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Pharmacological Effects and Biological Activity Evaluation of Marine Bioactive Substances

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Abstract Marine bioactive substances refer to compounds with biological activity extracted from marine organisms, including but not limited to algae, sponges, mollusks, etc. These compounds have attracted great attention due to their widespread applications in fields such as medicine, drug development, and ecology. With the increasing impact of humans on the Earth's ecosystem, the study of marine bioactive substances also involves ecology and environmental science. Protecting marine biodiversity while exploring its potential medical and ecological applications has become an important part of maintaining ecological balance and human health. This review delves into the pharmacological effects and bioactivity assessment of marine bioactive substances, including their concepts, diversity, separation techniques, pharmacological properties, practical application cases, and potential medical applications, challenges, and prospects. However, its research still faces challenges of resource sustainability, high costs, and time investment. To address these issues, researchers encourage in-depth research on marine biodiversity and provide new perspectives in this field.

Keywords Active substances; Marine extract; Drug effects; Biodiversity; Medical applications

The ocean is one of the most mysterious, diverse, and underexplored ecosystems on Earth, filled with various biodiversity and potential pharmaceutical resources. Since ancient times, humans have been searching for bioactive substances with medicinal potential in the ocean, from the legendary stories of ancient sea explorers to breakthroughs in modern molecular biology and biotechnology. Marine biological resources have always been a hot research topic in the fields of medicine and pharmaceuticals. Research has shown that marine organisms contain a variety of biologically active compounds with anti-cancer, antibacterial, anti-inflammatory, and immunomodulatory properties (Xiao et al., 2022), sparking widespread interest among researchers.

Over the past few decades, many studies have made significant breakthroughs in isolating and identifying bioactive substances from marine organisms. For instance, anticancer compounds found in Atlantic seaweed (Nicolini et al., 2023) and antibiotics discovered in Pacific sponges are successful cases. These achievements have provided valuable resources for drug discovery and development. With the advancement of modern scientific and technological capabilities, scholars are unveiling the infinite possibilities in the ocean, which are expected to not only revolutionize the field of drug research and development but also have profound implications for global healthcare. However, despite some successes, the full potential of marine biological resources remains largely untapped, requiring further research and evaluation.

This study aims to delve into the pharmaceutical effects and bioactivity of marine bioactive substances, providing a framework for better understanding the nature, potential applications, and future development of these potential drugs. Researchers will explore the discovery and mechanisms of action of marine bioactive substances, revealing their potential applications in the medical field from new perspectives. This will help guide future research and development, bringing more innovation and hope to the global healthcare sector. Through this study, the authors hope to encourage a better utilization of marine biological resources and propel advancements in the field of drug development.

1 Concept of Marine Bioactive Substances

Marine bioactive substances refer to compounds that are isolated, extracted, or synthesized from the marine environment and exhibit biological activity. These compounds possess potential pharmaceutical value and can be utilized for treating various diseases or playing a role in the biomedical field (Chen et al., 2018). These substances can originate from various marine organisms, including seaweed (Figure 1), sponges, corals, microorganisms, marine animals, and more. Marine bioactive substances typically manifest multiple biological activities, endowing them with a broad range of potential applications in drug development, biomedical research, ecology, and other fields.

