Bioactive Compounds and Nutraceuticals from Seaweeds

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Introduction

Studies delving into the natural product chemistry and chemical defense systems of seaweeds have unearthed a treasure trove of bioactive leads with significant pharmacological activities. Compounds like phlorotannins, sulfated polysaccharides, and polyphenols from seaweeds have demonstrated anti-proliferative effects against cancer cells and exhibited anti-inflammatory and anti-diabetic responses. These bioactive components also showcase the potential to modulate glucose-induced oxidative stress and regulate the presence of starch-digestive enzymes. In the quest for alternatives to synthetic drugs and their potential side effects, naturally obtained bioactive components from seaweeds have emerged as promising candidates for addressing persistent metabolic syndromes. Seaweed-derived functional food ingredients not only offer pharmaceutical advantages but also boast a myriad of bioactivities against various diseases. The last decade has witnessed a surge in scientific publications and patents, underscoring the growing interest in marine macroalgaebased bioactive compounds and functional food ingredients. Patents granted from 1995-2019 reflect the increasing importance of bioactive compounds from these species. The upward trend in patents related to marine natural product research, particularly their pharmacological effects, has captured the attention of marine natural product chemists and medical researchers, emphasizing the potential of this diverse phylum.

Exploration of seaweeds for bioactive compounds: a potential frontier in pharmaceutical and nutraceutical industries

The rich diversity of seaweeds along the Indian subcontinent's coastline represents an untapped reservoir of bioactive compounds with valuable pharmaceutical and biomedical applications. Brown and red seaweeds (classes Phaeophyceae and Rhodophyceae) stand out as potential sources of bioactive substances. While the global utilization of seaweeds is a multi billion-dollar industry, their bioactive potential remains underexplored. Traditionally limited to traditional and folk medicines, the medicinal properties of seaweeds have gained attention from industries in cosmetics, pharmaceuticals, and food in recent years.

The Central Marine Fisheries Research Institute in India has played a pivotal role in unraveling a database of seaweeds with small molecular weight bioactive molecules, combatting various life-threatening diseases. Nutraceutical products addressing arthritis, type-2 diabetes, osteoporosis, dyslipidemia, hypothyroidism, hypertension, and immune-boosting agents have been licensed to biopharmaceutical companies for commercial production and marketing in India and abroad. This initiative not only benefits health but also supports commercial farming in coastal habitats, benefiting marine macroalgal farming communities. Consumer interest in marine natural bioactive compounds and nutraceuticals as functional ingredients in foods is on the rise, positioning seaweeds as alternative sources for synthetic ingredients that contribute to consumer well-being. Marine macroalgae, being fast-growing and potentially renewable resources, are gaining attention as novel and sustainable sources for both pharmaceutical and nutraceutical applications. With the nutraceutical market in India growing at a compound annual growth rate of 20% over the past three years, and recent government efforts to clarify regulatory protocols, the future appears promising for this segment. The development of value-added products from underutilized marine macroalgal species holds the potential to expand opportunities for their downstream value chain, enhancing the livelihoods of resource-poor fisherfolk and budding entrepreneurs across the coastal belt. Coupled with renewed policy focus, the marine macroalgae-based value chain is gaining momentum, poised to create new market opportunities in the country.

Fig.1. Nutraceuticals from seaweeds for use against type-2 diabetes, obesity/ dyslipidemia, hypertension, osteoporosis, hypothyroidism, rheumatoid arthritis and as immune-boost agent

Seaweed nutraceuticals and bioactive compounds

Seaweeds are commanding increasing attention in the nutraceutical industry due to their potent protective capabilities against various chronic diseases (Chakraborty *et al.*, 2021; Dhara and Chakraborty, 2023). These marine wonders, often referred to as the 'wonder herbs of the ocean,' proliferate along the coastal shelves of India, showcasing significant pharmaceutical potential (Chakraborty *et al.*, 2018; Gangadhar *et al.*., 2021). The Indian nutraceutical market has experienced a robust compound annual growth rate of 20% over the past three years, with a focus on functional food products, antioxidants, and immunity boosters, fueled by increasing health awareness and a shift towards preventive healthcare (Chakraborty *et al.*, 2022). Nutraceuticals, defined as 'concentrated, isolated, or purified' pharmacologically bioactive molecules, find a distinctive intersection in seaweed-based products, serving as naturally derived concentrated pharmacologically active compounds, essentially functioning as 'Natural Drugs.' Recent government efforts to clarify regulatory protocols related to nutraceutical products have spurred rapid growth in this segment.

Beyond primary metabolites, seaweeds harbor a diverse array of structurally varied secondary metabolites that exhibit significant potential for various biological activities (Gangadhar *et al.*, 2020; Chakraborty and Anusree, 2020b). Synthesized in response to environmental stressors such as temperature fluctuations, changes in salinity, nutrient variations, exposure to ultraviolet radiation, and pollution, these bioactive compounds include polysaccharides, phenolics, proteins, peptides, terpenes, terpenoids, carotenoids, sterols, dibutanoids, acetogenins, alkaloids, and more (Chakraborty and Joseph, 2016). It is these compounds that underlie the health-promoting properties associated with seaweeds. Evolved as a defense mechanism to thrive in the complex oceanic environment, seaweeds' diverse bioactive secondary metabolites have been extensively studied, revealing numerous beneficial components (Dhara and Chakraborty 2021). These components offer a range of health benefits, including antioxidation, anticancer and antibacterial activity, chemoprevention against vascular diseases, and mitigation of complications arising from diabetes (Chakraborty *et al.,* 2017). Seaweeds are now hailed as a medicinal food of the 21st century, owing to their exceptional nutritional value and the wealth of bioactive compounds they possess.

