THE ROLE OF SEAWEEDS IN BLUE BIOECONOMY

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PREFACE

With the ever-increasing global population, the demand for food and all other services is rising, while the availability of suitable land for agricultural and other essential human activities is decreasing. In this context, marine bioresources have recently gained much attention as a sustainable alternative to meet the increasing demand for land-based agricultural activities. Thus, the term 'blue bioeconomy' has come into play, and many businesses are starting to consider marine bioresources as a sustainable approach to fulfill the growing demand gap associated with the increasing population and depletion of non-biogenic resources such as fossil fuel. With the growing demand for blue bioeconomy-related activities, it is necessary to understand and use the limited resources responsibly in a sustainable manner to ensure the use of these precious resources for future generations without degradation. Specifically, we want to prioritize major and minor marine bioresources in order to fully utilize them and conserve them. Just commercializing these precious marine bioresources without knowing their availability, applications, and potential could lead to another disaster for future generations.

With this basic idea, the editors have summarized the potential marine bioresources that play a significant role in the blue bioeconomy. Among the listed marine bioresources, seaweeds stand out as one of the ideal options that can be utilized in various industries, including food, biomedical applications, cosmeceuticals, nutraceuticals, functional ingredients, animal feeds, and the biofertilizer industry. Given these key roles, seaweeds have a substantial impact on the blue bioeconomy and are significant for future generations.

In this book, we aim to assist individuals, including industrialists, policymakers, scientists, and students globally, in understanding and effectively communicating the role of seaweed in the blue bioeconomy. We introduce important applications of seaweeds, starting with an explanation of the blue bioeconomy. The book then proceeds to highlight the morphology and nutritional profiles of seaweeds, along with other potential marine organisms such as microalgae, marine fungi and bacteria, and marine higher plants. Subsequently, the book delves into detailed explanations of major biomedical applications, including anticancer, antidiabetic, cardiovascular protection, and antivirus effects. Continuing the exploration, the book delves into various functional properties of seaweeds, with a particular emphasis on their antiaging and cosmeceutical-related applications. Extensive discussions in most chapters unravel the intricacies of these properties. As the narrative unfolds, the final chapters meticulously dissect additional commercial applications of seaweeds, shedding light on their significance as essential components in animal feed and biofertilizers.

We, the editors and authors of this book, are delighted to recommend this enlightening journey, "*The Role of Seaweeds in Blue Biotechnology*", to all interested parties, including industrialists, policymakers, scientists, and university students. This comprehensive exploration not only unveils the diverse applications of seaweeds but also serves as a valuable resource for understanding their pivotal role in shaping the future of blue biotechnology. We invite you to join us on this insightful expedition and discover the immense potential these marine wonders hold for various sectors and the for sustainable development of our blue planet.

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CHAPTER 1

A Basic Introduction to Blue Bioeconomy

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Abstract: The blue bioeconomy represents a transformative approach to harnessing the vast potential of marine resources for sustainable development. As the demand for food, energy, and materials continues to rise, the sustainable utilization of marine ecosystems offers a promising solution to meet these challenges while conserving terrestrial resources. The blue bioeconomy encompasses a broad range of sectors, including fisheries, aquaculture, marine biotechnology, and coastal tourism, among others. By capitalizing on the inherent biological diversity of the oceans, it seeks to unlock innovative pathways for economic growth, job creation, and environmental stewardship. This transition from traditional practices to a more sustainable and knowledge-based approach requires careful consideration of ecological, social, and economic factors. One of the primary advantages of the blue bioeconomy lies in its potential to provide alternative sources of protein and other essential nutrients through sustainable fisheries and responsible aquaculture practices. Additionally, marine biotechnology offers vast potential for the development of novel drugs, biomaterials, and biofuels, leveraging the unique properties of marine organisms. These innovations are Promising in addressing pressing global challenges, such as food security, climate change mitigation, and the transition to renewable energy sources. The blue bioeconomy represents a transformative pathway towards sustainable development, utilizing the diverse resources and ecosystems of our oceans. By adopting a holistic approach that integrates environmental, social, and economic considerations, the blue bioeconomy holds the potential to drive economic growth, enhance food and energy security, and contribute to the conservation and restoration of marine ecosystems. Embracing this approach is crucial for building a more sustainable and resilient future for our planet and future generations.

Keywords: Aquaculture, Biotechnology, Bioprospecting, Bioeconomy, Coast, Marine, Seaweeds.

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INTRODUCTION

The term bioeconomy generally refers to the part of the economy that is based on biology and biosciences. However, the definition of the term varies across different regions, and there is no single, universally accepted definition. In general, the concept is associated with the sustainable and renewable use of biological resources from both land and sea for the production of various goods and services in all economic sectors. Many definitions emphasize the importance of this approach at both the upstream and downstream stages of the value chain [1]. Different colors have been used to classify bioeconomy based on their focus and application. The green bioeconomy represents agricultural genetic engineering and other biotechnologies to improve crop traits and produce biofertilizers. The white bioeconomy focuses on the use of biotechnology to develop industrial products, such as ethanol, limonene, and polylactic acid through biorefinery, the red bioeconomy represents the production of diagnostic drugs using cell technology and genetic engineering for medicine and human health and the gray bioeconomy involves the use of waste as a resource for the production of energy and materials [2]. The colors of the biotechnology are summarized in Table **1**.

Table 1. Major categories of biotechnology by color.

Color	Fields	Reference
Black	Bioterrorism and crime	[9]
Blue	Marine (aquatic) resources for food, technology, medicine, and bioactive metabolites	[9, 10]
Brown	Biotechnology applied to deserts and arid regions	[9]
Gold	Nanobiotechnology and bioinformatics	[9]
Grey	Biotechnology related to environmental protection	[11]
Green	Agricultural genetic engineering and other biotechnologies to improve crop traits and produce biofertilizers	[9, 12, 13]
Red	Production of diagnostic drugs using cell technology and genetic engineering for medicine and human health applications	[11]
Violet	Related intellectual property, invention patents, and publications	[9]
White	Industrial biotechnology for the production of bio-based substances (ethanol, limonene, and polylactic acid) through biorefinery	[6, 11, 12]
Yellow	the fields of food biotechnology and nutritional science	[2]

Marine ecosystems play a significant role in promoting sustainable development and the overall health of the planet. Ocean ecosystems generate oxygen, absorb carbon dioxide, recycle nutrients, and regulate global climate and temperature, making them essential for all life on the Earth. Oceans are not only a fundamental partof the Earth's ecosystem, hosting a wide range of uncatalogued life diversity, but also an undervalued economic powerhouse with a high gross marine product value [3]. Furthermore, marine ecosystems serve as a source of food, livelihood, and tourism and have the potential to help achieve sustainable development goals, such as eliminating hunger and poverty [4]. Additionally, the deep sea or seabed provides hydrocarbons and mineral resources, accounting for 32% of the global supply. The ocean also offers renewable energy sources like wind, wave, tide, and thermal and biomass sources [3, 5]. Due to the increasing demand for resources to meet the global food-water-energy nexus and the rapid decline in land-based sources, oceans have become a crucial solution for promoting a sustainable environment and economy. Consequently, in the last decade, many industries and researchers have focused on developing marine bioresource-based products and applications (blue bioeconomy) [6, 7].

The blue economy consists of biological and non-biological components of marine bioresources. In 2012, UNEP published a synthesis report that introduced the concept of a “Green economy in a Blue world.” The report emphasized the significance of the marine environment as an essential component of a paradigm shift toward a sustainable bioeconomy, which was subsequently termed the “blue economy” by Pacific Small Island Developing States [3]. In general, the blue economy is a systematic approach to utilizing ocean resources, combining short and long-term economic activities based on principles of social inclusion, environmental sustainability, and innovation in and around the sea. However, instead of solely focusing on the blue economy, the concept of blue bioeconomy has gained prominence in recent years as a means of promoting the sustainable use of marine resources. Based on different definitions given by different agencies, the blue bioeconomy can be defined as a subset of the blue economy that specifically targets the extraction of marine biomass for various applications, such as material production, food and feed, energy generation (such as ethanol and biogas), and chemical production (such as fertilizers) [8].

MAJOR SECTORS OF BLUE BIOECONOMY

The blue bioeconomy represents an emerging economic paradigm that recognizes the importance of marine and freshwater resources for economic growth and sustainable development. Blue bioeconomy encompasses several sectors that deal with marine and freshwater ecosystems, such as marine fisheries, aquaculture, algal biomass and freshwater fishing fisheries, marine biotechnology, eco-tourism, etc [14, 15]. Over the past few decades, there has been consistent and gradual growth in the use of marine resource biotechnology for commercial purposes. By the year 2020, the market for products derived from marine

CHAPTER 2

What is Seaweed? General Facts about Seaweeds

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Abstract: Seaweeds are rich sources of various nutrients and bioactive compounds, which offer several health benefits. They contain high levels of vitamins, minerals, fiber, and protein, making them a valuable addition to a balanced diet. Seaweeds are particularly rich in iodine, an essential mineral that plays a crucial role in thyroid function and overall metabolism. They also contain significant amounts of iron, calcium, magnesium, potassium, and other trace minerals that are essential for human health. Moreover, seaweeds are known for their bioactive compounds, such as polysaccharides, phlorotannins, carotenoids, and polyunsaturated fatty acids, which have been linked to several health benefits, including anti-inflammatory, antioxidant, antimicrobial, and anticancer properties. Studies have shown that consuming seaweed may help to reduce the risk of chronic diseases, such as cardiovascular disease, diabetes, and certain types of cancer. Seaweeds may also improve gut health by acting as a prebiotic, promoting the growth of beneficial gut bacteria. In the present chapter, the authors focus on briefly summarizing the bioactive properties of secondary metabolites identified from seaweeds and their therapeutic potential as supportive information for the next chapters in this book.

Keywords: Macroalgal compounds, Macroalgal functional potentials, Macroalgal therapeutic effects, Seaweed bioactivities, Seaweed bioactive compounds.

INTRODUCTION

Seaweeds stand out as rich repositories of various nutrients and bioactive compounds, offering an array of health benefits. With elevated levels of vitamins, minerals, fiber, and protein, they contribute significantly to a well-rounded and

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nutritious diet. Seaweeds are also rich in minerals such as iron, calcium, magnesium, potassium, and other trace minerals essential for maintaining human health. Beyond their nutritional content, seaweeds are renowned for harboring bioactive compounds like sulfated polysaccharides, phlorotannins, carotenoids, and polyunsaturated fatty acids, all linked to a spectrum of health-promoting properties ranging from anti-inflammatory and antioxidant effects to antimicrobial and anticancer potentials. Extensive research suggests that the regular consumption of seaweed may play a role in reducing the risk of chronic diseases, encompassing cardiovascular ailments, diabetes, and specific types of cancer. Furthermore, the prebiotic qualities of seaweeds can positively influence gut health by fostering the growth of beneficial gut bacteria. This chapter serves to provide a concise overview, summarizing major categories of seaweeds, their ecological and evolutionary facts, and bioactive properties of secondary metabolites identified from seaweeds.

SEAWEEDS

Seaweeds are marine, photosynthetic, macroscopic, multicellular, and eukaryotic organisms and germinate in the intertidal and subtidal areas of the sea [1]. Algae, especially seaweeds, are an extremely fascinating source of nutritious foods as well as a naturally occurring source of biologically important compounds that could be used as functional ingredients, constituting a research area with many opportunities to explore food [2]. Seaweed consumption in Western diets has long been restricted to artisanal techniques and coastal communities, but in recent years, thanks to the health-food business, consumer interest has expanded [3].

In the food industry, seaweed is primarily employed as a source of hydrocolloids. Some seaweeds have gained attention in recent years just as a potential source of natural bioactive substances with potential uses in nutraceuticals, cosmeceuticals, and pharmaceuticals [4]. Approximately 27.3 million tonnes (96%) of the world's seaweeds are produced annually through aquaculture that is recognized as the most sustainable method. However, the rising demand for seaweed-based food ingredients necessitates the establishment of more rigid rules and regulations to ensure sustainability [3].

In China, Japan, and Korea as well as several Latin American nations like Mexico, seaweed has been used traditionally as food for many centuries [5]. Because of their widespread migration, the inhabitants of these nations brought this custom with them, and as a result, seaweed consumption is now commonplace in a large number of nations [6]. Seaweed has been successfully incorporated into European cuisine in recent years thanks to a strong movement in France, however, it is still viewed as an exotic ingredient on the menu [7].