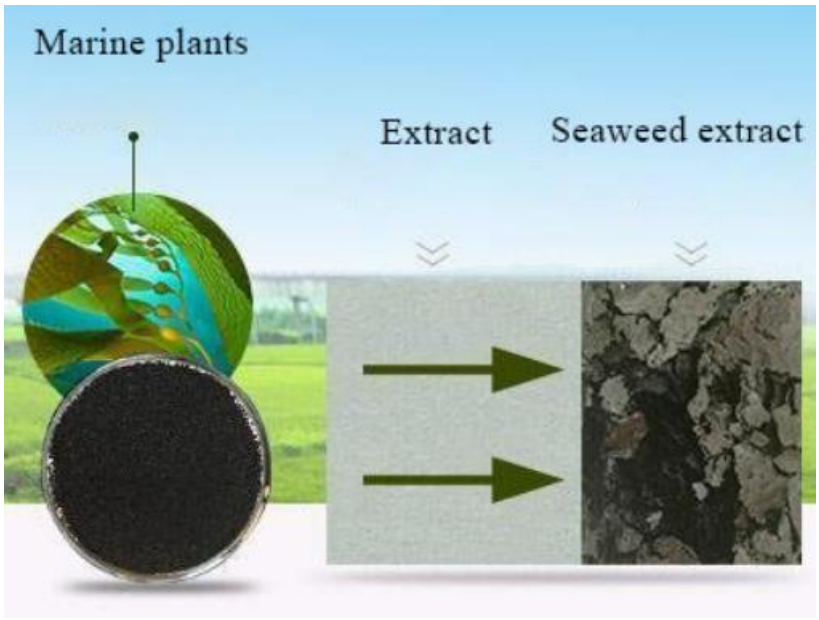

Figure 1 Active substances extracted from marine plants

1.1 Diversity of marine organisms

Marine ecosystems encompass a wide variety of life forms, ranging from microscopic plankton to massive whales, covering various kingdoms, phyla, and classes. The diversity of marine life is evident across different levels, including microorganisms, plankton, benthic organisms, seaweeds, corals, invertebrates, and vertebrates. The oceans harbor millions of species, many of which are yet to be scientifically described. An intriguing example is the microbial world, where the marine environment hosts an immense number of microbial communities, including bacteria, archaea, prokaryotes, and viruses. They play crucial roles in marine ecosystems, participating in vital ecological processes such as carbon cycling, nitrogen cycling, organic matter decomposition, influencing global climate, and maintaining ecological balance.

Additionally, the ocean contains a vast amount of plankton, including phytoplankton and zooplankton, which form the foundation of the marine food chain, providing a source of food for fish, whales, and other organisms. In the depths of the ocean floor, unique diversity of benthic organisms can be found. These organisms include various benthic invertebrates such as seabed crabs, sea cucumbers, corals, as well as various worms and sea stars. They constitute benthic ecosystems, offering essential ecological services such as water purification, waste decomposition, and maintenance of ecological balance.

The biodiversity in the ocean plays a crucial role in the stability and functioning of the global ecosystem. Marine organisms contribute to maintaining the balance of oxygen and carbon dioxide in the ocean and atmosphere, influencing climate regulation. Furthermore, marine life provides food, pharmaceuticals, and other resources, exerting a positive impact on the global economy and human society. It holds significant ecological, economic, and social value. Therefore, protecting marine biodiversity is essential to ensure that the Earth's largest ecosystem continues to provide a variety of ecological services and resources for humanity.

1.2 Definition of bioactive substances

Bioactive substances refer to compounds or molecules that exhibit biological activity or effects, capable of interacting with biomolecules within living organisms, triggering physiological or biochemical responses. These substances can originate from various biological sources, including plants, animals, microorganisms, and marine organisms, and find extensive applications in fields such as medicine, agriculture, food industry, and environmental protection. The diversity and functionality of bioactive substances make them a key area for scientific research and industrial applications.

Bioactive substances encompass a variety of biological activities, including anti-inflammatory, antioxidant, antibacterial, anticancer, immunomodulatory, antiviral, and more. They serve as active ingredients in pharmaceuticals, health supplements, cosmetics, and also find applications in ecological research, agricultural production, and environmental protection. The diversity of biological activities in these compounds stems from their structural and molecular characteristics, influencing biochemical pathways, metabolism, and signal transduction within organisms (Kandi et al., 2021).

Bioactive substances are often discovered in the natural world but can also be produced through chemical synthesis or biotechnological methods. Natural bioactive substances are sourced from diverse biological entities such as herbs, aquatic plants, marine organisms, microorganisms, insects, and animal organs. These natural products often possess complex chemical structures, including polycyclic compounds, polyphenols, alkaloids, and plant secondary metabolites. They play crucial ecological roles in ecosystems, such as attracting pollinators, resisting pests, and defending against predators.

Bioactive substances have significant applications in the field of medicine. Many commonly used drugs are derived from natural products or synthesized based on their prototypes, such as penicillin, aspirin, amoxicillin, etc., with widespread therapeutic applications. In the food industry, some bioactive substances serve as food additives, providing functions like antioxidant, antibacterial, and preservative properties. In agriculture, bioactive substances can be used for plant protection, fertilizer improvement, and growth regulation. From medicine to agriculture, food industry, and environmental protection, the diversity and functionality of bioactive substances make them an essential focus of biological research and industrial applications.

1.3 Discovery and isolation of marine bioactive substances

The discovery and isolation of marine bioactive substances is a complex and challenging process, typically involving multiple stages such as collection, extraction, separation, identification, and bioactivity assessment. This process requires the integrated application of techniques from various fields, including biology, chemistry, biotechnology, and analytical chemistry, to discover and study marine bioactive substances with potential pharmaceutical value. The discovery of marine bioactive substances usually begins with the collection of samples. These samples may include seawater, marine organisms, and seafloor sediments obtained from different marine regions and depths. Careful documentation of sample source information, including collection location, depth, and season, is essential for subsequent research and sample traceability.

