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Review Article

Pharmacological aquatic natural product: Screening for bioactive substances

Basit Fazal[1], Md. Javed Karim[2], Shantanu Ranjan[1], Mohammed Shadab Shahab[1], Archana[3,*]

[1]*Department of Pharmacy, Nibha Institute of Pharmaceutical Sciences, Affiliated to Bihar University of Health Sciences, Rajgir, India.*
[2]*School of Pharmacy, Bhabha University, Bhopal, India.*
[3]*Department of Pharmacy, MGM College of Pharmacy, Affiliated to Bihar University of Health Sciences, Patna, India*

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ABSTRACT

In recent years, there has been a significant increase in the exploration and development of drugs derived from marine-based natural compounds. A wide array of marine organisms—including fungi, halophytes, bacteria, cyanobacteria, and cone snails—have yielded promising chemical entities for pharmaceutical research. These biologically active compounds from natural marine sources are gaining considerable attention, especially those with potential to target key molecules involved in various diseases. Current studies are primarily focused on microorganisms such as bacteria and fungi isolated from marine sediments, algae, seaweeds, and invertebrates like sponges, mollusks, tunicates, and crabs. The marine environment presents promising opportunities for developing new therapies against bacterial, viral, fungal, and parasitic infections—particularly in light of growing resistance to conventional drugs and emerging infectious threats. Concerns such as bioterrorism, antimicrobial resistance, and newly arising infectious diseases have further fueled interest in marine-derived compounds, despite most clinical trials focusing primarily on cancer therapies. Marine natural products are generally categorized into three main biological sources: marine microorganisms (e.g., phytoplankton), marine algae, and marine invertebrates. Among these, the marine ecosystem is considered a highly productive reservoir of bioactive secondary metabolites. Compounds extracted from various types of algae—especially brown algae—are of particular interest due to their wide-ranging biological functions and compatibility with human systems. The vast biodiversity within the oceans remains a largely untapped resource, offering numerous plant, animal, and microbial species with the potential to produce novel bioactive agents.

Introduction

In recent decades, marine sources have become significant sources of lead compounds with various medicinal applications. [1].

*Corresponding author: Archana, Department of Pharmacy, MGM College of Pharmacy, Affiliated to Bihar University of Health Sciences, Patna, India.

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Marine microorganisms represent a largely underutilized source of several bioactive compounds. The distinctive environmental conditions of marine ecosystems—such as fluctuations in temperature, pressure, and light—allow specific marine species to synthesize unique secondary metabolites that are rarely present in terrestrial animals. Screening natural biological materials for therapeutic potential through high-throughput technologies can result in the creation of economically viable medications or products. Many marine natural chemicals serve as chemical defenses, effectively inhibiting physiological processes in competing marine species to facilitate prey capture or predator evasion. Bioprospecting endeavors seek to identify bioactive chemicals generated by marine microbes, frequently demonstrating antibiotic characteristics. At now, therapy choices for chronic diseases such as Alzheimer's, Parkinson's, rheumatoid arthritis, type 1 diabetes, heart disease, irritable bowel syndrome, allergies, asthma, cancer, and others are restricted. Furthermore, certain current drugs may induce significant adverse effects when misused, underscoring the necessity to investigate alternate treatments. Natural products have always been regarded as promising options for the treatment of numerous diseases, including bacterial infections. The marine environment, characterized by its extensive diversity and demanding conditions including variable salinity, temperature, pressure, pH, and nutrient concentrations, provides a distinctive source of new biomaterials. Organisms here have evolved specific metabolites employed for defense, communication, or offense [2]. A multitude of these metabolites exhibit structural uniqueness relative to terrestrial molecules and possess significant potential for medicinal advancement. Marine animals such as mollusks, corals, sponges, and tunicates are significant providers of these bioactive compounds. Moreover, marine associated micro-organisms such as cyanobacteria, actinomycetes, fungi, dinoflagellates, and uncultivable symbionts—are acknowledged for their capacity to generate innovative medicinal compounds. Natural products are essential in the process of medication discovery. Marine animals provide a more abundant and varied assortment of bioactive compounds than terrestrial creatures and non-marine microorganisms. The ocean's dynamic and frequently harsh conditions promote the synthesis of diverse secondary metabolites. Historically, numerous efficacious pharmaceuticals have derived from natural sources, including penicillin from fungi, digitalis glycosides from foxglove, and morphine from poppies. The inaugural marine-derived pharmaceutical licensed in the United States was ziconotide (branded as Prialt), a peptide sourced from the tropical cone snail, utilized for the management of chronic pain associated with spinal cord damage [3,4].

