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**REVIEW ARTICLE**

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# RECENT ADVANCES IN THE USE OF ALGAE AND MARINE PLANTS IN DRUG DISCOVERY AND DEVELOPMENT

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**ABSTRACT:** Marine plants and algae, in particular, are an uncharted territory in terms of resource potential for developing new bioactive compounds for introducing new drugs. Among these are peptides, lipids, polysaccharides, alkaloids, and polyphenols, which possess cancer fighting, bacteria killing, reducing inflammation and inflammation protecting, and nerve cell safeguarding abilities, among others. Organ sulfonates originating from the ocean are increasingly essential for expanding medicinal chemistry as structural motifs with remarkable properties since their chlorinated analogs. The recent advances in the genetic engineering and bioreactor systemization have brought the technology of utilizing marine life for various treatments to easier tracks, as in the recent past such compound production were done in a larger scale and sustainable way. In particular, algae express promising perspectives as the source of valuable bioactive chemicals regarded as an environmentally sustainable platform for drug development. Despite launch of dozens of drugs that Marine Bioactives inspired, there are challenges that span across multiple fields such as bioavailability, fetch, and reproducibility. The review provides information on contemporary developments in marine natural products for drug discovery. Included are the molecular aspects that render marine compounds bioactive, the results shown in clinical and preclinical studies of these compounds, and the identification of novel starting points via meantchology approaches such as computational aiding and omics. We emphasize the importance of sustainable use of the seas and colors cooperation with other fields while describing the great potential of medication created on the base of marine resources. Perhaps holding the key to better, less hazardous medication delivery, marine plants, and algae will become the stars of the field's future treatments.

**Keywords:** Marine plants, Algae, Bioactive compounds, Drug discovery, Marine biotechnology

## I. INTRODUCTION

Marine plants and algae are being considered more relevant in drug discovery because of the variety of different bioactive chemicals they contain. It is a fact that these sea animals synthesize many strange substances with strong bioactivities. Marine plants and algae harbor several natural products that may eventually be formally applied to emphatically cure cancer, infectious diseases, inflammatory disorders, and numerous other diseases [1]. The utility of these creatures is increasing in pharmaceutical manufacture since they present bioactive compounds that are rare in terrestrial plants. Seo has confirmed the folklore proverb that marine creatures are very effective in curing diseases in traditional medicine. From time immemorial people residing in island as well as coastal areas have been using marine angiosperms and seaweed for curing many diseases. Nonetheless, systematic research on the marine life for medicine wasn't conducted until mid-twentieth century [2]. Present marine anti-cancer drugs like trabectedin have drawn attention towards marine derived chemicals in pharmacotherapy thanks to tremendous advances in marine pharmacology. and among them polyphenols, alkaloids, lipids, peptides, polysaccharides to name a few of the bioactive compounds produced by marine plants and algae [3].

Many therapeutic functions such as antioxidant, antibacterial, anti-inflammatory, and anti-cancer have been found to be present in these substances. Due to their multidirectional chemical profile, compounds derived from the ocean are attractive new therapeutic assets. The main focus of this work is to bring updated information regarding new trends in the use of marine plants and algae in the search for new drugs. The premise of this research is to analysis the role of marine biotechnology in the amelioration of marine-derived Medicinal Chemistry, pharmacological action, and the therapeutic value of these bio species [4].

### 2. Biological Diversity and Sources of Marine Plants and Algae

It is said that there are many unexplored resources in the marine plant and algae specifically for the discovery of new medicine. These organisms are capable of producing an immense number of bioactive compounds, and can survive in vastly differing environments – from the shallow sea edge to the bottom of the ocean. The two broad classifications of marine flora variety are marine algae and marine plants each of which offers various materials that can be used in developing new medications [5].

**Marine Algae**

Macroalgae and microalgae represent two groups of marine algae that contain numerous bioactive compounds, however, the compositions of chemicals and sorts of molecules in these two types are quite distinct [6].

**Macroalgae**: Often known as seaweed though they are actually big algae forms, these are multicellular. Based on their pigmentation, they can be divided into three primary groups:

- **Brown Algae** (Phaeophyceae): Some of them include; *Sargassum, Fucus and Laminaria* etc. Some specific polysaccharides, including alginate, fucoidan, and laminarin, derived from brown algae have well-documented bioactivities including antioxidant, anticancer and antiviral properties [7].

- **Red Algae** (Rhodophyta): Some of the red algae include *Chondrus, Kappaphycus and Gracilaria.* The polysaccharides which include agar and carrageenan in plentiful in red algae, they find application as drug delivery agents, antimicrobial and immunomodulating agents too [8].

- **Green Algae** (Chlorophyta): Since then, several species of green macroalgae have been described, for examples, *Ulva and Codium.* What makes green algae possessing anti-inflammatory and antioxidant bioactive compounds are sterols, polyphenols and fatty acids [9].

**Microalgae**: This single-called algae are found in freshwater as well as in saltwater environment. Organisms that can synthesize many bioactive substances such as proteins, lipids and carotenoids are the bivalve's mollusks. Important classes of microalgae that have potential as medicines include:

- **Cyanobacteria** (Blue-green algae): Some of the most prominent are *Arthrospira and Spirulina.* Phycocyanin is one of the bioactive compounds formed by cyanobacteria with the features of antioxidant and ant inflammatory [10].

