IJP (2019), Vol. 7, Issue 9 **(Review Article)**

Received on 23 April 2020; received in revised form, 23 August 2020; accepted, 29 August 2020; published 01 September 2020

A BIRD'S-EYE VIEW ON MARINE BIOACTIVE COMPOUNDS WITH POTENTIAL HEALTH BENEFITS

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Keywords:

Marine flora, Bioactive compounds, Health benefits, USFDA approved marine drugs

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ABSTRACT: Marine natural products are currently acknowledged as the most significant source of bioactive substances and medications with phenomenal biodiversity. Marine plants and creatures, for example, algae, bacteria, sponges, fungi, seaweeds, corals, diatoms, ascidians, are significant sources of the ocean and contain over 90% of the complete ocean biomass. Because of its exceptional biodiversity, the sea world is a rich common asset for some biologically active compounds. About half of the world's biodiversity is a marine organism; thus, the seas and oceans are viewed as the biggest repositories with an immense assortment of new substances and natural molecules of benefit. During the previous four decades, various novel compounds have been confined from a marine organism, and a large number of these substances have been appeared to have intriguing biologic potential.This review is an ongoing update of data about efficient marine eugicons (proteins, peptides, amino acids, fatty acids, sterols, polysaccharides, oligosaccharides, phenolic compounds, photosynthetic pigments, vitamins, and minerals) and spotlight on their potential health benefits. Accordingly, the work assessed so far in this paper is planned to give the baseline data to directing marine plant-based research with modest, safe, and incredible medications to challenge the lethal human disease.

INTRODUCTION: Marine floras, for example, bacteria, Actinobacteria, Cyanobacteria, fungi, microalgae, Seaweeds, Mangroves, and other halophytes are exceptionally significant oceanic resources, establishing over 90% of the oceanic biomass. The marine plant is taxonomically assorted, biologically active, and chemically unique [1]. It is an extraordinary asset, which offers incredible opportunities for the revelation of new bioactive compounds with potential medical advantages [2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.IJP.7(9).217-22

The article can be accessed online on www.ijpjournal.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.7(9).217-22

The bioactivity of marine-inferred natural products is altogether higher than that of territorial origin compounds. For example, in the preclinical cytotoxicity screen at the National Cancer Institute, about 1% of the marine samples tried indicated anti-tumor potency, compared to 0.1% of the stable samples tested [3]. Oceans are an exceptional archive of structurally and chemically novel bioactive compounds with unique biological attributes not normally found in terrestrial natural products.

Over 6% of the active compounds of marketable formulations are natural products or their synthetic subordinates or imitates [4]. It is progressively perceived that the ocean contains an enormous number of natural products and novel chemical elements with extraordinary biological activity that can be helpful in the detection of potential drugs

with greater efficacy and explicitness for the treatment of human illnesses [5]. It cannot be denied that with 3.5 billion years of presence on earth and involvement with biosynthesis, the marine micro floras remain nature's best source of chemicals. The endeavors to extract drugs from the ocean began in the late 1960s. However, the orderly investigation started in the mid-1970s. During the decade from 1977 to 1987, about 2500 new metabolites were accounted for from a variety of marine organisms.

These investigations have unmistakably exhibited that the marine environment is an excellent source of novel chemicals, not found in terrestrial sources. Up until this point, in excess of 10,000 compounds have been separated from marine organisms with hundreds of new compounds are as yet being discovered every year.

About 300 patents on bioactive marine natural products were issued between 1969 and 1999 [1]. However, because of the absence of ethnomedical history engaged in comparing terrestrial populations, the development of marine floral compounds as therapeutic agents is still in their infancy, together with the technical troubles in gathering the marine floral samples.

Over the most recent couple of decades, critical attempts have been made by both pharmaceutical organizations and educational institutions, particularly for the introduction of new marine-derived, natural products from animal species. However, oceanic floras are just somewhat exploratory, and these works are reviewed as the reason for empowering further research in this area.

Compared with terrestrial organisms, marine life forms don't have a recognized history of utilization in conventional medication. However, in the last 50 years, advancements in new innovation and technology, such as scuba diving techniques, manned submersibles, and remotely operated vehicles (ROVs) have opened the marine environment for scientific exploration [6].

