POTENTIAL MARINE PHARMACOLOGICAL RESOURCES – A MINI REVIEW

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Abstract: Nature has been the traditional source of new pharmaceuticals. In recent years, a considerable number of structurally unique metabolites with biological and pharmacological activities have been isolated from the marine derived resource, such as polyketides, alkaloids, peptides, lactones, terpenoids and steroids. Some of these compounds have anticancer, antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, antibiotic and cytotoxic properties. This review discuss about the potential pharmacological properties of Marine Resource.

Keywords: *Marine pharmacology, Bioactive Compounds, Toxicology.*

I. 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 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 [1]. 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.

Marine bioactive compounds or Marine natural products (MNPs) are organic compounds produced by microbes, sponges, seaweeds, and other marine organisms. The host organism synthesizes these compounds as non-primary or secondary metabolites to protect themselves and to maintain homeostasis in their environment. Between 2002 and 2016, around 2500 new metabolites (MNPs) were reported from marine organisms ranging from microbes to fish, which accounts for less than 1.0% of the total marine organisms. 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). Covering the period from 1981 to 2008, around 68% of all the drugs used to curb infection (including antibacterial, antiviral, antiparasitic, and antifungal compounds) and 63% of anti-cancer drugs were naturally derived.

II. Chemical Diversity of Marine Environment

The ocean contains more than 200,000 described species of invertebrates and algae [2], however, it is estimated that this number is but a small percentage of the total number of species that have yet to be discovered and described. Conservative estimates suggest that oceanic subsurface bacteria could constitute as much as 10% of the total living biomass carbon in the biosphere [3]. From a relatively small number of these species that have been studied to date, thousands of chemical compounds have been isolated [4]. Moreover, only a small percentage of these compounds have been tested in clinically relevant bioassays. The ocean represents a virtually untapped resource for discovery of novel chemicals with pharmaceutical potential.

Marine plants, animals, and microbes produce compounds that have potential as pharmaceuticals. These "secondary metabolites," chemicals that are not needed by the organism for basic or primary metabolic processes, are believed to confer some evolutionary advantage. Because many of these plants and animals live in densely populated habitats are non-motile, and have only primitive immune systems, they have evolved chemical compounds to help defend against predators [5], to attract or inhibit other organisms from settling or growing on them [6], and to provide chemical cues to synchronize reproduction among organisms that expel their eggs and sperm into the water. The mechanisms by which they prevent encroachment or predation interact with the same or similar enzymes and receptors that are involved in human disease processes. For example, many natural products have been identified that inhibit cell division, the process that is the primary target of many anti-cancer drugs. In most cases, there is a greater understanding of the effect of the natural product on human disease processes than of the function in the marine organism from which it was isolated.

The marine environment became a focus of natural products drug discovery research because of its relatively unexplored biodiversity compared to terrestrial environments. The potential of marine natural products as pharmaceuticals was introduced by the pioneering work of Bergmann in the 1950s [7], which led to the only two marine-derived pharmaceuticals that are clinically available today. The anticancer drug, Ara-C, is used to treat acute myelocytic leukemia and non-Hodgkin's lymphoma. The

antiviral drug, Ara-A, is used for the treatment of herpes infections [8]. Both are derived from nucleosides isolated from a shallow-water marine sponge collected off the coast of Florida.

Marine sponges are among the most prolific sources of diverse chemical compounds with therapeutic potential (Plate XI). Of the more than 5000 chemical compounds derived from marine organisms, more than 30% have been isolated from sponges [8]. Sponges occur in every marine environment, from intertidal to abyssal regions, in all the world's oceans, and they produce a greater diversity of chemical structures than any other group of marine invertebrates. Other marine sources of bioactive molecules with therapeutic potential are bryozoans, ascidians, molluscs, cnidarians, and algae. Several strains of phytoplankton, especially cultured species of diatoms, have been described as exhibiting antibacterial and antifungal activity [9]. However, the levels of activity are low and hence the active compounds have not yet been isolated or characterized.