- **Diatoms**: The algae containing silica have displayed the prospect of synthesizing antiviral and anticancer substances [11].

- **Dinoflagellates**: Dinoflagellates have the ability to produce powerful toxins, like brevetoxins and saxitoxins, which could be used in the treatment of neurological disorders and pain [12].

**Marine Plants**

Many marine plants such as the seagrass, mangrove and some plants which may not be familiar, are sources of novel bioactive compounds that can be utilized in development of new medicines.

- **Seagrasses**: These large-seeded aquatic flowering plants– *Zostera and Thalassia* –have been described as possessing potent antibacterial, anticancer and anti-inflammatory effector chemicals. They are mostly found in the nearest shallow sea waters. Investigations on the prospective vaso, pro healing, and tissue repairing effects of sear water plant extract is also being conducted [13].

- **Mangroves**: Some of these adaptations include becoming adapted to survive in saline condition in which these coast plants grow along the brackish seas. The *Avicennia* and *Rhizophora* species contain tannins, alkaloids and flavonoids which contain potential usage in cancer, infections and inflamed conditions [14].

**Table 1: Classification of major marine algae and plants with examples of species studied for their bioactive properties [16]**

| *Category* | *Subcategory* | *Example Species* | *Bioactive Properties* |
|---|---|---|---|
| Marine Algae | Brown Algae | *Laminaria japonica* | Antioxidant, anticancer, antiviral |
| | | *Sargassum fusiforme* | Anti-inflammatory, antiviral, antimicrobial |
| | | *Fucus vesiculosus* | Antioxidant, anticancer, neuroprotective |
| | | *Ascophyllum nodosum* | Antioxidant, antimicrobial, anti-inflammatory |
| | Red Algae | *Gracilaria vermiculophylla* | Antimicrobial, immunomodulatory, anticancer |
| | | *Chondrus crispus* | Antioxidant, antiviral, antidiabetic |
| | | *Eucheuma cottonii* | Antiviral, anti-inflammatory, wound healing |
| | | *Kappaphycus alvarezii* | Antioxidant, anti-inflammatory, anticoagulant |
| | Green Algae | *Ulva lactuca* | Anti-inflammatory, antioxidant, anticancer |
| | | *Codium fragile* | Antioxidant, antibacterial, anti-inflammatory |
| | | *Chaetomorpha linum* | Antioxidant, anti-inflammatory, anticancer |
| | Cyanobacteria | *Spirulina platensis* | Antioxidant, anti-inflammatory, immunomodulatory |
| | | *Arthrospira* | Antiviral, antioxidant, anticancer |
| | | *Nostoc commune* | Anti-inflammatory, anticancer, antibacterial |
| Microalgae | Diatoms | *Phaeodactylum tricornutum* | Anticancer, antiviral, anti-inflammatory |
| | | *Thalassiosira weissflogii* | Antioxidant, antiviral, antimicrobial |
| | Dinoflagellates | *Alexandrium tamarense* | Toxins for neurological diseases, anti-inflammatory |
| | | *Karenia brevis* | Toxin production, neuroprotective, anti-inflammatory |
| | Seagrasses | *Zostera marina* | Antimicrobial, anti-inflammatory, wound healing |
| | | *Thalassia testudinum* | Antioxidant, antimicrobial, anticancer |
| Marine Plants | Mangroves | *Rhizophora mangle* | Anti-inflammatory, antimicrobial, anticancer |
| | | *Avicennia marina* | Antiviral, anti-inflammatory, anticancer |
| | Other Marine Plants | *Padina pavonica* | Antimicrobial, anti-inflammatory, anticancer |
| | | *Spartina alterniflora* | Antioxidant, antimicrobial, anti-inflammatory |

- **Other Marine Plants**: A large number of plants commonly found along the coast line, such as seagrasses, mangrove, salt marsh-grass (*Spartina)* etc. have given evidence for the synthesis of biologically active compounds with anti-inflammatory, anti-oxidant and anti-cancer potential. Greater attention has been paid to the pharmacological impact of these plants since they are mostly seen in the tidal areas [15].

**3. Bioactive Compounds from Marine Plants and Algae**

Several phytochemicals with potential therapeutic uses are available in marine angiosperms and seaweed sources. These databases are valuable tools when considering drug discovery and development since these molecules exhibit a range of biological activity. Here, the therapeutic uses and main categories of bioactive chemicals derived from marine plants and algae are described [17].

**Polyphenols: Antioxidants and Their Therapeutic Applications**

There are numerous chemicals in the plant referred to as polyphenols and they have well appreciated antioxidant properties. It is accepted that free radical mediated oxidative stress is responsible for many chronic diseases, and polyphenols which are found in large amounts in marine plants and algae exert antioxidant effects to stabilize free radicals [18].

**Therapeutic Applications:**

- **Antioxidant:** Free radicals are controlled by polyphenols and thus they have cell and tissue protecting antioxidant effects.