Seaweeds are taxonomically classified into three main phyla: Phaeophyceae (brown), which have a brown color due to the presence of the xanthophyll pigment fucoxanthin; Chlorophyceae (green), which contain chlorophylls 'a' and 'b' as well as other specific xanthophyll pigments; and Rhodophyceae (red), which obtain their color from phycobilins [8, 9]. There are about 4000 red seaweeds, 1500 brown seaweeds, and 900 green seaweeds in existence today [10]. Seaweeds play a remarkable role in aquaculture around the world. Brown seaweeds and red seaweeds, which were among the largest species categories in worldwide aquaculture in 2019, provided roughly 30 percent of the 120 million tonnes of aquaculture production in 2019 when assessed in wet weight [11].

EVOLUTIONARY AND ECOLOGICAL FACTS ABOUT SEAWEEDS

It has been suggested that seaweeds may have had a more significant ecological impact in the past, particularly during the early Paleozoic [12]. However, due to the scarcity of seaweed fossils and the focus on animal development, seaweed evolution and ecological effects have largely been disregarded, leaving us with a partial understanding of early marine ecosystems. There are still some unanswered questions regarding the evolution of macroalgae over time. The estimates from molecular clocks show that significant evolutionary events took place in the Proterozoic period [12]. Seaweeds are made up of red, green, and brown lineages that separately develop from unicellular algae progenitors. Rhodophyta or red algae have existed for ages. Both Bangiomorpha and Raffatazmia, which may be interpreted as red algal fossils, suggest that multicellular red algae first appeared in the Mesoproterozoic era between 1.0 and 1.6 billion years ago [13].

Marine ecology depends significantly on macroalgae for its ecological health. They create oxygen and absorb carbon dioxide. Seaweeds react to several climatic and physicochemical elements. Their ability to grow, survive, and reproduce depends on and varies with a wide range of critical environmental factors, including temperature, hydrodynamics and wave exposure, salinity, nutrients, pH, and carbon dioxide. Because they are the main and secondary producers, and because they safeguard coastal areas and serve as nursery grounds, algae perform a crucial regulatory role in the aquatic ecosystem. Additionally, seaweeds provide a variety of food for aquatic animals, and also provide for a wide spectrum of invertebrates. Additionally, seaweeds have economic significance for society and contribute to the cultural history and distinctiveness of each region [14]. The interaction with its microbiota has a significant influence on how seaweed functions and, consequently, the ecological benefits and economic uses it offers. The effects of this interaction on seaweed's morphology, settling, reproduction, and generation of physiologically active metabolites are only a few examples. The

CHAPTER 3

Potential Blue Bioresources to Develop Functional Foods

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Abstract: Functional foods are foods with therapeutic properties that enhance health along with nutritional properties. This review provides information about the potential of using marine ingredients to develop functional foods by elaborating on the nutritional and therapeutic effects of bioactive compounds found in marine bioresources. Microalgae, marine fungi, bacteria, marine invertebrates, vertebrates, and marine plants are marine resources, and some of the bioactive compounds obtained from marine resources are polysaccharides, fatty acids proteins, peptides, amino acids, many types of essential macro and trace elements, pigments, and phenolic compounds. Marine bioactive compounds have shown many therapeutic properties, including anticancer, antimicrobial, antioxidant, anti-proliferative, anti-inflammatory, anti-diabetic, and immune regulatory activities. These compounds can be used in the functional food industry in the form of nano or micro-particles, liposomes, gels, liquids, solids, pastes, and emulsions to overcome the challenges that could occur during product formulation and processing. Overall, this book chapter reveals the important facts about marine bioresources (except Seaweeds) and their functional potentials that the majority are unaware of. It also identifies that future research studies should be carried out.

Keywords: Functional foods, Marine functional ingredients, Marine bioresources, Therapeutic marine compounds.

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INTRODUCTION

Among the principal needs, foods perform a fundamental role in the existence and survival of human beings, and apart from getting the nutrients from food, most people pay attention to the health aspects of the foods they consume. Foods with health benefits along with nutritional properties, also known as functional foods, are becoming more popular around the globe [1]. The Food Agriculture Organization (FAO) defines functional foods as those that look like traditional food, are meant to be consumed regularly as part of a diet, and include biologically active substances that have the potential to improve health or lower the risk of disease [2]. There are numerous ways to make functional foods. Conventional foods with bioactive ingredients may be advertised with claims of improved health [3]. Functional foods are said to improve immune functions, fend off sickness, aid recovery from particular medical conditions, manage physical and mental ailments, and slow down aging [4]. Dietary supplements, antioxidants, citrus fruits, minerals and vitamins, grains and cereals, milk and other fortified dairy products, and herbal products are all examples of nutraceuticals. Cancer, diabetes, coronary heart disease, inflammation, high blood pressure, spasmodic disorder, and other diseases can all be treated with nutritional supplements [5]. According to a survey carried out by the International Food and Nutrition Council with 1005 participants, 45% of them showed that they were interested in functional foods, and 86% of them said that they wanted to learn more about functional foods [6].

The use of marine bioresources to develop functional foods has a wide research focus since the properties of marine bioresources are countless. Seas and oceans cover most of the Earth's surface, which is over 70% [7], making it more possible to explore the prosperity effects and social and economic benefits of the marine ecosystem. With the majority of its inhabitants (95%) living in underdeveloped nations, 10% of the global populace depends on the ocean for a readily available protein source and employment [8]. When compared to terrestrial organisms, marine species consist of specific traits and biologically important substances since they undergo harsh living conditions such as temperature fluctuations, high salinity, light, pressure, and nutrition. According to research [9], due to the various characteristics of the marine environment, including changes in the levels of salt, temperature, and light, compounds made from marine species are particularly fascinating. To increase the attainability and chemical diversity of marine-derived functional components, more research focuses are directed toward identifying and synthesizing marine-derived chemicals utilizing biotechnological techniques.

The marine environment is a logical place to look for natural items with a variety of health advantages because of its incredible biodiversity. The most typical types of creatures with potential interest as wholesome food or as a source of active compounds, including proteins, lipids, vitamins, and polysaccharides, are marine macroalgae, crustaceans, fish and fisheries byproducts, and microbes [10]. Seafood serves as an illustration of what is available and what is dangerous. It provides crucial micronutrients with positive health consequences, such as reducing the risk of acquiring non-contagious diseases. It is a vital source of protein for a sizeable fraction of the world's population (especially in economically struggling coastal towns) [7].

MICROALGAE

Microalgae are organisms with a size ranging from 1μm to 1 mm [11] and have properties such as single-celled, microscopic, and autotrophic [12] with more than 50,000 species. A few notable examples include *Aphanizomenon flos-aquae*, *Arthrospira platensis, Nostoc commune, Chlorella pyrenoidosa,* and *Chlorella vulgaris* [13]. The growth and development of microalgae are influenced by many factors, such as temperature, light intensity, and several invasive species [14]. Some of the main advantages of microalgae are the ability to manufacture complex metabolites with little resource input, better biomass productivity, and faster growth rates. The abundance of biomolecules with economic and biological value found in microalgal species is a result of their extensive taxonomic and inherent biochemical diversity [15].

There are a few categories into which the microalgae are subdivided, namely, blue-green algae (Phylum Cyanobacteria), dinoflagellates (phylum Myzoza), diatoms (phylum Ochrophyta), and yellow-brown and green flagellates (chlorophyte, prasinophytes, Prymnesiophyta, and others) [16]. The FAO, which is the UN's food and agriculture organization, recorded 87.0 tons of microalgae production in 11 countries in 2018, with 86.6 tons produced in China. In a recent study, the European Union showed 23 nations with 447 producers of algae and spirulina on a map. Germany, Spain, and Italy were the primary regions for producing microalgae. The production of microalgae in Brazil is also expanding, and energy firms, start-ups, and pilot projects are all involved [11].

NUTRITIONAL AND BIOACTIVE COMPOUNDS IN MICROALGAE

Microalgae consist of numerous compounds such as proteins, lipids, polysaccharides, vitamins, and minerals [17]. These compounds have many therapeutic properties, such as antidiabetic, anticancer, antimicrobial, anti-obesity effects, *etc* [18]. and can be incorporated with food items to enhance the functional valuables of the food product.

CHAPTER 4

Seaweed Metabolites as a Novel Source of Drugs to Treat Inflammatory Diseases

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Abstract: Inflammation is a complex adaptive response to harmful circumstances such as infection and tissue damage. While inflammation is curable in the acute stage, continuous inflammation can lead to chronic diseases such as diabetes, arthritis, neurodegenerative and cardiovascular diseases, inflammatory bowel disease, and metabolic diseases. The inhibition of inflammatory cell infiltration and excessive cytokine production is beneficial to reduce chronic inflammation. Seaweeds have significant medicinal value due to their bioactive compounds, including seaweed metabolites with anti-inflammatory properties such as sulfated polysaccharides, polyphenols, terpenes, and fatty acids. Marine algal compounds with anti-inflammatory characteristics have recently gained attention in medical research as natural therapeutics that provide a significant protective effect over synthetic drugs. Therefore, this review aims to summarize the current knowledge on the anti-inflammatory activity of seaweed metabolites, including their underlying mechanisms and impact on several chronic inflammatory diseases.

Keywords: Anti-inflammatory properties, Inflammatory diseases, Natural therapeutics, Seaweed metabolites.

INTRODUCTION

Inflammation is an important biological process that helps maintain the homeostasis of the body and develop tissues during a pathogen attack. However, inflammation can also result from innate and adaptive immune responses. While

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inflammation is vital in addressing acute abnormalities, such as rheumatoid arthritis, asthma, chronic inflammatory bowel diseases, type 2 diabetes, neurodegenerative diseases, and cancer, it can also lead to chronic diseases if it not properly controlled [1]. Excessive or uncontrolled inflammation can also lead to autoimmune or autoinflammatory disorders and neurodegenerative diseases. Various drugs can be categorized by their role in reducing inflammation, such as non-steroidal anti-inflammatory drugs, glucocorticoids, immunosuppressant drugs, and biological agents [2]. Non-steroidal anti-inflammatory drugs are known for inhibiting cyclooxygenase (COX) enzymes, specifically COX-2, which generate inflammatory mediators such as prostaglandins (PGE2) and are utilized to treat many inflammatory diseases [3]. Glucocorticoids, derived from the enzyme cortisol, can effectively treat autoimmune diseases such as osteoarthritic joints and tendonitis by restricting the expression of cytokine-induced genes. Biological agents act as chemokines that suppress the action of pro-inflammatory cytokines such as IL-1, TNF, IL-6, IL-12, IL-17, IL-18, or IL-23 to treat inflammation and allergy. Crohn's disease, an inflammatory bowel disease caused by the immune system, has been treated using chemokine receptor antagonists that are small molecules [4]. However, despite the abundance of drugs discovered for inflammatory diseases, completely effective inflammatory therapies have not been identified yet due to drug resistance and side effects. As a result, there is a growing focus on using natural compounds as anti-inflammatory therapies in recent literature.

SEAWEEDS AS A SOURCE OF BIOACTIVE COMPOUNDS

Seaweeds, commonly known as macroalgae, are easily found in coastal regions and are classified as eukaryotic organisms that live in saltwater or freshwater rich in bioactive molecules. Unlike higher plants, seaweeds do not have a proper root system, leaves, or any vascular system, and they are nourished through osmosis. Seaweeds can be further categorized into four main groups based on their pigmentation and shape: Chlorophyta (green algae), Phaeophyta (brown algae), Rhodophyta (red algae), and Blue-green algae [1]. There are over 15,000 species of seaweed in all marine water bodies worldwide, although only 8,000 marine macroalgae have been documented, with 2,000 being brown, 1,200 being green, and 6,000 being red [4]. In the Indian coastal area alone, 814 seaweed species associated with 217 genera have been identified [5]. Seaweeds are widely used in various industries due to their large bioactive compounds, such as proteins, polysaccharides, lipids, and polyphenols, which have been reported to possess antioxidant, anti-inflammatory, and anticancer activities [4]. Seaweeds contain bioactive compounds such as brominated phenols [6], nitrogen heterocyclics, kainic acids, guanidine derivatives, phenazine derivatives, amino acids, amines, sterols [7], sulfated polysaccharides [8 - 10], and prostaglandins [11]. These compounds are secondary metabolites that provide enrichment to seaweeds. Furthermore, various beneficial effects have been attributed to fucoxanthin, which is classified as a type of xanthophyll and serves as an accessory pigment in the chloroplasts of algae [12].

These compounds possess numerous anti-inflammatory and antioxidant properties that are beneficial in the treatment of various inflammatory diseases, such as endothelial dysfunction, lung disease, gastrointestinal dysfunction, and atherosclerosis [13 - 16]. Fig. (**1**) provides a summary of seaweed metabolites that exhibit antioxidant and anti-inflammatory activities.