Pharmacological Potential of Marine Natural Compounds

Marine algae, or seaweeds, are autotrophic organisms that thrive in saline environments and employ chlorophyll for photosynthesis. These algae synthesize several chemicals with prospective medical applications and can be effectively farmed in bioreactors to yield substantial quantities of biomass and bioactive molecules for research purposes. Carotenoids derived from seaweed, particularly fucoxanthin found in brown algae and some microalgae, demonstrate anticancer effects by impeding the growth and proliferation of cancer cells. Research indicates that fucoxanthin and its derivatives can elicit antiproliferative effects on colorectal cancer cells [5].

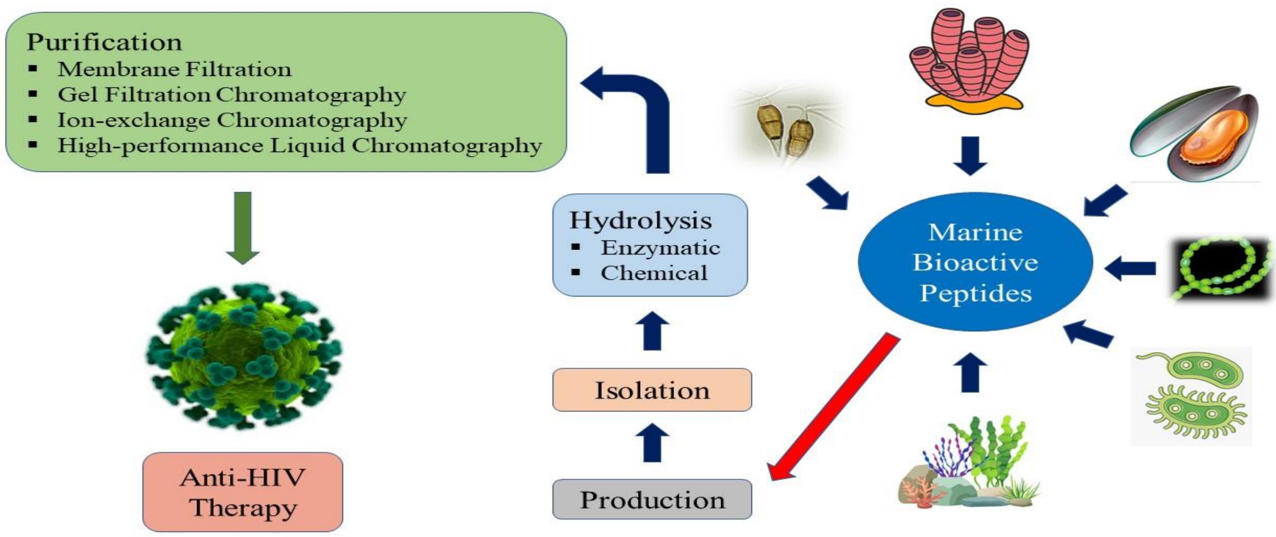

Figure 1: Infographic on marine bioactive peptides with antiviral potential (Source: MDPI – Marine Drugs Journal).

Polysaccharides, prevalent in marine algae both intracellularly and inside cell walls, exhibit diverse pharmacological activity, including anticancer properties. Fucoidan, sourced from brown algae, and carrageenan, obtained from red algae, are significant sources of alginic acid and have been investigated for cancer therapy. Studies integrating fucoidan with synthetic agents such as rutin have demonstrated increased anticancer efficacy, triggering apoptosis and mitochondrial impairment in cancer cells while sparing normal cells. Extracts from Ulva lactuca, a species of green algae, exhibit anti-inflammatory, antiviral, anticoagulant, antioxidant, and anticancer effects [6].

Sea cucumbers, marine creatures akin to starfish and sea urchins, possess essential elements like vitamins, calcium, fucoidan, triterpene glycosides, and sphingoid bases. Compounds extracted from sea cucumbers exhibit cytotoxic properties against human cancer cell types. Marine sponges, classified under the phylum Porifera, represent some of the most abundant sources of marine natural goods. More than 60 chemicals, including nucleosides, sterols, alkaloids, and amino acid derivatives, have been extracted from sponges, many of which exhibit potential as chemopreventive and anticancer medicines by influencing apoptosis, inflammation, and cell cycle control [7].