Extraction is the next crucial step in discovering bioactive substances. The extraction process involves isolating the target compounds from collected biological samples. This can be achieved through various extraction methods, such as solvent extraction, supercritical fluid extraction, microwave-assisted extraction, etc. The choice of extraction method often depends on the nature of the target compounds and the type of samples. Separation is the subsequent step used to isolate complex extracts into individual purified compounds. This is typically accomplished through chromatographic techniques, which can separate compounds from a mixture based on their characteristics such as polarity, molecular size, molecular mass, etc. After separation, researchers obtain relatively pure target compounds.

Identification is the process of determining the structure and properties of the isolated compounds. This usually involves using a series of analytical techniques such as mass spectrometry (coupled with chromatography techniques), nuclear magnetic resonance (NMR) spectroscopy, infrared spectroscopy, and ultraviolet-visible

spectroscopy. These analytical methods help determine the molecular formula (Figure 2), structure, and chemical properties of the compounds.

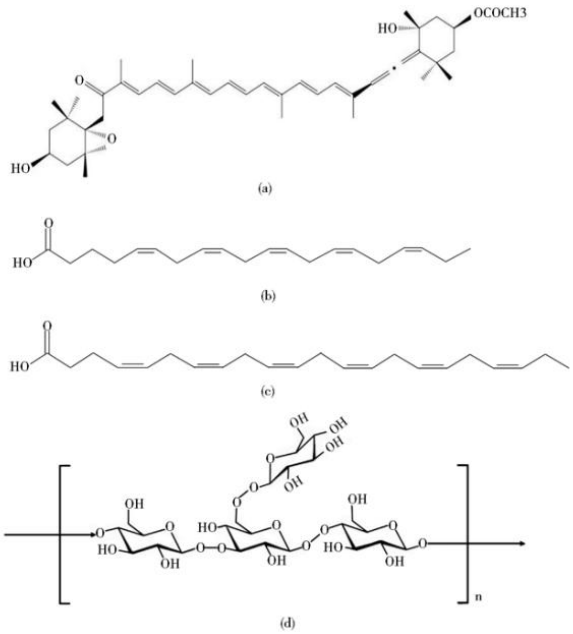

Figure 2 Separation of active substances from marine diatom production

Bioactivity assessment is a crucial step in understanding whether the isolated compounds possess biological activity. This involves both in vitro and in vivo experiments to determine the biological effects of the compounds within living organisms. In in vitro experiments, cell culture systems or biochemical analysis methods can be used to assess the biological activities of compounds, such as antioxidant, anti-inflammatory, anticancer, and antibacterial activities. In in vivo experiments, animal models can be employed to study the toxicity and pharmacological properties of the compounds. Once the bioactivity and pharmacological characteristics of marine bioactive substances are identified, researchers can further explore their potential applications. This may involve additional drug development, clinical trials, industrial applications, or ecological research.

2 Medicinal Effects of Marine Bioactive Substances

Marine bioactive substances exhibit a variety of medicinal effects, including anticancer, anti-inflammatory, antibacterial, antioxidant, neuroprotective, cardiovascular effects, and more. These bioactive substances have the potential to impact the field of medicine, offering new avenues for cancer treatment, management of autoimmune diseases, antibiotic development, cardiovascular health, antioxidant therapies, and the treatment of neurological disorders. The vast potential of marine biological resources brings new hope to the fields of medicine and biological sciences.

2.1 Drug discovery and development

The drug discovery and development of marine bioactive substances is a complex, multi-stage, and interdisciplinary process aimed at isolating, identifying, and studying compounds with potential pharmaceutical effects from marine organisms (You, 2019). This process typically begins with the collection of various types of marine biological samples, ranging from seaweed to sponges, corals, and microorganisms. These samples may originate from different global marine regions, as organisms in different areas may contain various types of bioactive substances. Once samples are obtained, researchers conduct preliminary bioactivity screening to identify which samples may contain potential drug activity.

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While the discovery and development of drugs from marine bioactive substances are time-consuming and expensive, it holds enormous potential for the discovery of new drugs and medical research. However, to protect marine biodiversity and ensure sustainable resource utilization, researchers and pharmaceutical companies typically adopt sustainable and responsible approaches. The continuous development of this field is expected to bring new hope and opportunities to global health and the medical field.