III. Current Status – Marine Pharmacology

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.

Bryostatin, isolated from the bryozoan Bugula neritina, is a polyketide with both anticancer and immune modulating activity [10-14]. Its mechanism of action is through activation of protein kinase C mediation of cell signal transduction pathways. This compound is currently in Phase II clinical trials for non-Hodgkin's lymphoma, chronic lymphocyte leukemia, and multiple myeloma through a Cooperative Research and Development Agreement (CRADA) between the NCI and Bristol-Myers Squibb.
Ecteinascidin 743, a complex alkaloid derived from the ascidian *Ecteinascidia turbinata* [15- 16] and licensed by the University of Illinois to PharmaMar S.A. is in Phase I clinical trials for ovarian cancer and other solid tumors in the United States and Europe.
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* [17]. The Marine Ascidian, *Didemnum psammathodes* against against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Vibrio* and *Shigella boydi* bacteria was isolates from diabetic foot ulcer patient [18].

Discodermolide, a polyketide isolated from deep-water sponges of the genus Discodermia [19] is a potent immunosuppressive and anticancer agent which inhibits the proliferation of cells by interfering with the cell's microtubule network [20]. This compound may be effective against breast and other types of cancer that have become resistant to other microtubule disrupting drugs. Discodermolide has been licensed by Harbor Branch Oceanographic Institution (Fort Pierce, FL) to Novartis Pharmaceutical Corporation, and is in advanced preclinical trials.

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 [21]. Analgesic and CNS Depressant Activities of Sea Anemone Heteractis aurora [22]. *In vitro* study on Antiinflammory assessment of Protein Denaturation activity and Antiprotease activity from Marine Ascidian, *Didemnum psammathodes*[23].

In each of these cases, however, bulk supply of the chemicals for continued clinical development is a problem. It is often neither economically nor ecologically feasible to rely on large-scale collections of the source organisms from their natural habitats for supply of marine drug candidates. Whether a drug company decides to support the clinical development of a new drug is dependent on identifying an adequate supply of the source material. This could be through culture of the organism or through synthesis of the compound using an economically feasible, industrial-scale process. Research is in progress on options for biological supply (e.g., aquaculture, cell culture, microbial fermentation, and genetic engineering) to address this critical issue in the development of chemicals from natural sources. Unfortunately, neither the NIH nor must drug companies are prepared to invest funds in basic research to develop general models for biological supply of marine natural products with therapeutic potential.
Despite the emphasis on identifying new anticancer compounds, marine natural products have also been found to have other biological activities, including mediation of the inflammatory response. The pseudopterosins are glycosides derived from the Caribbean soft coral Pseudopterogorgia elisabethae [24]. These are in advanced preclinical trials as anti-inflammatory and analgesic drugs.

A number of marine derived compounds have been discovered with antiviral and antifungal activity. Indeed, one of the two clinically available marine derived drugs is used for the treatment of herpes infections. Although no marine natural products are currently in clinical trials as treatments of infectious diseases, there is high potential for future development.

IV. Future Trends in Marine Pharmacology

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 produce the bioactive molecules [25]. Sustainable supply of isolated and identified lead compounds sometimes pose a problem because the lead compound is present only

in low quantity and 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 [25].

Some limitations of the marine drug development includes the development of universal expression systems for biosynthesis of small molecules with high yield, development of genetic tools to access the *in vivo* potential of cultured marine microorganisms, and the regulatory arousing of silent biosynthetic pathways for small molecule discovery. The subsequent levels of development of drugs comprises *in vivo* evaluations of safety and efficacy in animal models, determination of the mechanism and site of action, development of structure activity relationships, formulation and characterization of pharmacokinetics parameters and pharmaceutical properties including improvements through the use of medicinal chemistry.

V. Conclusion

Marine environment generate a stressful condition where inhabitants acclimate to survive. Most of the survivors are rich in secondary metabolites which are medically useful for human kinds. Mostly these biomaterials are directly applied as drugs substitute or used as template for synthetic drug development. Marine drugs are new hope for future drug development.

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