The effective conversion of marine natural products (MNPs) into medicines underscores its potential in medication development. Notwithstanding the problems encountered—such as the difficulty in acquiring adequate amounts of therapeutically pertinent chemicals from natural sources—substantial progress has been achieved to surmount these barriers, highlighting the considerable promise of MNPs in medicine [8].

Data Collection

The present paper was constructed by a comprehensive examination of literature obtained from regulatory and publicly available databases and websites. The literature search strategy employed a combination of several keywords and a weight of evidence methodology when appropriate. The search included many pharmaceutical, medical, and chemical databases, such as PubMed, Scopus, Embase, Web of Science, Google Scholar, ScienceDirect, HerbMedpro, NatMed Pro, Cochrane Library, Health Source, WHO, and CABI. Furthermore, comprehensive searches were performed utilizing Google to guarantee extensive coverage.

Comprehension of previous works

Marine Natural Products (MNPs) are bioactive substances obtained from marine organisms, including sponges, mollusks, corals, algae, and particularly microbes. These chemicals are produced via metabolic pathways and can be reproduced through chemical synthesis. They are essential in drug discovery because of their structural complexity and significant biological activity, demonstrating potential in the treatment of infections, cancer, and other disorders [9].

Marine bacteria represent a prolific and inadequately investigated reservoir of secondary metabolites with prospective medicinal and biotechnological applications. The distinctive circumstances of the marine environment (e.g., pressure, temperature, salinity) facilitate the synthesis of new chemicals not commonly present in terrestrial sources. [10]

Natural products have always played a significant role in the development of life-saving pharmaceuticals, and marine sources are currently receiving heightened interest owing to the rise in antibiotic resistance and the necessity for novel therapeutic agents. In addition to medicine, marine-derived chemicals are utilized in cosmetics and agriculture [11].

MNPs constitute a crucial and expanding field of study, with marine creatures providing exceptional chemical variety. These products are classified according to the producing species (microorganisms, algae, invertebrates) and their chemical structures (e.g., terpenoids, alkaloids, peptides) [12].

Marine natural compounds demonstrate a diverse array of pharmacological activity, encompassing antibacterial, antidiabetic, antiproliferative, anti-inflammatory, antioxidant, and neuroprotective properties. The bioactivities are primarily ascribed to the secondary metabolites generated by marine creatures, including algae, sponges, seaweeds, and snails, particularly in response to environmental stress.

Antimicrobial: Marine creatures produce antimicrobial chemicals as defensive strategies, effective against drug-resistant infections [13].

Antidiabetic: Seaweeds, particularly red algae, are abundant in bioactive substances such as carrageenan and agar, which exhibit antidiabetic properties.

Antiproliferative: Brown algae generate secondary metabolites that exhibit possible anticancer effects.

Anti-inflammatory: Compounds such as fucoidan derived from brown seaweed demonstrate significant anti-inflammatory and neuroprotective properties.

Antioxidant: Marine polysaccharides and polyphenols, such as phlorotannins, mitigate oxidative stress, a significant contributor to neurodegeneration [14].

Neuroprotective: Marine extracts (e.g., from Ulva, Sargassum) safeguard against neurodegeneration by mitigating inflammation and oxidative damage.

The categorization of marine natural products is determined by their source (e.g., algae, microbes, invertebrates) and their function (e.g., antibacterial, antiviral, anti-inflammatory, anticancer, analgesic).
Numerous marine-derived substances, such as ziconotide, fucoidan, and exo-polysaccharides, have demonstrated therapeutic potential and are under investigation for pharmacological and cosmeceutical uses [15].
Moreover, marine mollusks such as conchs, whelks, tulips, and snails fulfill ecological and commercial functions and serve as sources of bioactive chemicals.

Discussion

Marine natural products are essential in the research and development of novel medications. Marine species provide a more broad and abundant range of bioactive substances than terrestrial creatures and non-marine microorganisms, rendering them significant repositories for natural product study. The marine ecosystem promotes the synthesis of a diverse array of bioactive secondary metabolites, which possess significant promise for innovative pharmaceutical development [16].