The concurrence of numerous species in these habitats of limited extent increases their competitiveness and multifaceted nature. For example, marine macroscopic organisms such as algae, corals, sponges and a variety of other invertebrates are in consistent fight and most of the species have evolved chemical means to defend themselves against predation or overgrowth by contending species, or on the other hand, to stifle motile prey species for ingestion.

These chemical adaptations by and large appear as ‘‘secondary metabolites,’’ and include such well-known chemical classes as terpenoids, alkaloids, polyketides, peptides, shikimic acid derivatives, sugars, steroids, and a multitude of mixed biogenesis metabolites [7]. In this way, marine organisms have been demonstrated to be outstanding reservoirs of natural products, some of which have different structural characteristics in comparison to terrestrial sources.

Because of its phenomenal biodiversity, the marine environment is a vast and generally undiscovered source for new bioactive components of polyunsaturated fatty acids, polyphenols, sterols, proteins, sulfate polysaccharides, antioxidants, and pigments.

Chemical Diversity of Ocean: Thirty-four of the 36 known phyla are represented in the ocean. By comparison, the land has just 17 of the known phyla, with twelve phyla being solely marine. The ocean contains more than 200,000 described species of invertebrates and algae. Nonetheless, it is evaluated that this number is a small percentage of the total number of species that have yet to be discovered and portrayed [8].

Marine Bioactive Compounds: Attributable to its rich biodiversity, the marine environment is a tremendous and generally undiscovered source for new bioactive components derived from marine algae, coral reefs, marine herbs, marine sponges, marine fungi, seaweed and marine bacteria. In most recent five decades more than 20,000 compounds have been discovered from various marine organisms. **Table 1** contains lists of the bioactive compounds isolated from various marine floras.

Potential Health Benefits of Marine Natural Compounds: The chemical uniqueness of marine organism-derived compounds has quickened drug discovery from those marine sources which have the highest probability of having novel molecules and intriguing biological activity [30]. Marine flora is a productive source of bioactive constituents including polysaccharides, oligosaccharides, ter-

penoids, steroids, alkaloids, polyphenols, and anti-oxidants [2]. The different marine natural bioactive compounds with their potential health benefits are presented in **Table 2**.

TABLE 1: LISTS OF THE BIOACTIVE COMPOUNDS ISOLATED FROM DIFFERENT MARINE FLORA

Source	Compounds Isolated	References
Marine algae	Nitrogen-containing heterocyclics, kainic acids, guanidine	9
	Sulfated polysaccharides	10
	Prostaglandins	11
Corals reefs	Cytosar-U	12
	Dolastatin	13
	Sterols	14
	Noncembranoidalditerpene (5-Episinuleptolide acetate)	15
Marine herbs	Sorbicillactone A and Sorbicillactone B	16
	Fucoidan	17
	Stigmast-4-en-3-one, Stigmast-4, 22-dien-3-one	18
	Lophocladine A & B	19
Marine sponges	Heteronemin	20
	Manzamine A,	21
	8- hydroxymanzamine A	22
Marine fungi	A pimarane-type diterpenes, Scopararane I	23
	Varioloid A	24
	Azaphilonidal, penicilazaphilones B and C	25
	Secalonic acid D	26
Sea weeds	Dexcyanidanol, catechuic acid and trihydroxybenzoic acid	27
	Laminarin (β-1,3 glucan)	28
Marine bacteria	Quinine derivatives analogues like driamycin, daunorubicin, mitomycin C,streptonigrin, and lapachol,Anthroquinone family resembles parimycin, trioxacarcins and gutingimycin	29