2.2 Pharmacological characteristics of marine bioactive substances

The pharmacological characteristics of marine bioactive substances refer to the properties of these compounds in terms of their mechanisms of action, physiological effects, metabolic pathways, and interactions with biomolecules within a living organism. Understanding these characteristics is crucial for drug development and clinical applications, as they determine the efficacy and safety of the compounds.

The pharmacological characteristics of marine bioactive substances typically include their mechanisms of action. This refers to how compounds influence biochemical processes and physiological functions within a living organism. For example, some marine bioactive substances may interact with specific receptors through particular pathways, triggering physiological responses (Fakhreddin et al., 2021). These responses may involve the regulation of cell signaling, changes in gene expression, promotion, or inhibition of protein synthesis, among others. Understanding the mechanism of action helps determine the potential therapeutic effects of the compounds.

Metabolic pathways are also essential pharmacological characteristics of marine bioactive substances. Metabolic pathways involve the processes of metabolism and transformation of compounds within a living organism. Understanding metabolic pathways helps determine the bioavailability, pharmacokinetics, and drug interactions of compounds. Some compounds may become more active or inactive after metabolic reactions, and they may be excreted from the body through metabolic pathways. Additionally, pharmacological characteristics encompass bio-distribution, including the distribution, absorption, secretion, and accumulation of compounds within an organism. Different compounds may distribute within the body in different ways, influencing their bioavailability and efficacy.

2.3 Currently marketed marine-derived drugs

There are currently several drugs derived from marine organisms available in the market, and they are widely used in various fields, including medicine, ecology, and biotechnology (Gammone et al., 2020). Arabinose is a five-carbon sugar commonly found in plants and microorganisms rather than marine organisms. It is typically obtained through the hydrolysis of plant polysaccharides or microbial fermentation processes. Arabinose is a biologically active substance with diverse applications, particularly in the food industry, biotechnology, and medicine.

Arabinose, a polysaccharide compound derived from seaweed, has found extensive use in the food industry and biotechnology. In biotechnology, it serves as a carrier, providing stability and protection in cell cultivation and protein production processes. Arabinose is also utilized in the preparation of lyophilized drugs and oral formulations due to its excellent protective properties.

In the food industry, arabinose is employed as a food additive to enhance the texture, taste, and stability of various food products, including sauces, jellies, candies, yogurts, and ice creams. In biotechnological applications, arabinose is a crucial carrier molecule used in molecular biology and genetic engineering experiments (Figure 3).

It is widely employed in cell and microbial cultivation to stabilize and protect target molecules such as DNA, RNA, and proteins. Although arabinose is not a drug itself, it plays a significant role in the pharmaceutical industry. It can be used as an excipient to enhance the stability and bioavailability of drugs. Additionally, arabinose is employed in the preparation of lyophilized drugs to extend their shelf life. From the food industry to biotechnology and drug preparation, as a polysaccharide, it exhibits excellent water solubility and multifunctionality, thus playing a crucial role in these fields.

Figure 3 Arabinose used in industry

3 Potential Medical Applications of Marine Bioactive Substances

Marine bioactive substances exhibit a wide range of potential medical applications. Some of these compounds have made significant strides in pharmaceutical research, offering new possibilities for treating various diseases. For instance, Eribulin derived from marine sponges has been approved for the treatment of breast cancer and soft tissue sarcoma. It inhibits tumor cell proliferation and migration by disrupting microtubule dynamics, providing a novel therapeutic option for cancer patients. Additionally, certain marine bioactive compounds demonstrate anti-cancer, anti-tumor, and anti-angiogenesis activities, opening new avenues for cancer treatment.

Marine bioactive substances also show potential in the fields of anti-inflammatory and immune regulation, contributing to the treatment of autoimmune diseases and inflammatory conditions. Some marine-derived extracts have displayed potential efficacy against immune-related diseases such as rheumatoid arthritis. Moreover, certain components of marine bioactive extracts exhibit antibacterial and antiviral activities, contributing to the development of new antibiotics, antiviral drugs, or antimicrobial compounds, playing a role in addressing antibiotic-resistant bacteria and emerging viruses. Ziconotide, a marine-derived toxin, has been utilized in treating refractory pain through its regulation of neural signal transmission.