Algae are categorized as microalgae—comprising diatoms, cyanobacteria, dinoflagellates, and other brown and red algae—and macroalgae, popularly known as seaweeds, which encompass green, brown, and red algae. The microalgae group is renowned for its chemical diversity and pharmacological potential, frequently recognized for producing several bioactive compounds present in marine ecosystems. Red algae are distinguished as prolific makers of several physiologically active chemicals. Seaweeds, or phycocolloids, are utilized industrially as sources of gums and also provide nutritional benefits to the human diet [17].

Phycocolloids, including alginic acid, carrageenan, and agar-agar, largely located in the cell walls of red and brown algae, are extensively employed across multiple sectors. Algae possess a diverse array of bioactive compounds that augment their adaptation to environmental conditions [18].

Inflammation in the human body is a fundamental innate immune response aimed at addressing detrimental stimuli, including physical injury, pathogenic microorganisms, poisons, UV radiation, endotoxins, and specific disease conditions. The maritime environment sustains a diverse array of organisms—including bacteria, fungus, algae, corals, sponges, and mammals—that demonstrate significant structural and functional diversity [19].

Invertebrates represent a substantial category within marine fauna, including principal taxa such as Porifera, Cnidaria, Mollusca, Arthropoda, and Echinodermata, as well as several minor phyla. These marine invertebrates have traditionally served as abundant sources of marine natural products (MNPs) with diverse medical applications. Marine invertebrates, characterized by the absence of a vertebral column, frequently exhibit exoskeletons or shells and are categorized into more than 30 phyla, demonstrating an extraordinary diversity of body structures. They constitute the predominant portion of substantial marine fauna and were the initial organisms to evolve, preceding vertebrates [20].

Marine snails, particularly cone snails, are primarily located in tropical waters and are distinguished by their conical, frequently vibrant shells. Cone snails employ a sophisticated venom apparatus featuring barbed radula teeth to incapacitate prey, administering a complex array of peptides with significant physiological effects. Although their venom poses a threat to people, cone snail toxins exhibit potential for medicinal uses [21].

The class of gastropods has thousands of species, including marine snails, slugs, and both freshwater and terrestrial forms. They represent one of the most ecologically viable and diversified assemblages within the Mollusca phylum, inhabiting a wide range of settings, including forests, deserts, rivers, oceans, and extreme habitats such as hydrothermal vents. Marine gastropods encompass species with coiled shells, including abalones and whelks, but certain limpets forfeit their shell coiling post-larval stage [22].

Marine corals, classified under the subphylum Anthozoa within the phylum Cnidaria, are colonial entities that create extensive, dense colonies of polyps. Tropical reef-building corals manufacture calcium carbonate skeletons, forming enormous reef structures over generations. Coral polyps reproduce by both asexual and sexual means, frequently coordinating gamete release during full moons, resulting in the formation of new colonies from motile planula larvae. Numerous corals depend on symbiotic photosynthetic dinoflagellates (Symbiodinium) for energy, while others may collect plankton via stinging tentacles [23].

Octocorals, a subgroup of Anthozoa, encompass sea fans and soft corals, characterized by their eight-branched tentacles, in contrast to hard corals, which possess multiples of six. These corals occupy many environments, ranging from tropical shallow seas to deep-sea habitats, exhibiting numerous growth styles from creeping to erect fan-like structures [24].

Recent advancements in the last twenty years have associated marine algae with nanotheranostics, wherein engineering and medical sciences converge to create nanoparticle-based formulations that address the limits of peptide therapeutics. Red algae, characterized by distinct cellular attributes and supplementary pigments known as phycobiliproteins, exhibit a spectrum of colors from green to deep red to nearly black in deeper aquatic environments. The majority of red algae are multicellular and have intricate life cycles that encompass several generations. Coralline red algae play a crucial role in coral reef formation through the deposition of calcium carbonate. Green algae are part of the Viridiplantae group and encompass several forms, including colonial, filamentous, and unicellular varieties, many of which possess flagella. Green algae function as a photosynthetic resource for several marine animals and establish symbiotic associations with species such as lichens, flatworms, and ciliates. Multiple genera of green algae engage in these mutualistic interactions [25].