TABLE 2: DETAILS THE DIFFERENT MARINE NATURAL BIOACTIVE COMPOUNDS WITH THEIR POTENTIAL HEALTH BENEFITS

Marine Natural Product	Bioactive Compounds	Source	Health Benefits	References
Proteins	*Chrysophsins major*	*Chrysophrys* (*pagrus*)	Antimicrobial	31
	Peptides	Bonito	ACE inhibitor	32
	Peptides	Sardine	ACE inhibitor, Antioxidant	33
	Parasin I, Pelteobagrin Catfish	(*Parasilurus asotus, Pelteobagrus fulvidraco*)	Antihypertensive ACE inhibitor, Antimicrobial	33
	Protein hydrolysates	*Sargassum horneri*	Antioxidant, Anticoagulant	34
	FPH	Pacifichake (*Merluccius productus*)	Antioxidant	35
	Peptides	Cuttelfish	Antihypertensive, Antioxidant	36
Lipids	Omega-3 PUFA (DHA and EPA)	Salmon	Anticardiovascular, Anti-obesity	37, 38
	Omega-3 PUFA (DHA and EPA)	Sardine	Anticardiovascular, Anti-obesity	37, 38
	Omega-3 PUFA (DHA and EPA)	*Undaria pinnatifida*	Antiallergic	39
Polysaccharides	Polysaccharide	Cuttlefish (*Sepiella maindroni, Euprymn aberryi*)	Antimutagenic, Antimicrobial	40
	Chitin and chitosan	Crustaceans (shrimp, crab, crayfish)	Antimicrobial, Anticancer Anti-inflammatory, Hypocholesterolemic	41
	Fucoidan	*Laminaria japonica*	Anticoagulant, Antioxidant	42
	Galactan	*Codium fragile*	Antiviral, Immunostimulating effect	42
	Mannans	*Nemalion helminthoides*	Antiviral, Immunomodulatory effect	24, 45
Alkaloids	*Axinella verrucosa* and *Acanthella aurantiaca*	Marine sponges	NF-kappa B-specific inhibitors	44
	Convolutamydine A ISA003 and ISA147	Marine bryozoans	Migration of leucocytes, and expression of COX-2, PGE2, iNOS, IL-6, and TNF- α in RAW 264.7 cells	45

	Chaeto globosin Fex	*Chaetomium globosum,*	Suppresses IL-6, TNF- α and monocyte chemotactic protein-1(MCP-1) inLPS-stimulated peritoneal macrophages and RAW 264.7 cells.	[46]
Polyphenols	Phlorotannin sub-fraction	*Fucus distichus*	Reduces TNF- α, IL-10, MCP-1 and COX-2 expression	[47]
Steroids /Sterols	Solomonsterol A	*Theonella swinhoei*	Inhibits the development of arthritis caused by anti-collagen antibodies in transgenic mice harboring a humanized PXR2. Solomonsterol A reduces the expression of the inflammatory markers TNF- α , IFN-γ and IL-17 and chemokines MIP1- α and RANTES, which reduces the inflammatory response	[2]
	Pregnane-type steroids	*Seleronephthya gracillimum*	Anti-inflammatory activity	[2]
	Ergosta-7, 22-dien-3-ol	*Marthasterias glacialis*	Anti-inflammatory activity	[48]

US - FDA Approved Drugs from Marine Origin: Regardless of significant difficulties, some marine compounds landed in the market and are currently used in treatment, providing a useful roadmap for future translational efforts. It has been about five decades since the segregation of spongothimidin and spongoridine from the marine sponge Tethyacrypta by Bergman that in the end prompted the advancement of Ara-C (cytarabine, an anti-leukemia agent) and Ara-A (vidarabine, an antiviral agent), agents which received United States-Food and Drug Administration (USFDA) approval in 1969 and 1976, respectively. After the approval of Ara-C and Ara-A as therapeutics, it was not until 2004 that the next MNP would be approved, ziconotide (Prialt1), for the treatment of severe chronic pain. This was soon followed by the orphan drug status granted to trabectedin for the treatment of soft-tissue sarcomas and ovarian cancer, and its enlistment in 2007 in the EU for the treatment of soft-tissue sarcoma. To date, the worldwide marine pharmaceutical pipeline comprises of seven endorsed drugs from the marine source in clinical use, four of which are anticancer medications. Regardless, after various extended lengths of research basically by the educational system and sporadic association of significant pharmaceutical organizations, only a few MNP were endorsed. As demonstrated by the latest data, the USFDA endorsed medications of the marine source right now being promoted are enlisted in **Table 3**.