Antioxidants represent another crucial application of marine bioactive substances, aiding in defense against oxidative stress caused by free radicals. This can slow down the aging process, prevent chronic diseases, and improve skin health. These antioxidants find applications in cosmetics and skincare products and hold potential uses in nutritional supplements. Marine bioactive substances also demonstrate neuroprotective properties, offering potential treatments for neurological disorders such as Parkinson's disease, Alzheimer's disease, and neurodegenerative diseases. These compounds can alleviate damage or death of nerve cells, providing potential therapeutic options for these diseases. Furthermore, certain components can influence the cardiovascular system, including lowering blood pressure, improving cardiovascular health, and reducing the risk of heart disease, holding significance for patients with hypertension and cardiovascular conditions.

4 Potential Challenges and Prospects of Marine Bioactive Substances

Marine bioactive substances hold exciting potential, yet they face certain challenges that must be acknowledged and addressed for broader applications and sustainable resource management. One significant challenge is the

sustainability of resources. While marine biodiversity is one of the richest ecosystems on Earth, overharvesting and environmental degradation may threaten the continuous existence of this valuable resource. Protecting marine biodiversity and ensuring responsible resource management require international cooperation to develop and enforce policies and regulations that uphold the sustainability of marine biological resources.

Another challenge involves the cost and complexity of collecting and extracting biological samples. Deep-sea collection requires expensive research vessels and submersibles, and the extraction and isolation of compounds demand sophisticated laboratory equipment and techniques. This increases the costs of research and development, limiting the involvement of many researchers. Therefore, scientists need to develop more cost-effective collection and isolation methods to reduce expenses and facilitate widespread research. Additionally, the time and resources required for drug development pose a significant challenge. Moving from the discovery of new compounds to bringing them to the market demands substantial time and funding. Clinical trials, regulatory approvals, and large-scale production all entail considerable investments, potentially hindering the further development of promising marine bioactive compounds due to resource constraints.

With the continuous advancement of scientific technologies, researchers are expected to unlock more marine biological resources, discovering new compounds and applications. These compounds exhibit diverse biological activities applicable to treating various diseases, from cancer to infectious diseases and neurological disorders. The diversity of marine bioactive substances positions them as potential sources for multi-sector applications. Beyond drug development, they can find utility in the food industry, biotechnology, cosmetics, and environmental protection, presenting opportunities for different industries to enhance product quality and performance.

Most importantly, the research and application of marine bioactive substances offer new hope for global health and medical advancements. Novel drugs and treatment methods have the potential to improve patients' quality of life, enhance the efficiency of disease treatment, and address emerging threats such as antibiotic-resistant bacteria and viruses. Research on marine bioactive substances also contributes to expanding our understanding of biodiversity, providing new insights into ecology and environmental science.

5 Summary

This study delved into the pharmaceutical potential and bioactivity assessment of marine bioactive substances, covering their definition, diversity, discovery and isolation, pharmacological properties, practical applications, potential medical uses, challenges, and prospects. Marine bioactive substances are a valuable resource with enormous potential for drug development and application.

These substances have already provided new treatment options in various medical applications, including anti-cancer, anti-inflammatory, antiviral, antibacterial, antioxidant, neuroprotective, and cardiovascular fields, improving patients' quality of life and enhancing disease treatment efficiency (Riccioni et al., 2021). Furthermore, research in this field contributes to expanding our understanding of biodiversity, offering new insights for ecology and environmental science, and promoting sustainable resource management and environmental protection.

In future research directions, scholars are encouraged to delve into marine biodiversity, discover new bioactive substances, and unravel their pharmacological properties. Additionally, promoting interdisciplinary research and fostering collaboration between medicine, ecology, and biotechnology is a direction that requires effort. Better leveraging the precious resource of marine bioactive substances can be achieved through such collaborative efforts. The potential medical applications of marine bioactive substances offer new hope for global health and sustainable development, requiring collective efforts from the global community to realize their potential and provide broader prospects for future research and applications.

Maintaining the sustainability of marine biological resources has potential impacts on preserving marine bioactive substances. This involves establishing and enforcing resource management policies and regulations to control the quantity and methods of collection and fishing, preventing overexploitation and destructive fishing activities. Additionally, establishing marine protected areas at the national level is an important method to protect specific

marine organisms and ecosystems, limiting human activities. Continuous scientific research and monitoring help understand the status of marine biological resources, enabling better management strategies and alerting to any adverse trends. Adopting sustainable fishing and collection methods can reduce damage and waste, ensuring the renewability of resources. International cooperation is crucial to share information and best practices, protecting and managing global marine biological resources. The integrated application of these methods can help fully utilize this precious resource while safeguarding marine ecosystems to benefit future generations.

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