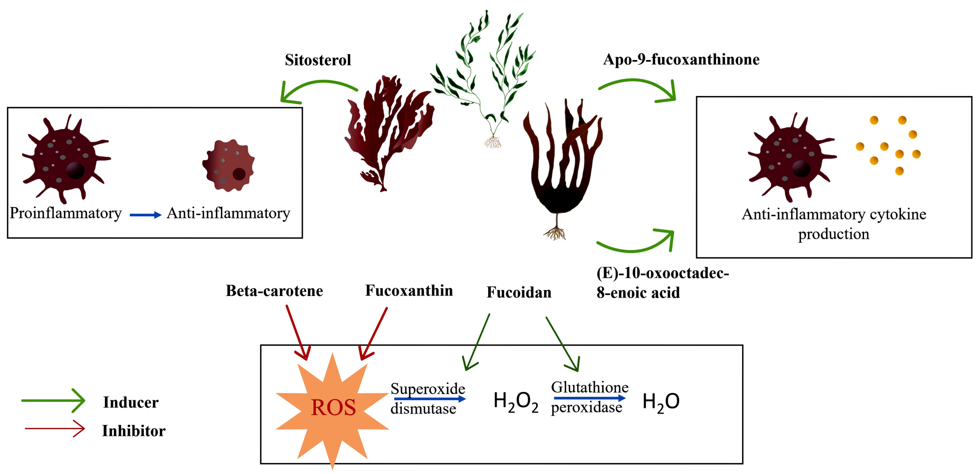

Fig. (1). Summary of seaweed metabolites with antioxidant, anti-inflammatory activities.

BIOACTIVE COMPOUNDS OF SEAWEEDS WITH ANTI-INFLAMMATORY PROPERTIES

Seaweeds are a rich source of bioactive compounds that have been found to have anti-inflammatory properties. These diverse compounds include polysaccharides, phlorotannins, carotenoids, and fatty acids [17].

Polysaccharides

Polysaccharides extracted from seaweeds have demonstrated significant anti-inflammatory properties, making them a promising candidate for developing natural therapeutics [18]. Fucoidan, laminarin, ulvan, and carrageenan are some polysaccharides extensively studied for their anti-inflammatory properties. Fucoidan, which is a sulfated polysaccharide present in brown seaweeds, has been found to have anti-inflammatory effects by suppressing the production of pro-inflammatory cytokines [1, 19 - 21].

CHAPTER 5

Structure of Fucoidan and Isolation Techniques

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Abstract: Fucoidans exhibit various biological activities, including immunomodulation, anti-cancer, and pathogenic inhibition. This approach can be used to isolate numerous natural resources and various applications in the pharmaceutical, food, and cosmetic industries. Fucoidan surrounds sulfated L-fucose as a vital monosaccharide and small amounts of mannose, galactose, glucose, xylose, arabinose, uronic acid, and glucuronic acid. Structural analysis revealed that purified fucoidan consists of a carbohydrate chain composed mainly of (1→3)-linked or (1→4)-linked L-fucose residues, with sulfate groups at C-2 and C-4 positions. Fucose residues at C-3 or C-4 serve as branch sites for galactose residues with 1–4)-linkages. Low molecular weight fucoidan, medium molecular weight fucoidan, and high molecular weight fucoidan are the three different types of fucoidan based on molecular weights. The structure of fucoidan determines its bioactivity and its economic and commercial value depending on the species, geographical location, and harvest season. Therefore, shortened phases, low temperatures, and low acidity are used in the extraction technique to determine the distinct structures of fucoidans. In industrial manufacturing, the extraction techniques must be environmentally friendly and cost-effective. In this chapter, classical extraction and purification procedures such as hot water, acidic or alkaline extractions, and chromatographic techniques are discussed and detailed. Microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), and enzyme-assisted extraction (EAE) are innovative techniques for fucoidan extraction. Optimization strategies for pH, temperature, pretreatment conditions, extraction time, and yield parameters also discussed in detail.

Keywords: Acidic and alkaline extraction, Anion exchange chromatography, Bioactivities, Classical extraction methods, Enzyme-Assisted Extractions, Extraction, Fucoidan, Hot water extraction, Isolation techniques.

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INTRODUCTION

Natural products are essential for human health and daily existence. In contemporary society, natural products are favored over synthetic products for product development on account of their extensive accessibility, economical operation and processing costs, and negligible occurrence of adverse effects [1]. Fucoidan is a naturally derived compound, and brown algae is a promising source of agents for fucoidan synthesis [2]. Fucoidan is a sulfated polysaccharide, and fucose is the main component of its structure. Apart from the two aforementioned elements, galactose represents the third highest proportion of fucoidan. Composition alongside galactose, glucose, xylose mannose, and rhamnose contributes significantly to the formation of the entire structure [3].

Owing to its various structural components, fucoidan possesses many bioactive properties that can be used to treat a range of disorders such as cancer and inflammation and is effective as an anti-coagulant, anti-oxidant, anti-viral, immunomodulatory, anti-diabetic, and antithrombotic agent [3, 4]. Therefore, fucoidan has the potential to be used in the production of drugs and functional foods. *Fucus vesiculosus, Undaria pinnatifida,* and *Macrocystis pyrifera* are used to produce some commercial fucoidan products in the current market [5].

Therefore, the primary emphasis of this chapter is to distinguish fundamental structure of fucoidans and extraction of fucoidans from diverse sources found in nature.

STRUCTURE OF FUCOIDAN

Fucoidan was originally isolated from brown seaweed by Kylin in 1913, and its structure consists mainly of fucose and sulfates. Fucoidans can form many structures that vary slightly depending on the source, especially the type of algae used in the extraction and isolation. The biochemical properties and branching patterns vary from one isolate to another and ultimately form different structures. Therefore, it is a challenge to predict the structure as one entity at a time [6]. When considering fucoidan structure, the fucoidan backbone, monosaccharide configuration, quality and position of sulfate groups, and molecular weight are highly recommended features that are directly relevant to the functional properties.

Fucoidan Backbone and Monosaccharide Composition

Fucose residues are the main components of the pentose sugar backbone and are responsible for the formation of the basic fucoidan backbone. Fucoidan backbone varies slightly between species. Using *Fucus vesiculosus,* three different types of linkages can be identified in the pentose backbone known as α-(1–3), α-(1–3)-α-(1–4), or α-(1–3)-α-(1–2). In type 1, α-(1–3), α-L – fucopyranose residues always bind with 1,3 positions and R groups present on the 2nd and 4th carbon of each pentose, which should be a sulfate group or a monosaccharide. In type 2, α-(1–3)-α-(1–4), the α-L – fucopyranose residues are arranged sequentially at the positions 1,3 and 1,4 like writing patterns. Similar to type 1 fucoidan, the same components also represented in the R group. In type 3, the α-L – fucopyranose residues is almost similar to type 2, but the sulfate groups bind to the oxygen atom present in carbon 2 and 4 (Fig. **1**).

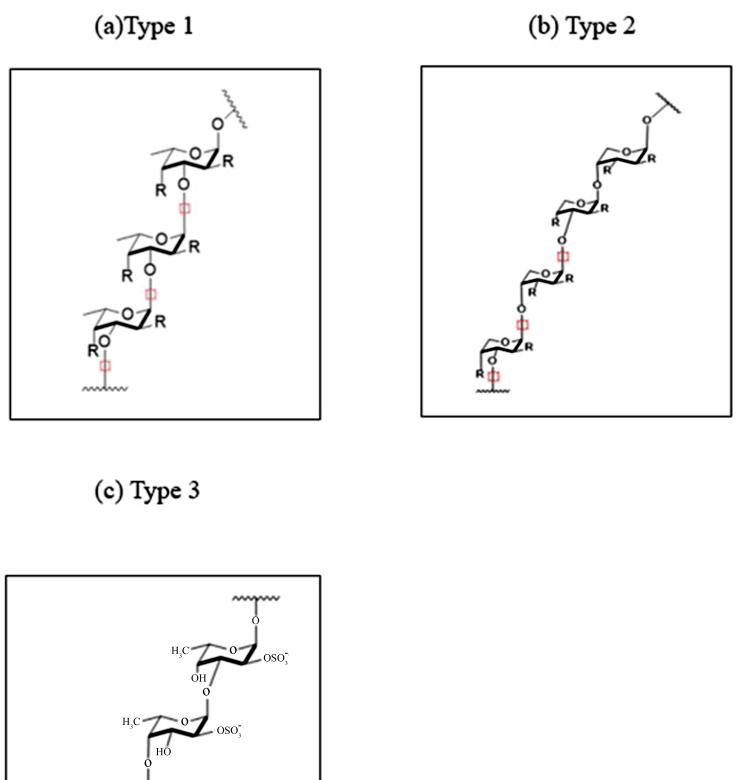

Fig. (1). The backbone structure of fucoidan. **(a):** Type 1 fucoidan, **(b):** Type 2 fucoidan, **(c):** Type 3 fucoidan.

CHAPTER 6

Functional Proteins Isolated from Seaweeds

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Abstract: Several functional proteins are identified and extracted from seaweeds. Red seaweeds contain a higher amount of proteins compared to green and brown seaweeds. Based on the structure, functional proteins in seaweeds can be categorized as glycoproteins and lectins, phycobiliproteins, mycosporine-like amino acids, and peptides and hydrolysates. Glycoproteins are oligosaccharides (glycans) bound to the proteins with N-glycosylation or O-glycosyl linkages. Lectins are also a type of glycoprotein with a carbohydrate-binding domain that binds to specific sugar residues. Phycobiliproteins (PBP) are water-soluble fluorescent pigments mostly found in red seaweeds. There are several types of phycobiliproteins, such as phycoerythrin, phycocyanin, phycoerythrocyanins, and allophycocyanin. Mycosporine-like amino acids (MAA) are secondary metabolites produced by marine organisms, including seaweeds. Peptides and hydrolysates are produced by gastrointestinal digestion or hydrolyzation processes. Several studies suggested that seaweed functional proteins exert unique health benefits, including antioxidant, anti-obesity, antimicrobial and antihypertensive activities. In this chapter, we will briefly describe the bioactive properties of proteins isolated from seaweeds.

Keywords: Antioxidants, Antimicrobial, Antihypertensive, Anti-diabetic, Functional proteins, Glycoproteins, Lectins, Phycobiliproteins, Phycobiliproteins, Peptides and hydrolysates, Seaweeds.

INTRODUCTION

Seaweeds are heterogenous macroalgae that belong to groups of red, brown, and green algae [1]. Over 10,000 seaweed species have been identified, but approximately 145 are used for human consumption [2]. Seaweeds are abundant with macro and micronutrients, including bioactive substances. Most of the

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identified macroalgal species' carbohydrate, protein, and fat contents range from 237–557 g kg−1 dry weight (dw), 59–201 g kg−1 dw, and 7–18 g kg−1 dw, respectively [3, 4]. Seaweed proteins are considered high-quality proteins owing to their essential amino acid composition and bioactivity. Red seaweeds contain more proteins compared to the other two groups. Generally, functional proteins serve unique health benefits other than their nutritional value. Functional macroalgal proteins can be categorized as glycoproteins, lectins, phycobiliproteins, mycosporine-Like amino acids, and protein-derived hydrolysate and peptides [5]. Through different mechanisms, these functional proteins exert several bioactive properties, including antioxidant, antibacterial, antiviral, antihypertensive, anti-inflammatory, anti-tumoral, anti-diabetic, and anti-obesity. Therefore, seaweeds can be used in various applications in cosmetics, pharmaceuticals, and functional foods [5].

Protein content and composition in seaweeds change due to many factors such as season, type of seaweed, habitat, environmental conditions, and extraction method. Seaweed proteins can be extracted by several methods categorized into significant groups, such as physical process, chemical extraction, and enzymatic hydrolysis [6]. Physical methods include homogenization, osmotic stress, and high shear force. Enzymatic hydrolysis uses enzymes such as cellulase, xylanase, and κ-carrageenase to degrade the polysaccharide wall. Chemical extraction methods include acid-alkaline, alkaline, and aqueous treatment systems. Novel protein extraction methods such as ultrasound-assisted extraction, pulsed electric field, microwave-assisted extraction, and membrane filtration are used commercially to increase the availability and bioactivity of the proteins [7].

THE UNIQUENESS OF SEAWEED PROTEIN

Seaweeds are popular as protein-rich non-animal sources among vegetarians. The protein percentage varies from 3% to 50% between different seaweed species. Table **1** shows that brown seaweeds contain a lower amount of proteins, and red seaweeds contain a higher protein amount than others. A variety of seaweeds have similar amino acid composition to soybean proteins but the digestibility and availability could be low. Seaweeds have protein content similar to animal sources (Tables **1** and **2**). Red algae, such as *Porphyra spp.,* has been reported to have higher protein content than other seaweeds [8]. The comparison between algae and animal proteins is challenging because algae protein primarily represents the percentage of dry mass. These protein contents of seaweeds can highly variy by environmental conditions and extraction methods. The amount of essential amino acids (EAA) and digestibility and bioavailability of amino acids are the basic criteria for determining the quality of a protein source. Amino acid composition is a critical parameter regarding the quality of the proteins. Animal protein sources are generally considered high-quality proteins due to their digestibility and availability of essential amino acids. Nine EAAs (Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan, and Valine) can be found in nature, and plant proteins lack most of these. In contrast to terrestrial plants, seaweed proteins contain almost all the EAA in the expected ratio for human nutrition (Table **3**).