- **Cardioprotective:** The influence of both on lipid profile and blood pressure is proven to decrease the risk of cardiovascular disease.

- **Neuroprotective:** Studies indicate that marine polyphenols could have some neurodegenerative diseases of aging like Parkinson's and Alzheimer's ailments.

- **Anticancer:** Scientists have also pointed out that polyphenols obtained from marine organisms exhibit anticancer effects in inhibition of cancer cells formation, induction of apoptosis in various types of cancer [19].

**Alkaloids: Bioactive Compounds with Anticancer, Antimicrobial, and Anti-inflammatory Effects**

Algae and marine plants contain alkaloids as nitrogen-containing chemicals present in various marine organisms. In particular for their effect on cancer, infections and inflammation, these chemicals exhibit high biological activity [20].

**Therapeutic Applications:**

- **Anticancer:** It has been shown that the obtained alkaloid compounds isolated from marine organisms have a cytotoxic effect in terms of cancer cell growth and proliferation inhibition and induction of apoptosis [21].

- **Antimicrobial:** Marine alkaloids hold ant- microbial, antifungal and antiviral potentials and thus have potentials for use in combating infections [22].

- **Anti-inflammatory:** Marine alkaloids have the tendency to suppress pro-inflammatory mediators, thus a simple inflammation condition such as arthritis can be controlled with the aid of this product [23].

**Lipids and Fatty Acids: Potential in Cardiovascular and Metabolic Diseases**

Polyunsaturated fatty acids and lipids including omega 3 fatty acids are richly available in the marine algae and plants important for human health. These chemicals have other physiological functions: mediating inflammatory responses and maintaining cell membranes [24].

**Therapeutic Applications:**

- **Cardiovascular Health:** Discoveries made in this field indicate that omega-3 extracted from the marine algae including Schizochytrium enhances the endothelial production of nitric oxide thus reduce cholesterol and Gen2 as well as triglyceride levels to block cardiovascular diseases [25].

- **Metabolic Diseases:** Multiple studies have evidenced that marine lipids affect insulin sensitivity and lipid profile which appears to be useful to combat obesity, type 2 diabetes, and metabolic syndrome [26].

- **Anti-inflammatory:** The three main chronic diseases, autoimmune disorders, cardiovascular diseases, and arthritis, are usually caused by inflammations, which marine lipids, especially omega-3s, help in decreasing [27].

**Polysaccharides and Peptides: Immunomodulatory and Anti-inflammatory Properties**

The ability of marine polysaccharides and peptides, primarily drawn from the seaweed and algae, to regulate immunity and reduce inflammation is of much interest. Products such as bioactive peptides with multiple pharmacological actions, and sulfated polysaccharides, fucoidan and carrageenan are examples of such substances [28].

**Therapeutic Applications:**

- **Immunomodulatory:** It has been found out that polysaccharides present in brown algae including fucoidan, enhances the immune system. This is because they introduce natural killer cells and macrophages into the body hence act as immune system triggers [29].

- **Anti-inflammatory:** That is why there are therapeutic possibilities for inflammatory diseases including inflammatory bowel disease and rheumatoid arthritis due to the combination of anti-inflammatory and pro-inflammatory abilities of different marine polysaccharides and peptides [30].

- **Wound Healing:** Marine peptides enhance the rate and efficiency of tissue repair because of its action on cell proliferation and collagen synthesis for wound healing and other tissues [31].

- **Antioxidant:** Further, Marine polysaccharides also contribute for avoiding age related ailment by helping the cells to protect from oxidative stress [32].

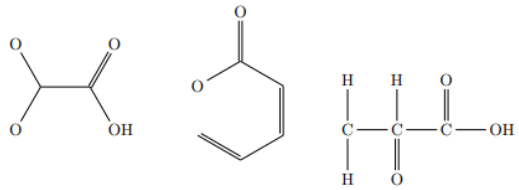

**Fig. 1: Chemical structures of representative bioactive compounds derived from marine plants and algae. [33]**

**4. Mechanisms of Action of Bioactive Compounds**

Marine plant and algal bioactive compounds exert pharmacological effects from molecular and cellular targets through various molecular routes of action. Therefore, information regarding these mechanisms is important for the development and optimization of marine-based therapies. The list of molecular targets and cellular pathways preferred by bioactive chemicals derived from marine sources is as follows [34].

**Molecular Targets**

Interest in enzymes Many bioactive chemicals isolated from marine organisms act on the regulation of enzyme activity since enzymes are often involved in cellular regulatory processes. These chemicals may modulate disease processes because they possess the capacity to either potentiate or inhibit enzymatic activity [35].

- **Protein Kinases:** Protein kinases are a family of proteins that are involved in the control of diverse cellular processes protein targets. Some marine alkaloids and polyphenols target protein kinases that regulate various signaling modules controlling cell division and cell death. For instance, marine polyphenols have hit particular MAPK pathways that are again related with inflammation and cancer cell proliferation [36].

