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MARINE ORGANISMS: A NEW CHALLENGE FOR DRUG DEVELOPMENT

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ABSTRACT

Disease ailments are changing the patterns, and the new diseases are emerging due to changing environments. The enormous growth of world population has overburdened the existing resources for the drugs. And hence, the drug manufacturers are always on the lookout for new resources to develop effective and safe drugs for the increasing demands of the world population. Seventy-five percentage of earth's surface is covered by water but research into the pharmacology of marine organisms is limited, and most of it still remains unexplored. Marine environment represents countless and diverse resource for new drugs to combat major diseases such as cancer or malaria. It also offers an ecological resource comprising a variety of aquatic plants and animals. These aquatic organisms are screened for antibacterial, immunomodulator, anti-fungal, anti-inflammatory, anticancer, antimicrobial, neuroprotective, analgesic, and antimalarial properties. They are used for new drug developments extensively across the world. Marine pharmacology offers the scope for research on these drugs of marine origin.

KEYWORDS: Marine organisms, Bryostatin, Cytarabine, Mariculture, Sponge.

INTRODUCTION

Ocean represents a source of a varied type of organisms due to the diversified environment offered by different oceanic zones. The enormous ecological resources of the sea have been exploited since ancient times and included the use of marine animals like fish and preparations from algae as the sources of medicine. Fish oils are the classic example of marine-derived product in use since ages. Marine pharmacology is a branch of

pharmaceutical sciences which focuses on the substances with active pharmacological properties present in marine species of plants and animals. Marine environment is an exceptional store house of novel bioactive natural products, with structural and chemical features generally not found in terrestrial natural products. The marine organisms also provide a rich source of nutraceuticals and potential candidates for the treatment of several human diseases. The modern day focus of marine pharmacology is on microbes.[1] This includes the discovery of new pharmaceutical candidates from marine microbes.[1] The ocean provides enormous opportunities to discover new compounds as it has more than 13,000 molecules described out of which 3000 are having active properties.[3] Marine natural products are generally secondary metabolites. They are not generated by biological or regular metabolic pathways and have no primary function associated with the development, growth, or propagation of a species.[4] Sixty-three percentage of the new drugs are classified as naturally derived (i.e., modified natural product, unmodified natural product or synthetic compound with a natural product as pharmacophore).[5]

Biodiversity of marine environment

Marine environment is a natural habitat for a broad variety of living organisms having different physiology and capacity to adapt their environment. Out of over 33 animal phyla known today, a total of 32 phyla are embodied in the marine environment out of which 15 varieties are exclusively present in the marine environment.[6] Such genetic diversity renders chemical diversity which is promising for new drug development.

O ceans contain more than 80% of diverse plant and animal species in the world. Marine organisms such as sponges, tunicates, fishes, soft corals, nudibranchs, sea hares, opisthobranch Molluscs, echinoderms, bryozoans, prawns, shells, sea slugs, and marine microorganisms are sources of bioactive compounds (viz. oils and cosmetics).[7] The first biologically active marine natural product was formally reported in late 1950 by Bergmann.[8] It was established that marine plants and animals are genetically and biochemically unique. Around 15,000 such unique natural compounds have been described and out of them 30% products have been isolated from sponges.[9]

Marine focus in India

India has over 8000 km of coastline with clusters of marine habitats like inter-tidal rocky, muddy and sandy shores, coral reefs, and mangrove forests. The potential of Indian marine habitat has remained largely unexplored for their potential of new drugs and biotechnological

programs. Some of the selected institutes such as National Institute of Oceanology, Goa; Central Drug Research Institute, Lucknow; Bose Institute, Kolkata; Central Institute of Fisheries Education, Mumbai; Regional Research Laboratory, Bhubaneswar of Council for Scientific and Industrial Research are presently working for exploration of life saving drugs from marine sources. Many other Indian institutes, universities, and pharmaceutical companies have also recognized the significance of this subject.[10]

Marine pharmacology has been reviewed extensively in the past all over the world as well as in India, but still there is a need to review the potential of the oceans as source for the development of new drugs, considering the advantage of their abundance in nature and large scale production. At present, the drug industry is working on screening and isolation of novel molecules with unreported pharmacological properties that can be exploited for the development of new therapeutic agents for commercial use. This review has largely focused on different classes of marine drugs currently in use and at different stages of trials for approval and marketing in future. The review has also tried to delve into the limitations and future trends of the drugs from marine sources.