Table 1. The protein percentage of brown, green, and red seaweeds (Adapted from Thiviya *et al.* (2022).

Type	Species	Protein (% Dry Weight)	Reference
Phaeophyceae (Brown Algae)	*Ascophylum nodosum*	3–15	[9]
	Fucus serratus	3–11	[8]
	Fucus vesiculosus	9.24–12.9	[10, 11]
	Fucus spp.	3–11	[9]
	Himanthalia elongata	6–11	[9]
	Laminaria digitata	8–15	[8]
	Durvillaea incurvata	6.5	[12]
	Lessonia berteroana	8.6	[12]
	Lessonia spicata	8.4	[12]
	Undaria pinnatifida	11–24	[9]
Chlorophyta (Green Algae)	*Caulerpa lentillifera*	19.38	[13]
	Cladophora rupestris	29.8	[8]
	Capsosiphon fulvescens	31.76	[14]
	Enteromorpha linza	12.5	[15]
	Enteromorpha compressa	17.48	[15]
	Enteromorpha tubulosa	19.09	[15]
	Ulva lactuca	7.06–29.0	[8]
	Ulva pertusa	17.5–26.0	[9]
	Ulva rigida	15–25	[11, 16]
Rhodophyta (Red Algae)	*Agarophyton vermiculophyllum*	17	[17]
	Chondrus crispus	21–27	[9]
	Gracilaria salicornia.	9.58	[18]
	Gracilaria vermiculophylla	15.9	[11]

CHAPTER 7

Seaweed as a Functional Food to Increase Digestive Tract Health

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Abstract: Seaweeds are known as a delicacy and are a well-known source of vital dietary components. Seaweeds make up some of the most important sources of novel medicinal substances for human use. Additionally, as food, they have been proven to possess diverse health benefits. The distinctive characteristics of the marine environment where seaweed grows are thought to be primarily responsible for most of its traits. Compared to terrestrial plants, marine seaweeds contain higher amounts of health-promoting molecules and materials. Clinical trials and mechanistic research on isolated and extracted compounds from seaweeds have shown potential benefits to gastrointestinal health. The present review emphasizes the major seaweed compounds having nutritive value with special reference to the potential to improve gastrointestinal disorders and gut health.

Keywords: Bioactive entities, Cancer, Cytokines, Extraction, Functional food, Gastrointestinal, Inflammatory disease, IBD, Intestinal health, Prevention, Microbiome, Pro-inflammatory, Prebiotics, Probiotics, Polysaccharides, Polyphenols, Signaling pathways, Seaweed, Therapeutic targets.

INTRODUCTION

Foods have long been linked to human illness prevention, and this knowledge dates back many millennia. It is important to realize that the desire to maintain and enhance health continues to be the primary driver in the consumer products sector, even with rising consumer expectations for quick foods. It appears that dietary knowledge among consumers is steadily expanding, and rising health consciousness among modern consumers stresses the larger concept of "wellness" attained *via* ideal nutrition.

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Furthermore, consumers are forced to reassess the nutrition and lifestyle choices they have adopted over the years due to health issues brought on by chronic illnesses, which are the most prevalent among the aging population. Due to this process of reevaluation, where consumers take an active role in lowering their risk of developing chronic diseases and work to manage such conditions without the assistance of a doctor, dietary transitions are becoming more widespread. Consumers are more open to functional foods and drinks in this setting as they look for nutritional ingredients that can promote health. As a result, the food industry has accelerated the development and marketing of a variety of functional food items by employing a variety of food sources on which biological tests have shown their positive effects in terms of the prevention of disease and the promotion of good health [1].

There are several ways to make functional meals. Conventional foods containing bioactive ingredients may be advertised with claims of improved health. These may be improved or fortified to lower illness risk among a certain population. Although every food has a specific purpose, the term "functionality" is used in this chapter to refer to a phenomenon that is widely acknowledged by the scientific community who work in this area. Functional foods refer to foods and food components that offer health advantages beyond fundamental nutrition for the target population [2]. These compounds frequently give more critical nutrients that are required for regular upkeep, growth, and development, including other biologically effective chemicals that possess beneficial health impacts or desired physiological consequences [3].

THE POTENTIAL OF SEAWEEDS FOR THE DEVELOPMENT OF FUNCTIONAL FOODS

Knowing the present demand for molecules with innovative modes of action to address developing illnesses, biochemists, biologists, food technologists and nutritionists are searching for the health advantages connected with these food sources, preferring a proactive strategy to "firefighting" with medicinal therapies. Photosynthetic algae are the most diverse group of organisms when it comes to the sustainability of various sources, and they are regarded as the planet's true survivors due to their survival in climatic changes. The marine environment contains a wide diversity of seaweeds. Seaweeds are taxonomically classified under three groups, namely, red seaweeds (Rhodophyta), green seaweeds (chlorophyte), and brown seaweeds (Phaeophyta). These saline-tolerant multicellular organisms are typically found attached to rocks, sand, and other hard surfaces in coastal areas. Seaweeds are popular as a culinary ingredient in nations such as China, Korea and Japan in Asia, whereas in the West, it is mostly used as a source for the extraction of food hydrocolloids such as agar, carrageenan and alginates. Seaweeds are a readily available source of cheap food virtually all year round, and their easy harvest potential makes them even more readily available [4, 5].

Similar to terrestrial plants, marine algae are also rich in nutritional elements. Seaweeds are abundant providers of vitamins, minerals, polysaccharides, proteins containing all necessary amino acids, and polyunsaturated fatty acids [6]. Seaweeds contain a significant proportion of carbohydrates, including structural, storage, and functional polysaccharides [7]. The total carbohydrate content varies among species and may range from 20% to 70% of dry weight [8, 9]. Seaweeds are not only a good source of nutrients but also a rich source of dietary fiber, which play a protective role in human health.

Seaweeds to Enhance Human Nutrition and Digestive Tract Health

The secret to human well-being is acquiring both good mental and physical health through optimal eating. The nutrients in our daily food or those created by the body from precursor molecules are crucial in controlling biological processes that are necessary for healthy growth and development [10, 11]. The body receives vitamins, proteins, lipids, carbohydrates, and proteins from a variety of dietary sources [12]. Like the majority of terrestrial plants, marine algae are a great source of the aforementioned nutrients. Compared to many popular vegetables, most edible seaweeds have higher quantities of fiber, minerals, and omega-3 fatty acids and moderate concentrations of lipids and proteins, which contribute to its status as a significant food source for human nutrition. The nutritional composition and the bioactivities of marine seaweeds are summarized in Fig. (**1**).

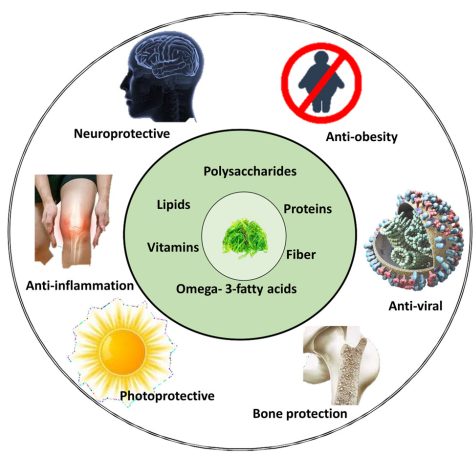

Fig. (1). Nutritional composition and bioactivities of seaweeds.

CHAPTER 8

Antidiabetic Properties of Seaweeds and Future Potentials

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Abstract: Seaweeds are a promising therapeutic target in drug development and nutraceuticals due to the presence of structurally different bioactive constituents in their composition. Diabetes mellitus (DM) is a major metabolic disorder that causes impaired insulin secretion, insulin action by the pancreas, or both. Despite the currently available synthetic antidiabetic drugs and insulin injections, there is a necessity for an effective natural approach to preventing or managing DM without long-term diabetes complications by eradicating adverse risk factors. Therefore, exploring the anti-diabetic properties of seaweeds has been revealed as an emerging and intact alternative target. Because of the significant contribution of bioactive metabolites in antidiabetic seaweed-based therapeutics, it is important to summarize the determinant factors, including the rich abundance of polyunsaturated fatty acids, minerals, dietary fibers, polyphenolic compounds, and carotenoids. In addition, seaweed extracts and their bioactive elements have anti-diabetic potential as they inhibit carbohydrate hydrolyzing enzymes *in vitro* and reduce blood glucose levels *in vivo* in random and postprandial blood glucose assays. Furthermore, they have been attributed to decreased weight gain in mice and rats, presumably by reducing mRNA expression of pro-inflammatory cytokines while raising mRNA expression of anti-inflammatory cytokines. Their advantageous effect on serum and hepatic lipid profiles, as well as antioxidant enzymes, suggests that seaweeds protect against free radical-mediated oxidative stress-induced hyperglycemia and related hyperlipidemia. Hence, seaweed-based therapeutic efforts for DM have a considerable potential to be used as perspective drugs or dietary supplements.

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Keywords: Anti-diabetic properties, Bioactive compounds, Diabetes Mellitus (DM), Natural therapeutic products, Seaweeds.

INTRODUCTION

Diabetes mellitus is a chronic and systemic disorder caused by defects in glucose regulation, where persistent hyperglycemia leads to serious complications over time. Mainly three types of diabetes have been identified, namely Type 1, Type 2, and gestational diabetes, which are caused by an autoimmune effect, imbalance of insulin functionality, and tentative imbalance of blood sugar levels during pregnancy, respectively (Fig. **1**) [1]. This disease has globalized as a major health crisis in the past few decades due to obesity, aging, lifestyle, diet habits, genetic factors, socioeconomic status, education, urbanization, *etc* [2]. Researchers are investigating the pathophysiology of diabetes mellitus, and treatments are being developed in accordance with the information obtained [3]. Unfortunately, a complete cure for this severe and progressive illness is not yet possible. Therefore, current therapeutic strategies primarily focus on controlling the symptoms and slowing down the progression of the disease. Treatment options include both pharmacological and non-pharmacological means, and they slightly change based on the type and severity of the disorder. Diet and exercise are non-pharmacological treatment options [4], whereas oral hypoglycemic drugs (OHD) and insulin treatment [5] are categorized under pharmacological approaches. However, insulin deficiency, insulin resistivity, or both conditions of the patient should be considered in selecting suitable pharmacological therapy. Insulin sensitizers, secretagogues, alpha-glucosidase inhibitors, incretins, pramlintide, bromocriptine, and sodium-glucose cotransporter 2 (SGLT-2) inhibitors, and insulin therapies (insulin and insulin analogs) are the most prominent treatment options [1].

Though the severity of the disease is controlled, there are some irreversible side effects of these drugs. The most common side effects include gastrointestinal disturbances like abdominal pain, bloating, diarrhea, loss of appetite, hypoglycemia conditions, anemia, lactic acidosis, liver inflammation, skin rashes, *etc* [6]. The researchers are searching for sustainable means of therapeutic efforts that cause the least damage to the body while having a significant effect on the disease. The possibility of seaweed as an alternative therapeutic candidate for diabetes mellitus has been revealed by recent research studies. This review summarizes the potential of seaweed as a therapeutic approach for diabetic mellitus management and future perspectives.

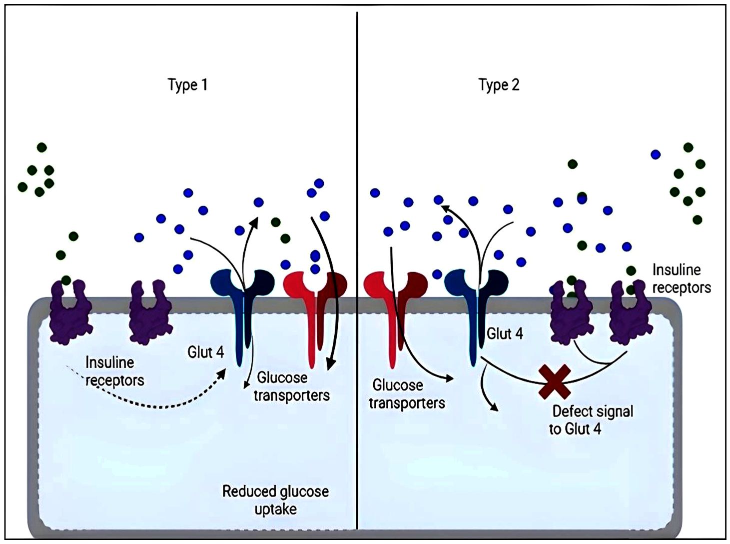

Fig. (1). Cellular action of type 1 and type 2 diabetics.