TABLE 3: UNITED STATES-FOOD AND DRUG ADMINISTRATION APPROVED DRUGS OF MARINE ORIGIN [8]

Compound Name	Marine Organism	Molecular Target	Indication	Approval Date
Trabectedin	Tunicate	DNA (minor groove)	Soft tissue sarcoma and ovarian cancer	October 23, 2015
Brentuximabvedotin	Mollusk/ cyanobacteria	CD30, microtubules	Anaplastic large T‐cell systemic malignant lymphoma, Hodgkin's disease	August 19, 2011
Eribulinmesylate	Sponge	Microtubules	Metastatic breast cancer	November 15, 2010
Omega‐3‐acid ethyl esters	Fish	Triglyceride‐producing enzymes	Hypertriglyceridemia	November 10, 2004
Ziconotide	Cone snail	DNA polymerase	Severe and chronic pain	December 28, 2004
Vidarabine	Sponge	Viral DNA polymerase	Herpes simplex virus infection	1976 current status: Discontinued
Cytarabine	Sponge	DNA polymerase	Leukemia	1969

Uniqueness of Marine Natural Products: Natural products represent validated beginning stages for drug discovery since they occupy biologically significant chemical space. There is an expanding requirement for novel therapeutics, particularly due to the existence of currently incurable diseases as well as rising microbial resistance to current therapeutics. The marine environment covers 70% of the earth's surface, is characterized by unique growth conditions, and encloses monstrous biodiversity. Biodiversity presumably delivers chemo diversity as well, giving more extensive opportunity for finding novel therapeutics with novel mechanisms of action.

Staggering Opportunities for Marine Drug Discovery: Marine natural products demonstrated their adequacy against a wide array of diseases, with some possessing novel mechanisms of action and others being the most strong among their inhibitor classes. Currently, there are four marine-derived drugs on the market and 12 more in different phases of clinical trials. Innovations in several fields beat the obstacles related to marine drug discovery and development. Advancements in several procedures, for example, sampling techniques, nanomole structure determination as well as genome sequencing and mining, upgrade the effectiveness of exploring marine samples for novel therapeutics. Several advanced strategies end up being effective in defeating the supply problem, including total chemical synthesis and microbial fermentation, as well as molecular biology tools. Numerous compounds at different phases of development that effectively use those innovations highlight marine natural products as a new wave of drugs.

CONCLUSION: Marine environment produces a distressing condition where inhabitants adapt to survive. A large portion of the survivors is rich in secondary metabolites, which are restoratively useful. Among the marine organisms, numerous unrefined extracts, improved fractions, and compounds obtained shown fascinating potential medical advantages along the years. These effects are mediated by compounds from different chemical classes including polysaccharides, ter-penoids, phenolic compounds, sterols, carotenoids, alkaloids, and fatty acids.

Owing to a diverse chemical ecology, marine floras are a potential source of bioactive compounds; however, they are least explored. Regardless of the unprecedented potential for sourcing new prescriptions from marine natural products, very few compounds have actually been utilized for treatment. Thus, endeavors should be made to develop marine functional compounds responsibly since their consumption could result in a decrease of the occurrence and gravity of chronic diseases. In order to meet the growing need for a wide range of pharmaceuticals, marine sources have a great promise for providing potent, cheaper and safer drug candidates for solving our most medical problems and which deserve further extensive exploration. This review takes bird's eye-view on marine anticancer compounds both known and as yet undiscovered, which hold answers to some of our biological queries and much more may be anticipated in near future.

ACKNOWLEDGEMENT: This work was supported by University Department of Chemical Technology, Dr. Babasaheb Ambedkar Marathwada University, Aurnagabad and Vilasrao Deshmukh Foundation, Group of Institutions, Latur, Maharashtra, India

CONFLICTS OF INTEREST: The author(s) declare that there are no conflicts of interest.

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How to cite this article:
Salunke MA, Wakure BS and Wakte PS: A bird's-eye view on marine bioactive compounds with potential health benefits. Int J Pharmacognosy 2020; 7(9): 217-22. doi link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.7(91).217-22.

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