Brown algae predominate in temperate and polar marine ecosystems, frequently located along stony coastlines. Kelp species serve as essential food supplies and habitats, whereas sargassum creates floating carpets in tropical oceans. Certain types of brown algae are harvested for human consumption [26].

Sponges, among the most ancient animal lineages, comprise a gelatinous matrix encased by cellular layers, including a porous body structure that enables water circulation for nourishment and breathing. Their pluripotent cells can differentiate into multiple types, and they lack intricate organ systems. Sponge fossils date back hundreds of millions of years, indicating their ancient evolutionary roots [27].

Tunicates, marine invertebrates classified under the subphylum Tunicata of the phylum Chordata, encompass both solitary and colonial filter feeders characterized by sac-like structures and siphons. Adult sessile ascidians adhere to substrates, while other tunicate families, including as salps and pyrosomes, are pelagic and free-swimming in the open ocean [28].

Sea snails have significant diversity, with certain species residing in marine, freshwater, or terrestrial habitats. Numerous sea snails utilize gills for respiration; however, certain species have developed lungs and are predominantly active during low tide, such as false limpets from the Siphonariidae family [29].

Table.1: Classification of Marine Natural Product Sources and Their Therapeutic Relevance

Biological Source	Examples	Common Habitats	Bioactive Compounds	Therapeutic Potential
Marine Microorganisms	Marine bacteria, actinomycetes, cyanobacteria, fungi	Sediments, hydrothermal vents	Polyketides, peptides, alkaloids	Antibacterial, antifungal, anticancer, antiviral
Marine Algae	Brown algae (*Sargassum*), red algae (*Gracilaria*), green algae (*Ulva*)	Intertidal zones, coral reefs	Phlorotannins, sulfated polysaccharides	Antioxidant, anti-inflammatory, anticoagulant, antiviral
Marine Invertebrates	Sponges, tunicates, mollusks, cone snails, crabs	Coral reefs, seabeds, rocky shores	Terpenoids, alkaloids, peptides, polyketides	Anticancer, neuroprotective, analgesic, antiparasitic
Halophytes	Salt-tolerant marine plants	Coastal marshes, mangroves	Phenolics, flavonoids	Antioxidant, hepatoprotective, antimicrobial
Phytoplankton	Diatoms, dinoflagellates	Open ocean, surface waters	Carotenoids, polyunsaturated fatty acids (PUFAs)	Anti-inflammatory, cardiovascular protection, immune modulation
Marine-Derived Fungi	*Penicillium*, *Aspergillus* species from marine environments	Sediments, decaying organic matter	Mycotoxins, polyketides	Antitumor, antimicrobial, enzyme inhibitors

Conclusion

Marine natural products have significant diversity, with the quantity of discovered chemicals rising each year. These chemicals originate from the secondary metabolism of diverse marine animals, underscoring significant patterns among numerous organisms. Marine algae, particularly brown algae prevalent in the cooler waters of the Northern Hemisphere, are significant resource for the development of novel medications. Green algae comprise several types, including colonial and spherical (coccoid), filamentous, and unicellular flagellates, the majority of which possess two flagella per cell, in addition to larger multicellular seaweeds. Red algae have a variety of thallus structures, including filamentous, branching, feathery, and laminar forms.

Marine invertebrates—including sponges, corals, bluebottles, worms, shells, sea urchins, starfish, crabs, sea cucumbers, and nudibranchs—are distinguished by their bioactive properties, which encompass antibacterial, antioxidant, antihypertensive, anticoagulant, anticancer, anti-inflammatory, wound healing, and immune-modulating effects. Cone snails predominantly interact with membrane proteins, specifically ion channels, receptors, and transporters. Gastropod snails facilitate the synthesis of structural proteins such as collagen and elastin. Marine corals excrete calcium carbonate to construct their skeletons, whereas octocorals comprise polyps featuring eight tentacles and mesenteries, situated within a gelatinous mesoglea. Sponges are immobile organisms devoid of physical defences. Tunicates exhibit diverse bioactive properties, encompassing antibacterial, antitumor, and anticancer activity, alongside distinct metabolic sources. Marine gastropods fulfill ecological functions by eliminating algae and assisting in the decomposition of plant detritus in aquatic ecosystems.

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Conflict of Interest

None declared.

Author Contributions

All the authors contributed to the study.

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