Classification of marine pharmacology

Marine pharmacology can be classified on the basis of source of the candidate drug.

Genetically engineered marine organisms

- Manufacture of pharmaceuticals and nutraceuticals of marine origin
- Chemicals produced by or found in marine organisms shown to have a wide variety of applications as pharmaceuticals.

Marine drugs can be broadly classified based on their actions as follows.

Antibacterial

Eicosapentaenoic acid, a polyunsaturated fatty acid, isolated from a diatom of marine origin *Phaeodactylum tricornutum* which has shown activity against an array of Gram-positive and Gram-negative bacteria, which also includes a multidrug-resistant variety of *Staphylococcus aureus*.[12]

Anti-inflammatory

The anti-inflammatory function of extracts and other parts of a Mediterranean sponge species *Spongia officinalis* in the *in vivo* study on rat model of carrageenan-induced paw edema assay.[13]

Neuroprotective

The extracts of South Indian green seaweed *Ulva reticulata* has shown neuroprotection by inhibiting acetyl-and butyryl-cholinesterases, efficacy comparable to agents currently approved for Alzheimer's disease treatment.[14]

Antiparasitic

Extracts of *Sarcotragus* sp. known as Tunisian sponge prepared in dichloromethane has demonstrated *in-vitro* anti-leishmanial activity by demonstrating the associated morphological alterations in promastigotes of leishmania major.[15]

Antiviral agents

Anti-herpes simplex virus-1 (HSV) activity found in high molecular weight exo-polysaccharides extracted from the *Celtodoryx girardae* (French marine sponge) and its associated symbiotic bacteria has been reported.[16]

Anticancer

Bryostatin, primarily obtained from the Bryozoan, *Bugula neritina*, although some forms have been extracted from sponges and tunicates. Sorbicillin-derived alkaloids sorbicillactone A and its 2', 3'-dihydro analog sorbicillactone-B has shown activity against leukemia cells free from any noteworthy cytotoxicity. Sorbicillactone-B has been derived from a salt-water culture of a bacterial strain *Penicillium chrysogenum* which has been isolated from a sponge *Ircinia fasciculata*, a Mediterranean sponge specimen.

Another promising anticancer drug used as an immunotherapeutic agent is keyhole limpet hemocyanin (KLH). KLH is a copper containing extracellular respiratory protein present in *Megathura crenulata*, a marine *Gastropod* species found in large numbers at the Pacific coast of California and Mexico. KLH is found in two isoforms KLH1 and KLH2.KLH is reported to possess remarkable immunostimulatory properties in experimental animals and human, used in experimental immunology and also clinically as an immunotherapeutic agent. KLH is specifically used in clinical setup for the treatment of bladder carcinoma, and its

efficacy is perhaps due to a cross-reacting carbohydrate epitope. KLH may also have significant potential for the treatment of other types of cancers, particularly the adenocarciomas derived from the epithelium, by using it as a carrier for gangliosides of carcinoma and mucin-like epitopes.[17]

Challenges and future trends

There are certain major challenges to derive the drugs from marine sources. The variable environmental conditions could result in the production of different metabolite every time from the same organism. A major challenge sometimes faced is that the microorganisms residing in the marine animal, and not the invertebrate marine hosts actually produces the bioactive molecules. Sustainable supply of isolated and identified lead compounds sometimes pose a problem because the lead compound is present only in low quantity and/or technically it becomes very difficult to isolate such compound. For any of intended use (drug, cosmetic, etc.,) of the compound, the required quantity may vary from few grams needed for preclinical drug development and safety studies in different setup; to quantities in kilogram required for clinical study in different phases and many of tons of cosmetics. And the availability of lead compound in such abundance can be a key issue.