THERAPEUTIC TARGETS OF DIABETES MELLITUS

One of the primary treatment approaches for diabetes (especially type II diabetes) is the reduction of postprandial hyperglycemia [7]. The inhibition of carbohydrate-hydrolyzing enzymes such as -amylase and -glucosidase may reduce postprandial hyperglycemia. Alpha amylase and -glucosidase are essential exo-acting glycoside hydrolase enzymes that regulate carbohydrate metabolism, and they interact to digest starch in the human body. Alpha amylase hydrolyzes the alpha bonds into insoluble starches, whereas -glucosidase catalyzes the final stage of starch and disaccharide digestion into glucose molecules. As a result, inhibiting such enzymes reduces postprandial blood glucose levels, and these enzyme inhibitors have been a possible target for the development of anti-diabetic drugs [8].

Carbohydrate-hydrolyzing inhibition enzymes such as aldose reductase, angiotensin-converting enzymes, dipeptidyl peptidase-4, and protein tyrosine phosphatase 1B may be combined to develop an alternative therapeutic approach for diabetes [9]. Aldose reductase is an important metabolic enzyme in the polyol pathway that transforms glucose into sorbitol in the presence of NADPH. High blood sugar levels in type 2 diabetes cause a rise in sorbitol synthesis *via* the polyol pathway. Sorbitol intracellular buildup leads to the formation of cataracts and diabetic neuropathy [10]. As a consequence, aldose reductase inhibitors may hinder the synthesis of sorbitol *via* the polyol pathway and thus lower complications associated with diabetes over time.

CHAPTER 9

Anti-Cancer Properties of Pure Compounds Isolated From Seaweeds

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Abstract: Cancer is a major public health concern, and there are no entirely effective treatments. Therefore, natural product-based alternative therapies have been suggested as effective therapeutics against cancer. Marine algae are a promising research tool considered a natural source of bioactive compounds embedded in marine ecology. Algae synthesize a vast variety of bioactive compounds, including polysaccharides, polyphenols, sterols, alkaloids, flavonoids, tannins, proteins, essential fatty acids, enzymes, vitamins, and carotenoids. These pure compounds are composed of intricate structures and exhibit a wide array of possible capabilities, including anticancer potency, in a plethora of *in vitro* and *in vivo* settings. Further, these bioactive constituents derived from seaweeds target crucial molecules that control the development of cancer. So, this chapter mainly focuses on the anti-cancer properties of pure compounds isolated from seaweeds and their therapeutic potential against a wide array of cancer types.

Keywords: Anti-angiogenesis, Anti-cancer, Apoptosis, Cancer therapeutics, Cell culture, Cell-cycle arrest, Chlorophyta, Seaweeds, Natural products, Phaeophyta, Phlorotannins, Polysaccharides, Primary metabolites, Rhodophyta, Secondary metabolites, Seaweeds, Therapeutics.

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INTRODUCTION

Globally, cancer is a major public health concern characterized by aberrant cell proliferation and invasion of nearby cells and tissues. Cancer etiology is multifactorial, and some factors, including drug use, unhealthy diet, infectious organisms, environmental toxins, genetic mutations, immune conditions, and hormones, act in sequence for the development of cancer [1]. In 2016, globally, there were 595,690 individuals diagnosed with this condition, and this figure. specifically pertained to patients in the United States. This represents a mortality rate of 1,630 per day in the USA [2]. In general, cancer treatments typically involve a combination of therapeutic approaches, such as radiotherapy, chemotherapy, immunotherapy, and surgeries, which are selected based on the specific stage of the cancer and its characteristics. The primary objective of any cancer treatment is to destroy cancer cells while minimizing damage to normal, healthy cells. Among these existing cancer therapies, chemotherapy is the most commonly used mode, where it targets all the healthy and tumor cells and tissues and destroys them without any selection [1, 3]. Thus, chemotherapeutic drugs exert a wide array of adverse effects, such as loss of appetite, alopecia, anemia, delirium, irreversible damage to organs, and peripheral neuropathy [4]. There is a prerequisite for novel substances with anti-cancer efficacy that are cell-selective, with fewer side effects, and that improve patient's quality of life, as currently, there is no effective treatment for cancer even after decades of study. In the hunt for compounds that can help in the treatment of ailments, natural products play a significant role in providing dependable substitutes [5]. Despite decades of research on the disease, there is still a need for highly effective anti-cancer medications with low tolerance and fewer adverse effects [6]. Since there are currently no anti-cancer medications that may significantly raise the median survival rate of cancer patients or enhance their quality of life, the need for more anti-cancer medications is daily upregulated [7]. In recent decades, more than 60% of the available anti-cancer medications that come from natural sources include unique biologically active substances [8, 9]. Due to their expansive habitats, high biodiversity, and unique living circumstances, seaweeds have gained relevance in recent years in natural product research, notably in the field of developing anti-cancer drugs [6, 10]. As some references revealed, seaweed-derived anti-cancer compounds kill cancer cells using a variety of signaling pathways and mechanisms [11, 12]. For instance, the seaweed-derived compound fucoidan blocks the generation of vascular endothelial growth factor (VEGF), the activation of natural killer (NK) cells, and other signaling pathways that lead to apoptosis, cell cycle arrest, and anti-angiogenesis. Numerous studies have examined the potential anti-cancer properties of natural seaweed products and signaling pathways engaged in anti-cancer mechanisms [13, 14]. Therefore, this chapter mainly focuses on the bioactive constituents derived from seaweeds and their composition that may lead to anti-cancer effects.

SEAWEED-DERIVED BIOACTIVE CONSTITUENTS

Many metabolites that are obtained from marine algae have biological properties. These bioactive substances have received a lot of attention due to the possible health advantages they may offer. Research has demonstrated a variety of biological actions of these compounds, including antioxidant, immunomodulatory, anticoagulant, and antiulcerogenic effects [6]. Recently, the significance of algae as a reservoir of structurally varied bioactive chemicals has been greatly emphasized. Natural pigments, lipids, polyunsaturated fatty acids, proteins, and polysaccharides are examples of commercial bioactive substances derived from algae [15] (Fig. **1**). Fucoidan and laminarins, which are prevalent in brown algae, carrageenan, which is present in red algae, and Ulva, which is found in green algae, are the main polysaccharides discovered in marine algae [16]. Galactans, sulfated polysaccharides found in Rhodophyta, are made of galactose or transformed galactose units. The sulfated l-fucose units known as fucans make up the Phaeophyta class. In addition to the evidence of homopolysaccharides, carrageenan may potentially possess antiviral, anticancer, and anticoagulant properties [17]. An agaran-type polysaccharide that was isolated from Grateloupia filicina and tested for its anti-angiogenic action is the main component of marine red algae [18]. Polysaccharides present in chlorophyta are polydispersed among heteropolysaccharides. Fucoidan is a sulfated polysaccharide that is abundant in marine brown algae and is also found in some types of bacteria, plants, and animals. It has been demonstrated that fucoidan has antiviral and anti-inflammatory effects [19]. Additionally, fucoidan could be considered a viable treatment for invasive metastasized human lung cancer. Bioactive phloroglucinol derived from seaweeds comprises a variety of chemical components and is extensively researched for its notably advantageous biological effects. Phlorotannins, physiologically active polyphenolic derivatives found in seaweed, have been the focus of the majority of research in this area. Phlorotannins are a group of polyphenols based on phloroglucinol and are accumulated by marine brown algae [19].

ANTI-CANCER POTENCY OF SEAWEEDS

Seaweeds generate diverse bioactive compounds based on their maturity and ability to adapt to environmental factors such as water pressure, radiation, and salinity. These specific compounds vary according to the species [3, 20]. Most commonly, seaweeds are composed of secondary metabolites, including pigments, polyphenols, terpenes, carotenoids, phycobiliproteins, polysaccharides, and

CHAPTER 10

Marine Seaweed Bioresources as Antiviral Agents Against RNA Viruses

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Abstract: Marine seaweed bio-resources (MSBR) have long been recognized for their therapeutic and disease-prevention benefits. They are utilized to prevent various non-communicable and communicable diseases as active components. In recent years, biotechnologists and pharmacologists have become interested in MSBR as a viable and almost limitless source of various biologically active compounds against a broad spectrum of diseases. The most recent global pandemic Covid-19 raised the scientific world's attention to discovering novel anti-viral agents against viruses. Oceans provide unlimited biological resources to develop therapeutic drugs for treating various human viral diseases. Our major intention of writing this chapter was to draw attention to the anti-viral potential of MSBR against various human viral diseases and gain the strength to conquer future viral pandemics.

Keywords: Anti-viral, Marine bioresource, Polyphenols, Polysaccharide.

INTRODUCTION

Oceans are considered a valuable natural resource on Earth, as they provide biologically active compounds, primarily in the form of primary and secondary metabolites accumulated in different organisms. Marine creatures produce a vast range of different and robust active chemicals unique to them due to their varied habitats and exposure to harsh environmental conditions [1]. Since at least a few thousand years ago, people have been aware that marine species contain chemicals with potent biological activity. However, the first comprehensive study on marine species began fifty years ago. Since then, the natural product composition of marine life has been studied [2 - 5]. Further, marine creatures have provided vital structures and compounds during the past fifty years, demonstrating

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their potential for commercial development as cosmetics, dietary supplements, fine chemicals, agrochemicals, and medicinal agents for various ailments. Over the past thirty years, tens of thousands of unique chemicals and their metabolites have been identified from various marine sources, some of which are now being used for various biological functions, from anticancer to antiviral. At the moment, significant pharmacological and therapeutic compounds are actively being sought from the ocean [2 - 7]. Industrial biotechnology and metabolic engineering provide advantages over traditional approaches for extracting biologically active chemicals from biomass that exhibit remarkable biological activities [8].

The microscopic particles known as viruses can be found in plants, animals, and other living organisms. They can occasionally spread illnesses like flu and COVID-19. These living organisms are the only place for viruses to live and reproduce. Some viruses can lead to illnesses, such as COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2). A virus may infect one host in one way while affecting another differently. This provides an insight into why a virus that causes illness in a bull may not affect a human. The virus can be considered a microscopic structure consisting of a core of genetic materials such as RNA or DNA covered by a protein capsid. Some viruses contain envelope-containing spikes that enable binding with the host cell receptors. Targeting the viruses or host cell components are the two main techniques for developing antiviral medications. Other than that, inhibitors of virus attachment, inhibitors of virus entrance, uncoating inhibitors, polymerase inhibitors, protease inhibitors, nucleoside and nucleotide reverse transcriptase, and inhibitors of integrase are some antiviral medications specifically targeting viruses [9]. RNA viruses that cause human diseases contain double-stranded RNA (dsRNA) or single-stranded RNA (ssRNA) as their genetic material. For genome replication, the virus utilizes RNA-dependent RNA polymerase, or in the case of retroviruses with a double-stranded RNA genome, reverse transcriptase can create viral DNA that can be incorporated into host DNA through its integrase activity. According to studies, endogenous retroviruses are long-terminal repeat (LTR)-type retro-elements that make up about 10% of the genomic DNA of humans or mice. HIV-1 is a lentivirus that infects humans. Its RNA genome is made up of two copies of a single-stranded, positive-sense RNA. The HIV-1 RNA genome is connected to the nucleocapsid protein and viral enzymes. Therefore, it is protected within the viral capsid principally generated by the p24 protein. Upon entry into the target cell, the viral RNA genome is reverse transcribed into the double-stranded DNA by a virally encoded reverse transcriptase that is carried together with the viral genome inside the virus particle. A virally encoded integrase and host co-factors import the viral DNA into the cell nucleus and integrate it into the cellular DNA. Once incorporated, the virus may go into a dormant state or be transcribed, producing new viral proteins and RNA genomes released from the infected cell as new virus particles that will infect other cells and start a new replication cycle. The actions of cellular proteins and RNA are closely related to numerous facets of the retrovirus life cycle. The dimerization of two RNAs in HIV-1 and Moloney Murine Leukemia Virus takes place in this process of replication. These infection and replication mechanisms provide great insight into developing antiviral agents against human RNA viruses, and the present chapter has discussed the antiviral potential of marine bioactive compounds against numerous RNA viruses through various therapeutic drug targets.

Identification of the Viral Infection Mechanism

Viruses can be infected through different mechanisms based on their structure and nucleic material. Further, viruses can be classified based on their morphology, structure, and functions. The major criteria of viral classification are summarized in Table **1** [9]. Scientists have discovered 26 virus families that cause human diseases. Further, in some circumstances, humans act as a virus's reservoir, and the connection between these viruses and human illness is evident. In other situations, humans may only serve as accidental hosts, or the connection with the disease may be unstable [9]. The identified virus families related to human diseases are summarized in Table **2**. Among these virus families, the authors discussed the infection mechanism of RNA viruses and the anti-viral potential of marine seaweed-derived compounds against RNA viruses responsible for human diseases

Table 1. Major classification criteria.

