for bioactive products,[27] in terms of productivity, diversity, and the saving of valuable freshwater resources.[28] Algae-based bioactivities seem to have a bright future as they reach the medicinal and cosmeceutical markets.

4. Conclusion

Marine is the major reservoir of millions of organisms that have their specialty which can perform various kinds of functions which can isolated successfully and can be used in various terms and requirements. MNPs are the major natural products that can replace and alter the use of hazardous chemicals in our daily life. A list of numbers of MNPs is listed which have various biomedical applications. Biomedical chemicals can be altered by the MNPs derived materials. Hence, we can say that the Marine has the solution to most of our problems if proper research is carried on.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Newman DJ, Cragg GM. Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. *J Nat Prod*. 2014;83(3):770–83. doi:10.1021/acs.jnatprod.9b01285.
2. Liang X, Danmeng L, Hendrik L. Advances in exploring the therapeutic potential of marine natural products. *Pharmacol Res*. 2019;147:104373. doi:10.1016/j.phrs.2019.104373.
3. Gerwick WH, Moore BS. Lessons from the past and charting the future of marine natural products drug discovery and chemical biology. *Chem Biol*. 2012;19(1):85–98. doi:10.1016/j.chembiol.2011.12.014.
4. Montaser R, Luesch. Marine natural products: a new wave of drugs? *Future Med Chem*;3(12):1475–89. doi:10.4155/fmc.11.118.
5. Andersen RJ. Sponging off nature for new drug leads. *Biochem Pharmacol*. 2017;139:3–14. doi:10.1016/j.bcp.2017.04.012.
6. Schorn MA, Alanjary MM, Aguinaldo K, Korobeynikov A, Podell S, Patin N, et al. Sequencing rare marine actinomycete genomes reveals high density of unique natural product biosynthetic gene clusters, Microbiology. *Microbiology*. 2016;162(12):2075–86. doi:10.1099/mic.0.000386.
7. Molinski TF. NMR of natural products at the' nanomole-scale. *Nat Prod Rep*;27(3):321–9. doi:10.1039/b920545b.
8. Lago J, Rodríguez, Blanco, Vieites AG, Cabado. Tetrodotoxin, an extremely potent marine neurotoxin: distribution, toxicity, origin and therapeutical uses. *Mar Drugs*;13(10):6384–406. doi:10.3390/md13106384.
9. Bane V, Lehane M, Dikshit A, O'riordan, Furey. Tetrodotoxin: chemistry, toxicity, source, distribution and detection. *Toxins*;6(2):693–755. doi:10.3390/toxins6020693.
10. Reena H, David JC. Conotoxins: Natural product drug leads. *Nat Product Rep*. 2009;2009(4):526–62.
11. Santostasi G, Kutty RK, Bartorelli AL, Yasumoto T, Krishna G. Maitotoxin induced myocardial cell injury: Calcium accumulation followed by ATP depletion precedes cell death. *Toxicol Appl Pharmacol*. 1990;102(1):164–73. doi:10.1016/0041-008x(90)90093-a.
12. Olivera BM, Hillyard DR, Rivier J, Woodward S, Gray WR, Corpuz G. Conotoxins: Targeted peptide ligands from snail venoms; 1990. p. 256–78.
13. Newman DJ, Cragg GM. Advanced Preclinical and Clinical Trials of Natural Products and Related Compounds from Marine Sources. *Curr Med Chem*. 2004;11(13):1693–713. doi:10.2174/0929867043364982.
14. Crews C, Collins J, Lane W, Snapper M, Schreiber S. GTP-dependent finding of the antiproliferative agent didemnin to elongation-factor 1-alpha. *J Biol Chem*. 1994;269(22):15411–4.
15. Wheeler LA, Sachs G, Goodrum D, Amdahl L, Horowitz N, Vries WD. Importance of marine natural products in the study of inflammation and calcium channels, in: Biomedical Importance of Marine Organisms (Memoirs of the California Academy of Sciences Number 13; 1988. p. 125–32.
16. Jacobson PB, Marshall LA, Sunf A, Jacobs RS. Inactivation of human sinovial fluid phospholipase ~ by the marine natural product manoalide. *Biochem Pharm*. 1990;39(10):1557–64. doi:10.1016/0006-2952(90)90521-L.
17. Gerald B. Biologically active compounds from marine organisms. *Phytotherapy Res*. 2001;15(2):89–94. doi:10.1016/0304-4203(83)90091-9.
18. Trivedi J, Bangwal AM, Kaul DP, Garg S. Algae based biorefinery-How to make sense? *Renewable Sustainable Energy Rev*. 2015;47:295–307. doi:10.1016/j.rser.2015.03.052.
19. Chew KW, Yap JY, Show PL, Suan NH, Juan JC, Ling TC. Microalgae biorefinery: High value products perspectives. *Bioresource Technol*. 2017;229:53–62. doi:10.1016/j.biortech.2017.01.006.
20. Fernando S, Kim M, Son KT, Jeong Y, Jeon YJ. Antioxidant Activity of Marine Algal Polyphenolic Compounds: A Mechanistic Approach. *J Med Food*. 2016;19(7):615–28. doi:10.1089/jmf.2016.3706.
21. Yamaguchi N, Yamaguchi KS, Ono M. In vitro evaluation of antibacterial, anticollagenase, and antioxidant activities of hop components (Humulus lupulus) addressing acne vulgaris. *Phytomedicine*. 2009;16(4):369–76. doi:10.1016/j.phymed.2008.12.021.
22. Wang MHD, Chen CC, Huynh P, Chang JS. Exploring the potential of using algae in cosmetics. *Bioresource Technol*. 2015;184:355–62. doi:10.1016/j.biortech.2014.12.001.
23. Stone MC, Mcnulty JJ, Sproul CD, Chastain PD, Flournoy EG, Zhou Y, et al. Effective intra-S checkpoint responses to UVC in primary human melanocytes and melanoma cell lines. *Pigm Cell Melonoma Res*. 2016;29(1):68–80. doi:10.1111/pcmr.12426.
24. Abu R, Jiang Z, Ueno M, Isaka S, Nakazono S, Okimura T. Anti-metastatic effects of the sulfated polysaccharide ascophyllan isolated from Ascophyllum nodosum on B16 melanoma. *Biochem Biophys Res Commun*. 2015;458(4):727–32. doi:10.1016/j.bbrc.2015.01.061.
25. Fan S, Zhanga J, Nie W, Zhou W, Chen JL, Lu X, et al. Antitumor effects of polysaccharide from Sargassum fusiforme against human hepatocellular carcinoma HepG2 cells. *Food Chem Toxicol*. 2017;102:53–62. doi:10.1016/j.fct.2017.01.020.
26. Syarina PNZ, Karthivashan G, Abas F, Arulselvan P, Fakurazi S. Wound healing potential of Spirulina platensis extracts on human dermal fibroblast cells. *EXCLI J*. 2015;14:385–93. doi:10.17179/excli2014-697.
27. Barlow J, Sims RC, Quinn JC. Techno-economic and life-cycle assessment of an attached growth algal biorefinery. *Bioresour Technol* ;220:321–9. doi:10.1016/j.biortech.2016.08.091.
28. Wijesekara I, Yoon NY, Kim SK. Phlorotannins from Ecklonia cava (Phaeophyceae): biological activities and potential health benefifits. *BioFactors*. 2010;36(6):408–14. doi:10.1002/biof.114.

Author biography

Sofia Khanam, Student

Aman Prakash, Student

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