- **Phosphatases:** Phosphatases counteract the action of kinases by stripping off phosphate groups from the proteins. Phosphatases may affect such signaling networks as those regulating cell cycling and apoptosis by inhibiting or activating these enzymes. Alkaloids and polysaccharide will enable the marine natural product to selectively inhibit phosphatases and aid in modulation of immune and inflammatory reactions [37].

**Receptor-Based Targets** A good number of the marine derived compounds also affect membrane receptors, which are responsible for transmitting signals received outside the cell to the inside of the cell and consequently regulating the behavior of the cell [38].

- **G-Protein Coupled Receptors (GPCRs):** GPCRs play a significant role in the modulating of various physiological processes, such as immune, signaling and metabolic processes. Marine-originated peptides, lipids and polyphenols affect GPCR operation pertinent to inflammation, pain and neuroprotection. For instance, marine natural products acting on cannabinoid receptors (CB1 and CB2) that decrease inflammation as well as alleviate pain [39].

- **Nuclear Receptors:** Certain bioactive compounds from marine algae have been shown to interact with nuclear receptors, such as peroxisome proliferator-activated receptors (PPARs) and retinoid X receptors (RXRs), which regulate gene expression involved in metabolic regulation, lipid homeostasis, and inflammation [40].

**Cellular Pathways**

Apoptosis, Autophagy, and Oxidative Stress Regulation The balance of cell life and death are essential regulatory aspects of diseases including cancer and neurodegenerative diseases. These molecules may modulate to these pathways and support cell survival or apoptosis in disease cells in the marine environment [41].

- **Apoptosis:** Some reviews have identified bioactive agents, including alkaloids and polyphenols obtained from marine sources that indicating potential to induce cancer cells death. This is realized through induction of intrinsic mitochondrial pathway which activates caspases. Each of these chemicals can enhance cell death by increasing levels of proteins Bax, which encourage apoptosis, and reducing levels of Bcl-2, which discourage it [42].

- **Autophagy:** Self-degradation of organelle structures is termed autophagy and some of the ocean derived chemicals can influence this process. As the invention, autophagy is involved in critical cellular maintenance and stress program. Studying the effects of marine

polyphenols and peptides it was found out that they have the capacity to induce autophagy. It helps in the process of elimination of detritus organelles or proteins and the avoidance of the formation of toxic compounds. Thus, these compounds can protect cells from damages under stress [43].

- **Oxidative Stress Regulation:** Long-term health decay, cancer and other diseases originate from oxidative stress which is a relative abundance of free radicals to antioxidants. Marine foods containing polyphenols and polysaccharides present antioxidants which are capable of combating free radicals and other oxidative related damages. It is invaluable in the protection it offers from cell damage, unhealthy aging, and diseases such as Alzheimer's and heart diseases [44].

**Inflammation Pathways and Immune System Modulation**
This condition has been connected with many diseases such arthritis, cardiovascular diseases and cancer. Marine bioactive compounds, almost all of contain significant anti-inflammatory activity that act through multiple mechanisms [45].

- **NF-kB Pathway:** A protein indispensable for the control of inflammatory gene activity is nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB). Fucoidan from brown algae and other marine compounds modulate the activity of NF-kB, resulting in a decline in such pro-inflammatory cytokines as TNF-α, IL-6, and IL-1β [46].

- **COX and LOX Pathways:** The formation of eicosanoids involves two enzymes; cyclooxygenase (COX) and lipoxygenase (LOX) that pro- inflammatory. The works on reducing inflammation by using drugs that would block the activity of COX and LOX. This is one of the ways of action of marine polyphenols, fatty acids and alkaloids in relief of inflammatory bowel disease and rheumatoid arthritis [47].

- **Immunomodulation:** There is evidence that the immune system could be modulated by marine polysaccharides, fucoidan and carrageenan stimulating macrophage, NK cells, dendritic cells. This helps the immune process of the body to monitor and check on any invasions of anything that is strange in the system. These materials help in the regulation of the overall immune system, innate immunity as well as adaptive immunity to prevent disorder through overactivation of the immune system [48].