Criteria	Description
Nucleic acid type	RNA or DNA
Strand type of nucleic acid	Double-strand, partially double-strand, and single-strand
Nucleic acid sense	Positive, negative, and negative with ambisense
Morphology of capsid	Helical, icosahedral or complex
Envelope	Present or absent
Genome segmentation	Number of segments
Genomic structure	Location of structural genes, caps, repeat sequences
Genome size	Large genome DNA viruses such as herpesviruses or small genome viruses such as hepadnaviruses
Nature of gene expression	Use of polyproteins, reverse transcriptase, multiple nested genes, and RNA ambisense coding

CHAPTER 11

Anti-Aging Properties of Seaweeds

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Abstract: Aging is a natural phenomenon that occurs due to diverse changes in cells and tissues over time, and it is impossible to halt or reverse the process. However, extrinsic skin aging, caused by environmental factors, is largely preventable. Natural products have long been used in skin anti-aging treatments. Seaweeds are multicellular, large-sized marine organisms that have a variety of economic values. They are used in cosmetics, cosmeceuticals, and nutricosmetics due to their versatility and richness in valuable bioactive compounds and other nutrients found in different species of seaweed. This category includes phenolic compounds [flavonoids (flavones, flavanols, flavanones, flavonols, anthocyanins, isoflavones); non-flavonoids (tannins, phlorotannins, lignans & stilbenes)], polysaccharides (sulfated galactans, ulvan, sulphuric acid polysaccharides, alginic acid, carrageenans, fucoidan or sulfated fucose, laminarin), peptides and amino acids, fatty acids (docosahexaenoic acid, eicosapentaenoic acid, stearidonic acid and eicosatrienoic acid), vitamins (vitamin B: B1, B2, B3, B5, B6 & B8, vitamin C, vitamin E), vitamin precursors (α-tocopherol, β-carotene, lutein, and zeaxanthin), pigments (chlorophylls, xanthophylls, and carotenoids), and minerals. The presence of these important bioactive compounds plays important roles in cosmeceutical applications by mediating antioxidant, photoprotective, anti-wrinkling, anti-inflammatory, antimicrobial, anti-collagenase, anti-elastase, and anti-metalloproteinase activities through multiple pathways. Furthermore, seaweed nutrients play vital roles in nutricosmetics and are also involved in vital technical features such as moisturizing, thickening, gelling, and emulsifying effects in different skincare products. This chapter specifically describes the skin anti-aging properties of seaweeds *via* different biological activities due to their unique composition.

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Keywords: Anti-aging, Bio-activities, Cosmetics, Cosmeceuticals, Nutricosmetics, Seaweeds, Skin anti-aging.

INTRODUCTION

Aging Process

Introduction to Aging

Aging is a phenomenon unique to most living organisms including human beings. The process of aging is characterized by a progressive decline of physiological integrity, leading to impaired function and increased vulnerability to diseases and death. The accumulation of diverse deleterious changes in cells and tissues over time with advancing age is responsible for the loss of an organism's structure and function. This deterioration is the primary risk factor for major human pathologies, including cancer, diabetes, cardiovascular disorders, and neurodegenerative diseases [1 - 3].

Worldwide Aging Statistics

Population aging has increased considerably in recent years throughout the world. It is projected that the rate of aging will unduly increase in most countries and regions in the coming years. The decline in fertility and mortality and the increase in longevity have caused a substantial increase in the aging population worldwide. The global population of older persons in 1990 and 2013 was 9.2 and 11.75%, respectively. In 2015, it went up to 12.3% and is projected to increase to 16.5% by 2030 and 21.1% by 2050. It has been reported that, by 2030, every one in six people globally will be over 60 years and this will reach one in every five people *i.e.*, nearly 2.1 billion by the middle of the twenty-first century [4, 5].

According to the United Nations World Population Aging Report 2015, Japan is home to the world's most aged population accounting for 33.1%. Other six countries or areas having the highest percentage of the aging population (aged 60 or over) included Italy (28.6%), Germany (27.6%), Finland (27.2%), Portugal (27.1%), Greece (27.0%), and Bulgaria (26.9%). Except for Bulgaria, all the other countries or areas belong to the high-income category. However, today the speed of population aging in many developing countries is substantially faster than in developed countries. By 2050, two-thirds of the world's population over 60 years will be living in low- and middle-income countries [4 - 6]

Globally, the number of people aged 80 years or over, the "oldest-old" persons, is growing even faster than the number of older persons overall. The number of persons aged 80 years or older is expected to triple between 2020 and 2050 to reach 426 million [4 - 6]. Population aging has major social, political, and economic consequences. The old-age support ratios are already low in both developed regions and some developing countries and are expected to continue to fall in the coming decades. In a number of developing countries, poverty is high among older persons, especially in countries with limited coverage of social security systems [4 - 6].

Introduction to Skin Aging

The human skin is the outer covering of the body. It is the largest and the most visible organ in human beings. Like other organs in the body, the skin also undergoes aging, and it is a complex biological organ [7, 8].

Etiology of Skin Aging

Skin aging is influenced by both endogenous or intrinsic and exogenous or extrinsic factors. Intrinsic aging (chronological aging) occurs as a natural consequence of aging and is genetically determined [9]. Some factors such as genetics, cellular metabolism, hormones, and metabolic processes dramatically influence the rate of intrinsic aging, which is largely inevitable and becomes evident generally around 30-40 years of age [10]. The intrinsic rate of skin aging is dramatically influenced and increased by extrinsic factors, particularly chronic exposure to solar radiation and some other factors such as pollution, harsh weather, chemicals, toxins, and cigarette smoke. Chronic exposure to solar radiation is the principal cause of extrinsic skin aging, and it is referred to as photo-aging or premature skin aging [9].

Characteristics and Clinical Signs of Skin Aging

The key difference between intrinsic and extrinsic aging is that the latter falls within the volitional control of the individual. Nevertheless, there are salient features exhibited by aged skin, regardless of the type and causes of skin ageing [9]. The anatomical changes occur throughout the epidermis, dermis, and subcutaneous tissue during skin aging [7] and result in skin atrophy, laxity, wrinkling, sagging, dryness, roughness, mottled hyperpigmentation, pigmentation, nail and hair changes and development of neoplasms [7, 9]. These changes are associated with numerous clinical alterations that affect all skin functions. Such clinical changes include decreased strength, impaired skin barrier, altered immunity, skin senescence, changes in skin appendages, vascular changes, and a decrease in skin protective functions [7, 9, 11].

CHAPTER 12

Anti-Obesity Potential of Seaweeds

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Abstract: An excessive buildup of body fat is a sign of the metabolic disease known as obesity. The primary etiological factor for obesity is thought to be an imbalance between energy intake and expenditure, where genetic factors can also play a significant role. The rise in obesity rates over the past few years has encouraged a focus on adipose tissue biology and the precise processes behind adipocyte differentiation and adipogenesis. Due to the advent of several *in vitro* cell models and molecular biology tools, adipocyte commitment and differentiation have become complicated processes that may be studied to gain a better knowledge of adipogenesis and adipocyte malfunction related to obesity. As the available anti-obesity drugs and surgical interventions cause adverse effects, it is important to rely on natural-based therapeutics in order to manage obesity and its associated complications. Seaweeds are a rich source of natural bioactive compounds that exhibit human beneficial effects. Fucoxanthin, phlorotannins, fucoidan, and alginate are some of the bioactive compounds present in seaweeds exhibiting anti-obesity potential mainly *via* the inhibition of digestive enzymes and adipocyte differentiation. Therefore, this chapter mainly focuses on the anti-obesity potential of seaweeds proved by many animal and human cell culture models using *in vitro* and *in vivo* mechanisms.

Keywords: Adipocyte differentiation, Adipose tissues, Anti-obesity potential, Bioactive constituents, Cell culture, Chlorophyta, *In vitro*, *In vivo* studies, Marine algae, Metabolic disorders, Natural products, Phaeophyta, Polyphenols, Polysaccharides, Primary metabolites, Rhodophyta, Secondary metabolites, Seaweeds.

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INTRODUCTION

Obesity is a metabolic condition characterized by abnormal fat accumulation within the body, leading to severe complications [1]. The main cause of obesity is the imbalance between energy consumption and energy expenditure [2]. However, genetic factors can also contribute to obesity in some individuals [3]. Individuals with obesity are at a higher risk of developing non-communicable diseases like hypertension, dyslipidemia, cardiovascular diseases, type-II diabetes mellitus, and certain cancer types [1]. Several parameters are available to measure overweight and obesity, in which BMI (Body Mass Index) and Waist Circumference (WC) are considered the most popular indices used to detect overweight and obesity. According to the WHO guidelines, obesity is described as a BMI more than or equal to 30 with an increased waist circumference [4].

Globally, obesity has become one of the main public health problems that alter the quality of life not only by causing serious disease conditions but also by decreasing the life expectancy of individuals substantially. With all of this, it increases the annual healthcare expenditure on diagnosing and treating obesity and obesity-associated disease conditions [5]. According to recent statistics published by the WHO, obesity is one of the main risk factors associated with mortality in both developing and developed countries more than underweight [6]. In 2016, over 650 million people aged more than 18 years belonged to the obese category worldwide. According to additional data, 39 million children under the age of five would be overweight or obese in 2020. However, a recent study projected the growing rate of obesity in men and women in 2025 as 6% and 9%, respectively [1].

In healthy individuals, adipose tissues play a significant role in contributing to homeostasis *via* metabolic, immunological, and hormonal processes. In obese individuals, adipose tissue becomes dysfunctional, which leads to metabolic disorders together with inflammatory conditions [7]. In general, obesity can be defined as "a condition in which an excessive amount of fat is accumulated in the adipose tissues". This excess fat causes the release of biologically active mediators, such as adipocytokines, that contribute to inflammation in obese individuals. Adipocytokines are a group of chemical mediators secreted by adipocytes, including leptin, tumor necrosis factor-alpha (TNF-α), resistin, and adiponectin. These mediators can lead to the development of various health problems associated with obesity, including hypertension, dyslipidemia, cardiovascular diseases, type-II diabetes mellitus, and certain types of cancer [8]. These chemical mediators activate the generation of (ROS) reactive oxygen species, thus leading to enhanced oxidative stress. It is known as one of the main mechanisms that enhance insulin resistance and inflammatory conditions in obese people. Therefore, obese people have more chances to develop type II diabetes mellitus [9].

Several treatment strategies are available to manage obesity, in which diet and physical activities play a main role. Therefore, it is recommended to consume less energy-dense foods rich in dietary fibers to manage obesity. Currently, anti-obesity drugs and surgical interventions are available to manage obesity. Bariatric surgery is the main surgical intervention used to manage severe obesity. However, it is associated with several complications, such as kidney injury, bowel obstructions, nutritional deficiencies, and gallstones [10]. Additionally, pancreatic lipase and carbohydrate hydrolyzing enzymes (α-amylase and α-glucosidase enzymes) are the main targets of anti-obesity medications in order to restrict energy absorption. Further, it aims to reduce fat mass by redistributing adipose tissue or by increasing energy expenditure. However, to date, very few drugs are available in the market to manage obesity, and these drugs are also associated with several side effects. For example, sibutramine is an anti-obesity drug that has been withdrawn from the market due to risks associated with cardiovascular diseases [11]. Therefore, it is important to search for natural-based products to eliminate the side effects associated with available anti-obesity drugs. In lieu of herbal medicines, seaweeds are enriched with ideal bioactive metabolites that exhibit different biological activities. Fucoxanthin, phlorotannins, fucoidan, and alginate are some of the bioactive compounds available in seaweeds that contribute to anti-obesity activity [12]. Therefore, this chapter mainly focuses on the anti-obesity potential of marine seaweeds.

Mechanisms of Anti-obesity Action

Obesity is a complicated disease with multiple causes with an increased risk for the development of health complications with a high rate of mortality [13]. Therefore, it is important to understand the mechanisms linked with anti-obesity action to prevent obesity and its associated complications.