Recognizing the significance of these bioactive compounds, the ICAR-CMFRI has established a research program systematically identifying seaweed species for developing promising bioactive molecules with potential applications in human health and medication. Over 12 bioactive products with nutraceutical applications have been successfully developed and commercialized, targeting lifestyle diseases such as

rheumatic arthritis, diabetes, hyperlipidemia, hypothyroidism, hypertension, osteoporosis, non-alcoholic fatty liver disease, boosting immunity, and reducing post COVID complications (Chakraborty *et al.*, 2018; Gopalakrishnan *et al.*, 2020; Chakraborty *et al.*, 2021; Dhara and Chakraborty, 2023). These efforts have led to technology transfer agreements, fostering business relations between the ICAR institute and various public and private organizations.

Traditional and medicinal marvels of seaweeds

Seaweeds boast a millennia-spanning history of traditional use across diverse cultures, with roots dating back thousands of years. These oceanic plants have played pivotal roles in traditional medicine worldwide, offering remedies for an array of ailments. In the present era, their applications are still unfolding in modern medicine, underscoring their potential as invaluable resources. As early as 13,000 - 300 BC, seaweeds were seamlessly integrated into traditional folk medicine in Japan, a practice mirrored in ancient China, Egypt (1,550 BC), and India (300 BC). Notably, *Sargassum* spp. found a place in traditional Chinese medicine around 2,000 years ago, addressing conditions such as goiter. Ancient Romans turned to seaweeds for wound care, burns, and rashes. *Capsosiphon fulvescens* was a traditional remedy for stomach disorders and hangovers, while *Ulva pertusa* addressed urinary diseases, sunstroke, and hyperlipidemia (Qi *et al.*, 2006). Codium fragile tackled dysuria, dropsy, and enterobiasis, and *Gloiopeltis tenax* was a traditional aid for diarrhea and colitis (Liu *et al.*, 2012; Pati *et al.*, 2016). The influence of seaweeds in medicine persists in the contemporary era. *Laminaria* sticks, for instance, assist in softening and dilating the cervix, aiding in surgical abortion or childbirth. Specific *Sargassum* species provide cooling and blood-cleansing effects. Iodine-rich seaweeds like *Asparagopsis taxiformis* and *Sarconema* sp. are harnessed to control goiter. Red seaweeds such as *Hypnea musciformis*, *Corallina officinalis*, and *C. rubens* serve as *vermifuges*, and *Gracilaria* and *Gelidium* are known remedies for stomach pain and intestinal disorders. Beyond these applications, seaweeds showcase therapeutic potential in antiviral properties. *Gelidium cartilagineum*, for example, exhibits activity against influenza B and mumps viruses (Nakashima *et al.*, 1987). Seaweed extracts, such as those from Enteromorpha, display effectiveness against tuberculosis. Compounds like fucoidan derived from seaweeds hold promise for treating chronic stomach inflammation, peptic ulcer diseases, and gastric cancers. Fucoidans also show potential in managing blinding diseases, including diabetic retinopathy and age-related macular degeneration. Seaweed consumption has been linked inversely to cardiovascular mortality, especially cerebral infarction, among Japanese men and women. Fucoxanthin, found in brown algae, proves beneficial in

improving insulin resistance, reducing blood glucose levels, and decreasing cytokine production in adipose tissue, thereby mitigating cardiovascular disease risks in diabetic patients. A seaweed extract nutrient complex demonstrates the ability to alleviate osteoarthritis symptoms in a dose-dependent manner when taken orally. Seaweeds are at the forefront of innovative antiviral drug development. Sodium oligomannate, an oligosaccharide from seaweed, has received approval in China for treating Alzheimer's disease, marking the first novel drug sanctioned for Alzheimer's treatment worldwide since 2003 (Syed, 2020). In essence, seaweeds persist as fountains of traditional remedies and frontiers for modern medicinal applications, offering a spectrum of potential benefits.

Conclusions

Seaweeds are often celebrated as the ocean's wonder plants due to their remarkable ability to biosynthesize valuable bioactive compounds and nutraceuticals. These marine resources are truly unique, offering a wide range of economic applications and ecological significance, positioning them as a cornerstone of the blue economy. Ecofriendly startups worldwide are dedicated to creating innovative products from seaweeds, such as bioplastics and functional foods. The exploration of bioactive compounds from seaweeds with potential health benefits is an emerging area of research. The Indian nutraceutical market has experienced significant growth, maintaining a consistent compound annual growth rate of 20 percent over the past three years. Driven by increasing health consciousness and a shift towards preventive healthcare, India's prospects in this sector appear highly promising. It is anticipated that India's nutraceutical industry will secure a substantial 3.5 percent share of the global market by 2023, with projected growth from an estimated $4 billion to an impressive $18 billion by the end of 2025.

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