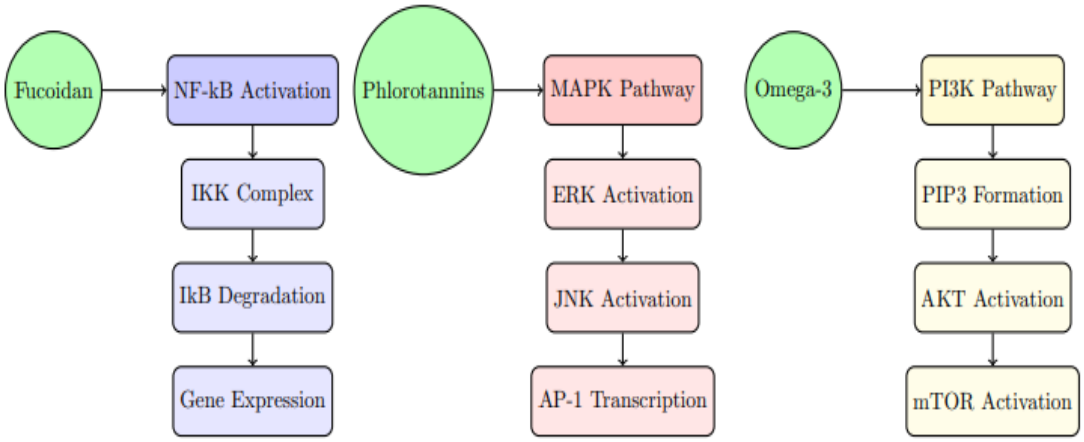


**Fig. 2: Diagram showing molecular pathways targeted by marine bioactive compounds (e.g., NF-kB, MAPK, PI3K). [49]**

## 5. Applications in Drug Discovery and Development

Due to the potential versatility of therapeutic application, bioactive chemicals coming from marine sources have been the focus of much attention which may be as new drug candidates. The substances are today being investigated in clinical and preclinical trials. But there are also certain challenges that must be resolved before they can be turned into commercial pharmaceuticals, including the challenge of boosting production and ensuring bioavailability [50].

### Preclinical Studies

It is necessary to conduct preclinical research prior to moving to the human trials in order to determine pharmacological profiles of drug coming from marine sources. Plant secondary metabolites and marine algae components are evaluated for efficacy, toxicity and mode of action by using in vivo and in vitro experimental models [51].

***In Vitro* Studies**: The effect of the marine chemicals is measured using cultured cell in vitro experiments. These investigations help to establish whether the chemicals interact with immune systems, suppress inflammation or inhibit creation of cancer cells. Fucoidan isolated from marine algae has pronounced immunomodulating properties in populations of immune cells, the polyphenols of the red alga Gracilaria vermiculophylla demonstrated significant cytotoxicity against human cancer cells grown [52].

***In Vivo* Studies**: For the assessment of the systematic impact of chemical products derived from the sea, there is a need to conduct in vivo study in animals. As for the characteristics, named by letters from ADME, which stands for absorption, distribution, metabolism, and excretion, these investigations are capable to predict bioactivity of a substance in real biological systems. One of them is Laminaria japonica, the brown algae extract, which has demonstrated a beneficial effect in the cardiovascular system in preclinical research. Both of these extracts have decreased cholesterol and hypertension in mice type [53].

That is why, together with the efficiency of the preparations, their possible toxicity and other side effects in case of using substances extracted from water is an equally important direction in preclinical research. Several marine bioactive compounds which have been believed to have a potential as clinical agents in the future are already known to more of them have been found to be nontoxic or less toxic in animals and have safe side effects [54].

**Clinical Trials**

Several products derived from marine organisms are currently being tested for viability in clinical trials in order to determine their effectiveness as human medicines. Before such molecules can be deemed potential marketable drugs, they are subjected to efficacy and safety tests, doses setting trials among others.

**Marine-Derived Drugs in Clinical Trials**:

- **Bremelanotide (Vyleesi®)**: Women suffering from hypoactive sexual desire disorder (HSDD) can now use bremelanotide, a peptide that can be traced from marine cone snails. In research some have showed that it is effective in enhancing sexual desire through the melanocortin receptors that are present in the brain [55].

- **Marinederived Anticancer Agents**: Various substances from marine organisms have been shown to possess potentially anticancer properties; several are currently undergoing clinical trial. An example would be Trabectedin (Yondelis®) which has been approved for use in soft tissue sarcomas and ovarian cancer because of clinical trial results. It is isolated from the marine creature *Ecteinascidia turbinata*, a tunicate [56].

- **Omega-3 Fatty Acids**: The focus of researchers is to determine whether supplements containing omega-3 polyunsaturated fatty acids, which make up fish oil and marine algae, helpful for metabolic syndromes and inflammatory diseases and also for heart health. Some clinical studies also show that they can enhance heart metabolism and reduce the concentrations of triglycerides [57].

- **Therapeutic Indications**: Amongst many diseases for which drugs derived from marine products are already in clinical trials, there is cancer, cardiovascular diseases, neurological disorder, and inflammation. Scientist are seeking marine bioactive compounds for a range of therapeutic applications such as anticancer agents, cardiovascular agents but also from neurological point of view, in the treatment of ailments like Alzheimer's and Parkinson's [58].

**Challenges in Drug Development**

Chemicals derived from marine sources hold promising agents for medicine, but many challenges lie ahead for these substances to be fully functional and affordable drugs.

- **Bioavailability Issues**: The major challenge facing the creation of drugs from marine sources is their bioavailability; the fact that there are several issues to be handled once the drug has to pass through several phases of development. Due to their extensive feature of molecular size or tendency to be broken down in the digestive system, many marine chemical compounds such as lipids, polysaccharides and peptides have low oral availability. To make these medicines more bioavailable, efforts are being made toward nanoencapsulation, lipid-based delivery systems and change in formulation. In order to increase practical applicability of these agents, it is necessary to make them even more soluble and stable in biological solutions [59].