Digestive enzyme inhibition is one of the key mechanisms linked with anti-obesity action. α-amylase and α-glucosidase are two enzymes involved in carbohydrate digestion, whereas lipase is involved in the digestion of fats [14]. The pancreas and salivary glands both secrete α-amylase, which breaks down starch's -1,4 glycosidic linkages into oligosaccharides that are then broken down by the enzyme α-glucosidase to create glucose in the small intestine. Glucose transporters are involved in the transport of glucose from the small intestine to the bloodstream [15]. A high glucose concentration in the blood induces several metabolic pathways, such as glycolysis, glycogenesis, and lipogenesis in the liver

CHAPTER 13

Antimicrobial Properties of Seaweeds

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Abstract: Antimicrobial activity is defined as the ability to destroy or inhibit the growth of microorganisms. Antimicrobial compounds are naturally occurring or synthetic organic compounds having antimicrobial activity. Recently, scientists have discovered many pharmaceutically active compounds that have antibacterial, antifungal, antiviral and antiprotozoal activities in seaweeds. To thrive in various environmental stresses, seaweed produces different metabolites such as polyphenols, polysaccharides, proteins, fatty acids, and pigments. These bioactive compounds are responsible for the antimicrobial activity exerted by seaweed. The antimicrobial activity of seaweed is influenced by various factors, such as the type of seaweed extract used, the target microorganisms, and the environmental conditions. The composition of the bioactive compounds from seaweed may depend on the extraction method and the solvent. It also depends on the seaweed sample, such as fresh or dried sample. Different mechanisms are followed by seaweed extract to acquire antimicrobial activities. Seaweed extracts exhibit various inhibition mechanisms, including disruption of the cell membrane, inhibition of target microorganism enzymes, and prevention of microorganism association with cellular receptors of the host cell. The location, salinity, temperature, *etc.* of the marine environment may affect the chemical composition of the bioactive compounds present in the seaweeds. The antimicrobial activity of seaweed can be evaluated in both *in vitro* and *in vivo* assays. Antimicrobial susceptibility tests and antimicrobial resistance tests are carried out by *in vitro* methods. The antimicrobial activity of seaweed can be a promising source in many applications, such as therapeutic applications, food industries, aquaculture, and biofouling.

Keywords: Antimicrobial, Antibacterial, Antifungal, Antiviral, Bioactive compound, Seaweed.

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INTRODUCTION

Antimicrobial refers to destroying (microbicidal) or inhibiting (microbistatic) the growth of a particular microorganism or group of microorganisms, especially if they are pathogenic to humans and animals. Basically, bacteria, viruses, fungi and parasites are the major pathogenic microorganisms. Antimicrobial compounds are naturally occurring or synthetic organic compounds, and they work at a cellular level to disrupt and prevent the growth of the respective microorganisms continuously (Fig. **1**). Some antimicrobial compounds are known for their ability to function at very low concentrations (*e.g.*, antibiotics in micrograms scale) [1]. Thousands of years ago, ancient Egyptian, Greek, and Asian cultures used antimicrobial agents to treat some infections. Later in the 19th century, Louis Pasteur and other microbiologists discovered the antagonism of bacteria, which led to the golden era of antimicrobial therapy [2].

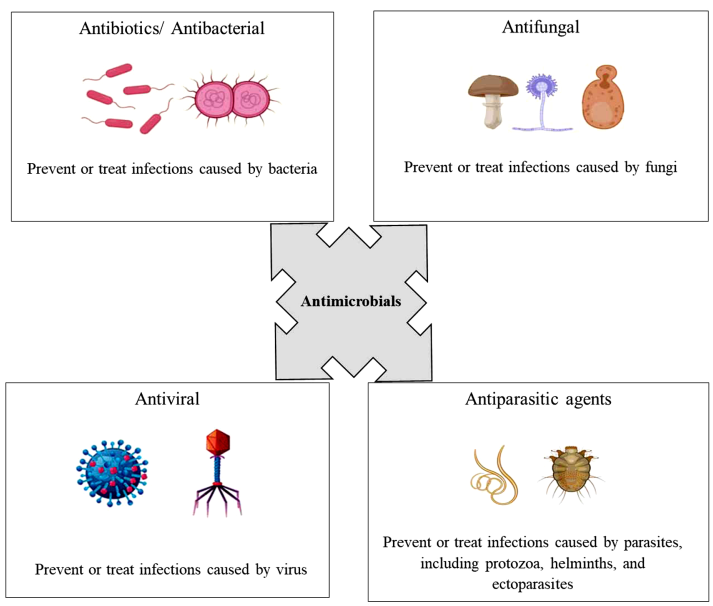

Fig. (1). Types of antimicrobial agents.

The ability of antimicrobials to inhibit or destroy microorganisms has applications in various sectors, including disease control in healthcare, food production, agriculture, aquaculture, cosmetics, animal feed production, and industries that use antifouling agents. The health sector utilizes antimicrobials to combat antibiotic-resistant pathogenic microorganisms [3]. In the food industry, antimicrobials are used as a food supplement for animals and to prevent food spoilage from microorganisms [4, 5]. Animal feed industry antimicrobial agents are used for therapeutic purposes [6]. Antimicrobial peptides are used in plant disease control and the production of biopesticides in agricultural industries [7]. Antimicrobials are reported to be used in aquaculture to control diseases [8]. According to Nabavi *et al*. (2015), antimicrobials are also used in the cosmetics industry [9].

Food and cosmetics industries are demanding more naturally originated ingredients and preservatives. In the food industry, synthetic antimicrobial compounds such as ZnO nanoparticles are reported to have negative health effects [10]. Pathogenic microorganisms can cause significant economic losses due to their negative impact on the aquaculture and agriculture industries. However, conventional antimicrobial agents used to exterminate these harmful microbes can have negative effects on the product and the environment [11].

The chemical industry, in the production of bio-fouling preventive agents, is also reported to exploit harmful antimicrobial agents [11]. According to Banerjee *et al*. (2011), silver nanoparticles are used as antimicrobials to prevent befouling, which are found to be toxic to mammalian cells [12]. Biofoul preventive paints are reported to contain toxic compounds, such as As, Hg or TBT (tributyltin) [11].

Discerningly, these problems need to be necessarily addressed. Hence, it has led to the discovery of better environmentally friendly alternatives that are more potent with minimal toxicity, lesser side effects and good bioavailability [11].

Naturally derived compounds are reported to be a promising source for drug development due to the presence of a greater number of chiral centers [13]. According to Li *et al*. (2015), chiral centers are important for the recognition of biologically active molecules and their interaction with their target [14]. Therefore, different living organisms from terrestrial and marine systems, such as plants, animals, fungi, and micro and macroalgae (seaweed), are under the spotlight for discovering natural antimicrobial agents [15].

Seaweed as Candidates for the Development of Antimicrobials

The marine environment accounts for more than 70% of Earth's total surface and hosts a broad variety of genetically and biochemically unique marine plants and animals. Before 1950, the therapeutic properties of marine resources were only used in traditional and folk medicine [16]. Later, the concept of 'drugs from the sea' emerged, and many bioactive metabolites were discovered from sources such as macroalgae [17], sponges [18], fishes, prawns, shells, marine microorganisms, *etc* [19]. Many novel compounds from marine plants and animals were identified during the period between 1987-1997, out of which, 35% were from algae [20]. Among algae, seaweed has obtained interest among the scientific community in

CHAPTER 14

Benefits of Seaweeds in Cardiac Diseases

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Abstract: Cardiovascular diseases encompass a wide range of disorders that can be categorized into several groups depending on different criteria. The prevalence of cardiac disease is rapidly accelerating in the world. Cardiovascular disorders are responsible for roughly 17.9 million annual fatalities, or nearly 32% of the total mortality globally. The etiology of cardiovascular disease is complex, consisting of both modifiable and non-modifiable risk factors, including metabolic abnormalities, aberrant protein function, genetic mutations, and other contributing elements. Atherosclerosis continues to be the most significant risk factor since it primarily defines the pathogenic processes of cardiovascular diseases. Both pharmacotherapy and surgical interventions are currently in use to alleviate disease symptoms and reduce fatalities. Nevertheless, they have limitations. Therefore, there is an urgent need to develop a novel treatment for cardiovascular disease. Seaweeds are comprised of bioactive compounds with different biological and chemical properties. These can be classified into two groups: primary metabolites and secondary metabolites. Constituents such as phlorotannins, polysaccharides (ulvan, fucoidan, carrageenan), peptides, sterols, and carotenoids (fucoxanthin and astaxanthin) have depicted beneficial effects in preventing cardiovascular diseases. Therefore, this chapter mainly focuses on the bioactive constituents derived from seaweeds and their composition that may benefit in preventing and treating cardiovascular diseases.

Keywords: Benefits, Bioactive compounds, Cardiovascular diseases, Seaweeds.

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INTRODUCTION

Cardiovascular disease refers to a collection of disorders that affect the heart and the circulatory system supplying the heart, brain, and peripheral tissues. Ischemic heart conditions, including myocardial infarction (MI), fall within this category, and these conditions exhibit serious health concerns, which require early precautionary measures [1].

The prevalence of cardiovascular disease is rapidly growing and is the primary cause of mortality in the developed as well as the developing world [2]. According to the World Health Organization (WHO), noncommunicable diseases take 41 million lives each year, equivalent to 74% of all deaths globally [3, 4]. Cardiovascular diseases account for the majority of these deaths, taking an estimated 17.9 million lives, representing 32% of all global deaths, and out of these deaths, 85% were due to heart attack and stroke. By 2030, it is anticipated that there will be 23.6 million cardiovascular disease-related deaths annually [5, 6]. Within the field of cardiovascular health, a diverse array of disorders exists, each capable of affecting the functioning of the heart and blood vessels. Coronary heart disease, hypertension, stroke, and congestive cardiac failure are among the most prevalent among these. The spectrum, however, encompasses additional ailments such as atrial and ventricular arrhythmias, congenital cardiovascular disorders, peripheral artery disease, rheumatic heart disease, and other conditions like deep vein thrombosis and pulmonary embolism that have a significant impact on the circulatory system [7].

The majority of cardiovascular diseases arise as a result of behavioral factors that are also known as modifiable factors, such as unhealthy dietary patterns, tobacco consumption, lack of physical activity, and excessive alcohol intake [8]. Apart from these, there are some risk factors that are unchangeable, including advancing age, ethnicity and genealogy, which contribute to the development of cardiovascular diseases [5]. The effects of the aforementioned risk factors might manifest in people as obesity, hypertension, hyperglycemia, and hyperlipidemia. Atherosclerosis continues to be the most significant risk factor since it primarily defines the pathogenic processes of cardiovascular diseases [9, 10]. Traditional biomarkers of cardiovascular diseases include metabolic factors like total and high-density lipoprotein cholesterol, fasting blood glucose, biological factors like blood pressure or others linked to lifestyle including smoking habit, along with age and gender, and some less significant factors like history of premature cardiovascular events, body mass index, physical inactivity, and genetic features [11].

Currently, pharmacotherapy and surgery are the major forms of treatment available for cardiovascular disorders [12 - 14]. Several cutting-edge therapeutic methods have evolved among these therapeutic strategies. Notably, pharmacological therapies include medications intended to support smoking cessation, suppress platelets or thrombosis, as well as those intended to lower cholesterol levels and blood pressure. Additionally, alternatives to drugs, including calorie restriction and the use of left atrial appendage closure devices, have drawn attention. In an effort to improve treatment effectiveness and advance general cardiovascular health, additional tactics like fixed-dose combination medications and community-based preventative programs have also been investigated [15 - 17]. While the aforementioned strategies work effectively to reduce mortality rates and alleviate the symptoms of the disease, both pharmacotherapy and surgical interventions have certain drawbacks. Traditional medication can also cause side effects such as damaging the kidneys, liver, and other organs [14]. The application of cardiac surgery in therapeutic settings faces limitations due to intricate procedures and potential post-operative complications [18]. Therefore, there is an immediate requirement to develop a novel, convenient, and effective method to deal with cardiac diseases [19].

The bioactive compounds abundant in seaweeds have depicted their potential to reduce the risk of noncommunicable diseases [20]. Research suggests that these bioactive secondary metabolites, including carotenoids, phycobilins, fatty acids, polysaccharides, vitamins, sterols, tocopherols, and phycocyanins, may have a role in preventing cardiac diseases [21]. Additionally, seaweeds contain peptides that may help control blood pressure [22], and the compound fucoidan has been demonstrated to increase high-density lipoprotein (HDL) cholesterol while inhibiting increases in serum total cholesterol, triglycerides (TGs), and LDL cholesterol [23]. Consuming these elements found in seaweeds may thereby reduce the risk of developing cardiovascular disorders [24]. Fucoxanthin, phlorotannins, fucoidan, and alginate are some of the bioactive compounds available in marine seaweeds that have proven effects on treating and preventing cardiovascular diseases [25]. Thus, the bioactive components derived from marine seaweeds and their nutritional composition are discussed in this chapter. Further, this chapter explains how these components may be useful in preventing and treating cardiovascular diseases.