Lack of sustainable supply of the candidate compound has sometimes held back further research and development of many extremely potent marine novel compounds. Attempts have been made to beat this hurdle by increased development of synthetic or hemisynthetic analogues derivatives with desired and customized properties, or designing a pharmacophore of lower complexity with easier synthesis method. Identification of a bioactive compound synthesized or hemisynthesized must be done with the reference to the compound derived from the biological source. The structural complexity of the isolated compound and meager yield which is generally faced with marine compounds, may lead to wrong assignment of chemical formula of the compound, its real constitution (planar connectivity), configuration of intramolecular bonds, configuration entirity, and incorrectly assigned one or multiple stereocenters. To overcome the issue of regular supply, the use of natural resources should be under control and need to favor the growth of marine organisms in its natural environment by farming which is also known as “Mariculture.”Another option is to culture the marine organisms under artificial conditions by the process called as “aquaculture”.

Fig 1: Scope of marine pharmacology.

REFERENCES

1. Kijjoa A, Sawangwong P. Drugs and cosmetics from the sea. Mar Drugs, 2004; 2: 73–82.
2. Mayer AM, Glaser KB, Cuevas C, Jacobs RS, Kem W, Little RD, et al. The odyssey of marine pharmaceuticals: A current pipeline perspective. Trends Pharmacol Sci, 2010; 31: 255–65.
3. Vignesh S, Raja A, James RA. Marine drugs: Implication and future studies. Int J Pharmacol, 2011; 7: 22–30.
4. Martins A, Vieira H, Gaspar H, Santos S. Marketed marine natural products in the pharmaceutical and cosmeceutical industries: Tips for success. Mar Drugs, 2014; 12: 1066–101.
5. Cragg GM, Grothaus PG, Newman DJ. Impact of natural products on developing new anti-cancer agents. Chem Rev, 2009; 109: 3012–43.
6. Margulis L, Schwartz KV. 3rd ed. New York, USA: W.H. Freeman and Company; 1998. Five Kingdoms – An Illustrated Guide to the Phyla of Life on Earth.
7. Donia M, Hamann MT. Marine natural products and their potential applications as anti-infective agents. Lancet Infect Dis, 2003; 3: 338–48.
8. Bergmann W, Stempien MF. Contributions to the study of marine products. XLIII. The nucleosides of sponges V The synthesis of spongosine. J Org Chem, 1957; 2: 1557–75.
9. Murti Y, Agarwal T. Marine derived pharmaceuticals-development of natural health products from marine biodiversity. Int J ChemTech Res, 2010; 2: 2198–217.

10. Thakur NL, Thakur AN, Muller WEG. Marine natural products in drug discovery. Natural Product Radiance, 2005; 4: 471–7.
11. Desbois AP, Mearns-Spragg A, Smith VJ. A fatty acid from the diatom *Phaeodactylum tricornutum* is antibacterial against diverse bacteria including multi-resistant *Staphylococcus aureus* (MRSA) Mar Biotechnol (NY), 2009; 11: 45–52.
12. Dellai A, Laroche-Clary A, Mhadhebi L, Robert J, Bouraoui A. Anti-inflammatory and antiproliferative activities of crude extract and its fractions of the defensive secretion from the mediterranean sponge. *Spongia officinalis*. Drug Dev Res, 2010; 71: 412–8.
13. Suganthy N, Karutha Pandian S, Pandima Devi K. Neuroprotective effect of seaweeds inhabiting South Indian coastal area (Hare Island, Gulf of Mannar Marine Biosphere Reserve): Cholinesterase inhibitory effect of *Hypnea valentiae* and *Ulva reticulata*. Neurosci Lett, 2010; 468: 216–9.
14. Ben Kahla-Nakbi A, Haouas N, El Ouaer A, Guerbej H, Ben Mustapha K, Babba H. Screening of antileishmanial activity from marine sponge extracts collected off the Tunisian coast. Parasitol Res, 2010; 106: 1281–6.
15. Rashid ZM, Lahaye E, Defer D, Douzenel P, Perrin B, Bourgougnon N, et al. Isolation of a sulphated polysaccharide from a recently discovered sponge species (*Celtodoryx girardae*) and determination of its anti-herpetic activity. Int J Biol Macromol, 2009; 44: 286–93.
16. Bringmann G, Gulder TA, Lang G, Schmitt S, Stöhr R, Wiese J, et al. Large-scale biotechnological production of the antileukemic marine natural product sorbicillactone A. Mar Drugs, 2007; 5: 23–30.
17. Harris JR, Markl J. Keyhole limpet hemocyanin (KLH): A biomedical review. Micron, 1999; 30: 597–623.