- **Sourcing and Scaling Production**: This paper reveals that some of the most damaging challenges faced by the pharmaceutical industry as they move towards sustainability lie primarily in the extraction of chemicals from the marine and the subsequent manufacturing of these for commercial purposes. The culture or harvest of large quantities of marine animals such as corals, sponges and algae which serve as reservoirs of many bioactive compounds may be difficult. This poses a big challenge in its ability to increase on the production rate while at the same time ensuring that raw materials are available in large quantity at the required time. The use of bioreactors that involve marine organisms and cell cultures of algae are among the outstanding achievements in today's marine biotechnology, which are currently considered as the possible solutions to these issues. But there's still a big obstacle: the cost for aspiring to upscale the production while maintaining standard harvesting methods sustainable [60].

- **Regulatory and Environmental Concerns**: There is thus the need to proceed with the harvesting of these organisms because many of the marine derived medications originate from marine systems that are normally diverse. A notable aspect in the process of generating drugs is to ensure that gathering marine species, does not jeopardize, the marine species diversity, or marine's ecosystem. Besides, all the drugs and medicines that originate from the sea are subject to the same standards of efficacy and safety like other medications to be used clinically [61].

**Table 2: List of marine-derived drugs in clinical trials with current status [62]**

| *Drug Name* | *Source* | *Therapeutic Indication* | *Current Status* | *Phase* |
|---|---|---|---|---|
| Bremelanotide (Vyleesi) | *Conus spp.* (Marine Snails) | Hypoactive Sexual Desire Disorder (HSDD) | Approved for use | Market Approval |
| Trabectedin (Yondelis) | *Ecteinascidia turbinata* (Tunicate) | Soft Tissue Sarcomas, Ovarian Cancer | Approved for use | Market Approval |
| Omega-3 Fatty Acids (Lovaza) | Fish Oils (derived from marine sources) | Hypertriglyceridemia, Cardiovascular Diseases | Approved for use | Market Approval |
| Marizomib | *Nereis virens* (Polychaete Worm) | Glioblastoma, Cancer | Completed Phase II | Phase II |
| Oltipraz | *Marine Algae* | Liver Diseases, Cancer | Completed Phase II | Phase II |
| Dolastatin 10 | *Dolabella auricularia* (Sea Hare) | Cancer (Various Types) | Ongoing Phase I | Phase I |
| Ecteinascidin-743 (ET-743) | *Ecteinascidia turbinata* (Tunicate) | Ovarian Cancer, Soft Tissue Sarcomas | Approved in Europe | Market Approval |
| Discodermolide | *Discodermia dissoluta* (Marine Sponge) | Cancer (Various Types) | Completed Phase I | Phase I |
| Fucoidan | *Fucus vesiculosus* (Brown Algae) | Immunomodulation, Cancer | Ongoing Phase I/II | Phase II |
| Spirulina Extract | *Arthrospira platensis* (Blue-Green Algae) | Immune Support, Antioxidant | Ongoing Phase I | Phase I |
| Salinomycin | *Streptomyces albus* (Marine Actinobacteria) | Cancer (Various Types) | Completed Phase II | Phase II |
| Gracilaria Extract | *Gracilaria spp.* (Red Algae) | Metabolic Diseases, Diabetes | Ongoing Phase I | Phase I |

## 6. Advances in Marine Biotechnology for Drug Development

Biotechnology in marine organism is a rising focal area in drug discovery and development due to the novelty of marine derived molecules. New breakthroughs in genetic engineering, bioreactor technology and drug delivery systems are enhancing development of marine derived drugs and improving ways of producing them for market [63].

### Genetic Engineering of Marine Organisms

Increasingly, marine organisms especially algae are being genetically engineered to enhance production of the biologically active agents. With a process called metabolic engineering, the process in which various forms of algae can be genetically modified, scientists are able to produce more bioactive compound and get such stuff to work as drugs [64].

- **Algal Strains Engineered for High-Yield Bioactive Production:** The biochemistry field of algae can be targeted to produce additional valuable compounds, such as lipids, polysaccharides and polyphenols, which are exceptionally overexpressed in the algae strains altered by genetic engineering. Since the polysaccharide fucoidan exhibits high anti-inflammatory and anticancer properties, the approaches undertaken for metabolic engineering of brown algae (Fucus vesiculosus) have been described in the article. The improved procedure allows for the industrial synthesis of these compounds in large quantities, thereby increasing their availability and reducing the costs of their synthesis for use in drug formulation [65].

- **Synthetic Biology Approaches:** Algae can be made to produce chemicals that are not available in the natural world due to synthetic gene networks that researchers are constructing using synthetic biology. This strategy has the capacity to produce new medicinal molecules such as bioactive peptides or antibacterial and anticancer alkaloids by controlling microalgal metabolic activities [66].

### Marine Bioreactors

Another issue that must involve bioreactor technology in large scale culture and production of bioactive chemicals derived from marine organisms [67]. For those species that have not been cultured to large quantities, the labor respecting and ecologically unfeasible conventional techniques for obtaining bioactive compounds from the muscular tissues of marine animals are even worse. However, unlike other forms of bioreactors, marine bioreactors present a controlled platform which is more efficient in cultivating these marine organisms.