Biological Pathways Underlying Cardiovascular Diseases

The development and progression of cardiovascular disorders are significantly influenced by several risk factors. For instance, dyslipidemia and hypertension, both of which are linked to atherosclerosis and thrombosis, are intimately related to obesity and other modifiable or behavioral risk factors, including hypertension

CHAPTER 15

Role of Seaweed as a Biofertilizer

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Abstract: Seaweed is considered the most important marine bioresource within marine ecology, enriched with ideal bioactive components, including macro and micronutrients, vitamins, amino acids, proteins, phytohormones, minerals, lipids, carbohydrates, antimicrobial compounds, and osmoprotectants. Currently, seaweed is a potential candidate for the production of human food, animal feed, fuels, fertilizers, chemicals, pharmaceuticals, phytoremediation, nutraceuticals, and hydrocolloids. Within the agricultural sector, seaweed-derived biofertilizers play a vital role. The utilization of seaweed compounds in agriculture and horticulture to nourish and condition the soil, as well as for the enhancement of pest management, are some of the major considerations that have enhanced the growth of the worldwide seaweed extracts market. Seaweed extracts are available as biofertilizers in various forms, including liquid fertilizers, powder, and flakes. In this chapter, our goal is to emphasize the utilization of seaweed-derived biofertilizers in sustainable agriculture and its significance in organic farming, which is a more environmentally friendly option for current and upcoming generations.

Keywords: Bioactive constituents, Biofertilizer, Bioresource, Chlorophyta, Horticulture, Macronutrients, Micronutrients, Natural products, Nutrient content, Phaeophyta, Phytohormones, Polysaccharides, Primary metabolites, Plant growth, Rhodophyta, Seaweeds, Seaweeds, Secondary metabolites, Sustainable agriculture, Therapeutics.

INTRODUCTION

The estimated global population by 2050 will be around 9.7 billion, with develo-

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ping countries expected to contribute the most to the population growth. Among the emerging challenges, maintaining food security with an increasing population is critical. Accordingly, agricultural production should also keep pace with it [1]. To address the circumstances of food demand paralleling a growing population, the agricultural sector should be developed with advances in the next few decades. Not to mention that relying too heavily on chemical fertilizers to increase crop yields inevitably harms both the environment and human health [2]. Recently, there has been a turn toward organic fertilizer usage, but slow among farmers. To address this challenge, the fertilizer production industry is continuously growing, as it is one of the main components for increasing food production. As the demand for fertilizer increases, the availability of one or two sources of organic fertilizer is not sufficient. The application of seaweed as a fertilizer is one of the possible options to be explored [3, 4].

All plants require specific minerals and nutrients to exist in the environment. The roots of plants absorb these minerals from the soil, where they naturally occur. This mineral content is often sufficient in most soils to maintain the health of plants. To ensure the plants' optimum growth and development, nutrients that are progressively absorbed by the plants or nutrients that are washed out of the soil must be supplied. N, P, and K are the most often lost minerals that need to be replaced [3]. Due to the repetitive cultivation of the plant, the soil's nutrients become depleted; therefore, fertilizers are needed to be added to the soil. Chemical fertilizers and organic fertilizers are the two categories under which fertilizers fall. The overuse of synthetic fertilizers in agriculture is expensive and has serious impacts on soil physio-chemical parameters, plants, animals, and humans [3]. Inorganic fertilizers are mostly resistant to the ecosystem, which can sometimes be detrimental to the environment, especially with regard to soil fertility. In fact, they contribute significantly to the degradation of soil and land because most microorganisms start to decline with the use of high levels of chemical fertilizers. Organic fertilizers are developed from substances found in nature that are living things. Because organic fertilizers must break down and transform into plant nutrients, they usually take longer to work than conventional fertilizers, but the results last longer. All natural fertilizers enhance soil parameters, including organic matter content, texture, and water-holding capacity, minimize issues with crusting, lower water and wind erosion, and release nutrients gradually over time [5]. Biofertilizer covers a wide range of materials, including plant extracts and manures, which enhance the nutrient availability and uptake by a particular crop [6, 7]. This would be a great achievement for the agro-industry because it would be helpful in nutrient enrichment of the soil, efficient uptake of nutrients from crops, suppression of soil-borne diseases, and improved crop production with reduced energy and fewer environmental issues [8]. Among biofertilizers, seaweed extracts have been used in different types, such as powder form and liquid fertilizer, and have been commercialized, and their beneficial effects have been studied for several years [9]. Among them are the enhancement of quality and quantity of edible biomass and reduction of biotic and abiotic stresses. Seaweed extracts have the potential to not only promote the yield and quality of edible plant biomass but also to reduce biotic and abiotic stress in crops, as well as environmental stress. The revealed significant activities of seaweed extracts include better seed germination and root development, greater climate resistance, higher nutrient uptake, modifications in plant tissue composition, increased pest and disease resistance (fungal diseases), greater harvest, and improved well-being of animal when livestock is fed with farming crops [10]. It has been demonstrated that seaweed fertilizers and animal manure have been effective. Overall, these activities of the seaweed extract can be very beneficial to those who are concerned about it as a source of microelements and as a soil conditioner for environmental protection and agricultural sustainability [5].

Nutritional Composition of Seaweeds

Large aquatic photosynthetic organisms called marine seaweeds can be found along coastlines. The ocean environment contains over 150,000 macroalgae, which are easily cultivated year-round on a huge scale and reproduce quickly. According to the color of their pigments, seaweeds are divided into three groups: rhodophyta (red), chlorophyta (green), and phaeophyta (brown) [11]. Seaweeds are a rich source of bioactive constituents, including alkaloids, polyphenols, tannins, flavonoids, proteins, sterols, enzymes, peptides, essential fatty acids, pigments, and vitamins. They have been shown to exhibit anti-diabetic, antimicrobial, antiviral, anticancer, anti-inflammatory, and anti-obesity effects. In addition to their medicinal effects, these seaweeds also contain valuable nutrients that are essential for plant growth and development [12, 13]. This section highlights the bioactive compounds present in marine seaweeds and their nutritional composition important for the production of biofertilizers in biopharming.

Seaweed extracts are frequently used to promote plant growth, although the processes that cause this stimulation are frequently poorly understood. Numerous studies have demonstrated that a range of key components found in seaweed extracts, such as various phytohormones, plant nutrients, or beans, are responsible for the stimulating effects [12, 13]. As a result of its nutritional content, organic matter found in seaweed biofertilizers is recognized to promote plant development (Fig. **1**) [14]. It has also been demonstrated that adding various seaweeds in the right amounts as organic fertilizers enhanced soil quality and field crop growth metrics [15]. Seaweeds increase the amount of N, P, and K in the soil as well as other essential minerals for plant growth [16]. The analysis of the mineral content

CHAPTER 16

Seaweed as Livestock Food

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Abstract: Seaweeds are a diverse group of plants with a complicated and contentious taxonomy. In general, seaweeds are classified into three groups, brown (Phaeophyceae), red (Rhodophyceae), and green (Chlorophyceae), based on pigment variability. Seaweeds have tremendous potential for human consumption, cosmetics, fertilizers, industrial gums, and chemicals. Researchers have also discovered that seaweeds have been used as animal feed in the livestock sector for thousands of years. However, out of the approximately 10,000 types of seaweeds, only a few are used in animal consumption, such as *Ascophyllum nodosum*, *Laminaria* species, *Lithothamnion* species, *Macrocystis pyrifera*, *Sargassum* species, *Palmaria palmata*, and *Ulva* species. According to previous studies, seaweeds have been incorporated into the diet of cows at less than 2% of the dry ingredients, but the isolation of compounds responsible for reducing methane production by cattle has not been done yet. It is crucial to isolate the various bioactive compounds in seaweeds and incorporate them into traditional animal feed to improve their nutritional and functional characteristics. Seaweeds have also been utilized in fish feed, where finely ground seaweed meal made from brown seaweeds acts as a binder in formulated feeds, with the alginate present in seaweed functioning as the binder. Although successful results have been achieved with seaweed consumption for animal feed, researchers have raised concerns about metal uptake from the surrounding water.

Keywords: Animal feed, Bioactive compounds, Livestock sector, Microalgae.

INTRODUCTION

The livestock industry plays a significant role in the global economy and is an essential source of food, income, and employment for millions of people worldwide. This includes the rearing, breeding, and processing of animals such as

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cattle, sheep, goats, pigs, and poultry [1]. The distribution of the livestock industry varies widely across different regions and countries. Asia is the largest livestock-producing region in the world, accounting for around 40% of global production. China, India, and Indonesia are among the leading producers in the region. Europe and North America are also significant livestock producers, with countries such as the United States, Brazil, Russia, and Germany among the leading producers. The type of livestock reared varies by region and country. For example, beef cattle are the dominant livestock in countries such as the United States, Argentina, and Australia, while dairy cattle are more prevalent in countries such as India and New Zealand [2].

The industry faces significant challenges, including disease control, climate change, environmental impact, feed availability, antibiotic resistance, and animal welfare. Addressing these challenges requires cooperation between stakeholders across the industry, including farmers, policymakers, researchers, and consumers, while meeting the growing demand for livestock products with increased efficiency and sustainability [3].

Ensuring adequate feed availability is a significant challenge for many livestock producers. Major strategies for providing a balanced diet include high-quality forages, supplements, and food additives that can improve the health, productivity, and welfare of livestock [4]. Feed strategies for livestock animals should aim to provide a balanced diet that meets all their nutritional requirements, with a focus on high-quality forages, supplements, feed additives, and good feeding management practices. Alternative feeds can also be used to supplement traditional feeds, reducing costs and improving sustainability [5]. However, livestock production requires a significant amount of feed, and the availability of feed can be affected by factors such as weather, pests, and disease outbreaks. The high cost of feed can also be a significant barrier for small-scale farmers.

Despite the availability of various feed strategies in the livestock industry, there are still some problems associated with them, including availability and cost, quality control, environmental impact, nutrient imbalance, antibiotic resistance, and animal welfare. Addressing these problems requires cooperation between stakeholders across the industry, including farmers, policymakers, researchers, and consumers [6]. However, more research is needed to fully understand their potential benefits and challenges and to develop cost-effective and palatable feed options.

Nutritional Properties of Seaweeds

Seaweeds have the potential to be a sustainable and nutritious alternative feed source for livestock due to their nutritional value, health benefits, positive environmental impact, versatility, and sustainability. The nutritional composition of seaweeds can have a significant impact on their use as livestock feed. Seaweeds are a rich source of protein, minerals, and vitamins. However, their protein content varies, ranging from 2-47% of dry matter [7] (Please refer to Fig. **1**). The proteins in seaweeds are generally of high quality, with a good balance of essential amino acids. Seaweeds with higher protein content may be more suitable as a direct feed supplement or as a replacement for traditional protein sources, such as soybean meal. These are also a rich source of minerals, including iodine, calcium, magnesium, and potassium. The mineral composition of seaweeds can vary depending on the species, location, and time of harvest. Iodine is an important nutrient for animal health, but excessive intake can be toxic. Therefore, it is important to carefully monitor the iodine content of seaweed-based feeds. The vitamin content of seaweeds can vary depending on the species, location, and time of harvest, though they are rich in vitamins like A, C, E, and B. Supplementing animal diets with seaweed can provide a source of vitamins that may be lacking in traditional feed sources [8].

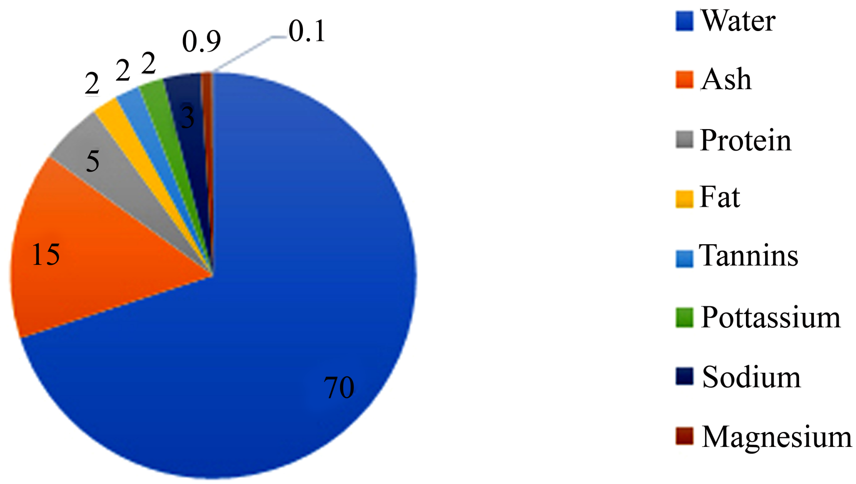

Fig. (1). Nutrition Profile of Seaweeds (Costa *et al*., 2021).

However, some seaweeds contain anti-nutritional factors, such as phytates and tannins, which can reduce the digestibility of other nutrients. However, these factors can be reduced through processing or by combining seaweed with other feed sources. In the same way, the taste and odor of seaweed can vary depending on the species, location, and time of harvest. Some seaweeds may have a strong taste or odor that can be unappealing to livestock. However, some seaweeds can be processed to improve their palatability, or they can be mixed with other feed sources to improve their acceptance. Careful selection, processing, and

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