- **Large-Scale Production of Bioactive Compounds from Algae:** The cultivation of micro and macro algae is possible in bioreactors, where light, temperature and nutrient supply can be manipulated for enhanced growth on production of bioactive compounds. For escalating the outputs of such compounds as astaxanthin for antioxidant purpose and eicosapentaenoic acid useful in cardiovascular diseases treatments, photographs are used to grow algae inside photobioreactors. That is why, in addition to the use as source of obtaining huge amounts of substances taken from the sea, bioreactors also enable large scale production of bioactive chemicals [68].

- **Continuous Bioreactor Systems:** Progress in a strategy of constant bioreactor has provided better growing conditions for algae and at the same time been more effective and economical through a system of continuous drawing of algal bio mass. These systems are suitable for growing bioactive compounds on an industrial scale because water and nutrients are recycled, eliminating costs and negative impact on the environment [69].

### Marine-Derived Biopolymers in Drug Delivery

More and more research are pointing to marine-derived biopolymers, such as algal proteins and polysaccharides, as potential components of effective medication delivery systems. Biodegradability, biocompatibility, and the capacity to be functionalized for targeted therapeutic uses are some of the distinctive features offered by these biopolymers [70].

- **Development of Drug Delivery Systems Using Algal Biopolymers:** Because of their gel-forming, drug-encapsulating, and controlled-release properties, polysaccharides derived from algae, such as agar, carrageenan, and alginates, are finding more and more applications in the creation of drug delivery systems. The mucoadhesive characteristics of alginates, which can improve gastrointestinal drug absorption, are one reason why they are being considered for use in oral drug delivery systems. Nanoparticles or hydrogels made from these biopolymers can be engineered to target particular organs or tissues, allowing for more targeted drug delivery with fewer unwanted side effects [71].

- **Nanocarriers for Targeted Drug Delivery:** Nanocarriers that can carry therapeutic compounds in a targeted manner are being designed using marine biopolymers, especially those generated from brown algae. By attaching targeting ligands to the nanocarriers' surfaces, anti-inflammatory chemicals or anticancer medications can be loaded onto them and delivered to specified areas of the body, such tumors or inflamed tissues. The medicine is both more effective and less harmful to healthy cells thanks to its focused delivery [72].

- **Marine Biopolymer-Based Hydrogels:** Researchers are looking into hydrogels consisting of biopolymers obtained from marine sources for uses such as controlled medication release, wound healing, and tissue regeneration. Improved therapeutic outcomes in chronic diseases and tissue damage can be achieved through the prolonged release of bioactive chemicals by these hydrogels. Regenerative medicine could benefit from marine polysaccharides because of their potential to aid in the repair of damaged tissues [73].

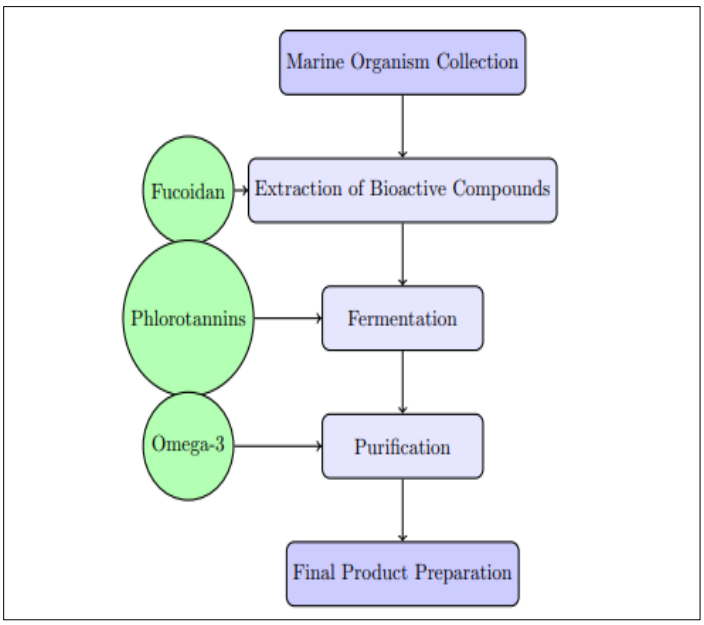


**Fig. 3: Schematic of biotechnological processes for marine bioactive compound production.** [74]

## 7. Current and Future Trends in Marine Drug Discovery

Exploring the enormous therapeutic potential of marine creatures, the dynamic area of marine drug development employs state-of-the-art technology and sustainable approaches. The development, manufacture, and discovery of pharmaceuticals derived from marine sources are being propelled forward by innovations in computational methodologies, sustainable sourcing, and omics technology [75].

### Omics Technologies

Genomic, proteomic, and metabolomic technologies have completely altered the way marine creatures and the bioactive substances they contain are studied. Scientists are able to discover novel therapeutic targets and decipher intricate chemical interactions with the help of these high-throughput technologies. Scientists can learn more about the molecular mechanisms of action and the pathways for production of bioactive chemicals in the ocean by using these technologies [76].

- **Genomics:** The discovery of new genes involved in the synthesis of bioactive chemicals has been made possible through the genomic sequencing of marine creatures, such as sponges, corals, and algae. By delving into genomic data, we can learn more about the evolutionary adaptations of marine animals and potentially identify the genes that give them their distinctive chemical characteristics. Metagenomics, which entails sequencing the genome of microbial communities as a whole, opens up new avenues for research into the genetic variety and bioactivity of marine microbes [77].

- **Proteomics:** Marine species' protein composition can be analyzed using proteomics technology, which could lead to the discovery of new therapeutic proteins or enzymes for medication development. Protein profiling and network identification allow scientists to learn more about the functions of marine proteins and how they could be used to treat cancer, inflammation, and other disorders [78].

- **Metabolomics:** Metabolomics involves the comprehensive analysis of metabolites in marine organisms, allowing for the identification of small molecules with therapeutic potential. By using advanced mass spectrometry and nuclear magnetic resonance (NMR) spectroscopy, scientists can identify bioactive metabolites, such as polyphenols, alkaloids, and lipids, which may be valuable candidates for drug development. Metabolomics can also provide a deeper understanding of how marine organisms adapt to their environments and how these adaptations can lead to the production of unique bioactive compounds [79].

**Computational Approaches**

The integration of computational methods in marine drug discovery is accelerating the identification and design of novel marine-derived drugs. These approaches enable researchers to screen large chemical libraries, predict drug-target interactions, and optimize the pharmacokinetic properties of bioactive compounds, making the drug development process faster and more efficient.

- **Computational Drug Design:** Virtual screening and molecular docking are commonly used to predict how marine-derived compounds will interact with biological targets. By using computational tools, researchers can simulate the binding of bioactive compounds to specific protein targets, assess their binding affinity, and predict their potential as therapeutic agents. This approach significantly reduces the time and cost of drug discovery by narrowing down the list of compounds for further experimental validation [80].

- **QSAR Models:** Quantitative structure-activity relationship (QSAR) models are used to predict the biological activity of marine-derived compounds based on their molecular structure. By analyzing the chemical structure of compounds and comparing them with known bioactive molecules, QSAR models can predict which marine compounds are likely to exhibit the desired therapeutic effects, such as anticancer or antimicrobial activity [81].

- **Machine Learning and AI:** Machine learning algorithms and artificial intelligence (AI) are increasingly being used to analyze large datasets generated from omics technologies and computational drug design. These tools can identify patterns in the data and make predictions about the potential efficacy and safety of marine-derived drugs. AI can also assist in optimizing the design of new compounds by suggesting structural modifications that may enhance bioactivity and reduce toxicity [82].

**Sustainability and Sourcing**

As the demand for marine bioactive compounds increases, ensuring their sustainable sourcing and production is critical to maintaining the health of marine ecosystems and meeting the growing needs of the pharmaceutical industry. Advances in biotechnology are helping to address these challenges by developing sustainable methods for harvesting and producing marine-derived compounds without depleting marine resources.

- **Sustainable Harvesting:** Overharvesting of marine organisms, such as algae and sponges, can threaten marine biodiversity and disrupt ecosystems. Sustainable harvesting practices, such as aquaculture and selective harvesting, are being developed to ensure that marine species are collected in an environmentally responsible manner. By establishing guidelines and regulations for sustainable harvesting, researchers and industries can minimize the ecological impact of marine drug discovery [83].

- **Biotechnological Production:** Advances in marine biotechnology, such as the use of marine bioreactors, offer a promising solution to the challenges of sourcing marine bioactives. Marine bioreactors allow for the large-scale production of bioactive compounds in controlled environments, reducing the need for wild harvesting. Furthermore, genetic engineering of marine organisms, such as algae and bacteria, can enhance the production of bioactive compounds in laboratory settings, ensuring a more reliable and sustainable supply of these compounds for drug development [84].

- **Marine Biotechnology and Circular Economy:** The concept of a circular economy in marine biotechnology is gaining traction, where waste products from marine organisms or industrial processes can be repurposed to create new bioactive compounds. For example, the by-products of algae cultivation, such as residual biomass, can be used to produce high-value bioactive compounds, reducing waste and promoting sustainability [85].

**CONCLUSION**

Marine organisms have long been a source of inspiration for drug discovery, and recent advances in biotechnology, omics technologies, and sustainable practices have significantly expanded their potential in pharmaceutical research. Through the identification and characterization of bioactive compounds from marine plants, algae, and microorganisms, we have gained valuable insights into their therapeutic properties and mechanisms of action. These compounds have shown great promise in addressing a wide range of diseases, including cancer, inflammation, cardiovascular disorders, and infections, positioning marine-derived drugs as vital contributors to modern medicine.

One of the most significant findings in recent years is the growing application of omics technologies, including genomics, proteomics, and metabolomics, which have enabled a deeper understanding of marine organisms and their biosynthetic pathways. These technologies, combined with computational methods like molecular docking and AI, are accelerating the identification and design of novel marine-derived drugs. Moreover, the development of marine bioreactors and genetic engineering techniques has improved the efficiency and sustainability of bioactive compound production, making these compounds more accessible for large-scale pharmaceutical applications.

Despite these advancements, challenges such as sourcing, bioavailability, and scaling production still exist. Addressing these issues through sustainable harvesting practices and biotechnological production methods will be key to ensuring a reliable supply of marine bioactives for drug development.

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