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EXPLORING THE POTENTIAL IMPACT OF SEAWEED DERIVED BIOACTIVES IN THE MANAGEMENT OF CHRONIC DISORDERS

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ABSTRACT

Seaweeds are marine autotrophic creatures that contain a variety of interesting bioactive compounds. It has been an integral part of various cultures for centuries due to its versatility in culinary, agricultural, and medicinal applications. Seaweeds have a wide range of medicinal uses because they contain rich stores of bioactive compounds which are not present in terrestrial food sources such as polysaccharides, polyphenols, pigments, vitamins, and minerals. It contains polysaccharides like alginate, fucoidan, and carrageenan that have anti-inflammatory, antioxidant, and immunomodulatory qualities. These compounds have shown their potential in the management and prevention of various types of chronic illnesses, such as cancer, cardiovascular disease, and inflammatory diseases. Seaweed is higher in certain health-promoting compounds and materials, such as dietary fiber, omega-3 fatty acids, essential amino acids, and vitamins A, B, C, and E, than terrestrial plants and animal-based diets. Moreover, the abundance of polyphenols found in seaweed, including phlorotannins, has been linked to their possible neuroprotective, anti-diabetic, and anti-cancer properties. These substances exhibit the capacity to scavenge free radicals, reducing oxidative stress and the health risks that are associated with it.

Keywords: seaweed, anti-oxidant, macroalgae, anti-cancer, bioactive compounds, cardiovascular, marine organisms

INTRODUCTION

Consumer interest in healthy food has grown in the present day, and consuming healthy food is the foundation of living a healthy life. The primary consideration in the formulation of food products is nutrition. Algae are organisms capable of providing bioactive compounds for producing novel medicinal and as a source of food and a number of pharmaceutical and industrial products for humans. Algae are used as functional foods and have been extensively researched for their nutritional value for humans.

The term marine algae is generally referred to as marine macroalgae or seaweed [1]. Seaweed is a marine algae, it is grown from natural shock or pond culture. Seaweed has no true roots or leaves. They are attached to substrates such as sand, mud, rocks, and shells or ranging from tide level to considerable depths in the ocean and seas [2]. Seaweed has been used in cuisine for ages, but its use in Asia began in China and Japan. They are traditionally

consumed in many Asian nations, including China, Indonesia, the Philippines, South Korea, North Korea, and Malaysia. Due to its useful qualities and the introduction of Asian cuisine, it has recently gained increasing recognition in Western nations and is being extensively consumed as food in the USA, South America, and Europe [3]. Seaweed and its products are particularly significant in the food business because of their usefulness as additions to functional foods, fertilizers, and animal feed supplements. Although they have a small amount of calories, they are high in proteins, polysaccharides, vitamins, minerals, vital trace elements, and dietary fiber. They are also high in polyunsaturated fatty acids. Apart from regular consumption, many studies have advocated the health benefits of seaweed supplementation alongside a regular diet [4]. They are also utilized as hydrocolloids, as emulsifiers, and as gelling agents in various food product preparations. Apart from the advantages of including seaweed in one's diet on a regular basis, the therapeutic capabilities of seaweed bioactives have long been acknowledged. Seaweed has a wide range of therapeutic uses in addition to being known for its antioxidant and bioactive polyphenolic components. Furthermore, two important benefits of algae for human health and wellness are their ability to prevent cancer and metabolic syndrome (METS), which is associated with diabetes, obesity, cardiovascular disease, and chronic inflammation. Furthermore, macroalgae contain essential components including both fermentable and insoluble dietary fibers known to improve digestive health, including colorectal cancer, gastrointestinal inflammation, aids probiotics, and other adverse health issues. Though some evidence suggests that the effect of bioactive compounds on the human body is moderate and may last over relatively short periods, they could contribute significantly if consumed routinely as part of the daily diet [5].

Seaweed is broadly classified into three groups based on pigmentation as red, brown and green. Botanists referred these groups as Phaeophyceae, Rhodophyceae, and Chlorophyceae, respectively. Among these, brown seaweeds are usually larger in size and range from the giant kelp that is often 20 a long, to thick, leather-like seaweeds from 2-4 m long, to smaller species 30-60 cm long. Red seaweeds are smaller in size, generally ranging from a few centimeters to about a meter in length . However, they are not always red but sometimes purple, even brownish red, but they are still classified by botanists as Rhodophyceae because of other characteristics. Green seaweeds are also small, with a similar size range to the red seaweeds [6].

This review focuses on the nutritional composition of seaweed along with the therapeutic role of seaweed derived bioactive compounds for health maintenance and disease prevention.

NUTRITIONAL COMPOSITION OF SEAWEED

Seaweeds are just the ocean's wealth, or as we can say, these are the resources of marine life. It's a good source of fiber, carbohydrates, proteins, vitamins, and minerals. Many types of seaweed are rich in minerals, including sodium, calcium, magnesium, potassium, chlorine, sulphur, and phosphorus, as well as micronutrients, including iodine, iron, zinc, copper, selenium, molybdenum, fluoride, manganese, boron, nickel, and cobalt. Apart from that, brown seaweed generally serves as the best provider of iodine. Although the amount of protein and calcium varies by species, it is generally low in fat. In general, the protein level of

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red and green seaweeds can reach up to 30%, while brown seaweeds have a lower protein content of up to 15% [7]. The nutrient composition of edible seaweed is shown in Table 1.

Table 1. Nutrient Composition of Edible Seaweed (% dry weight)

Species	Protein	Ash	Dietary fiber	Carbohydrates	Lipids
Chlorophyta (Green seaweed)					
Caulerpa lentillifera	10 – 13	24 - 37	33	38 - 59	0.86
C. racemosa	17.8 - 18.4	7 - 19	64.9	33 - 41	1.11
Codium fragile	8 - 11	21 - 39	5.1	39 - 67	9.8
Ulva compressa	21 - 32	17 - 19	29 - 45	48.2	0.5 - 1.5
U. lactuca	10 - 25	12.9	29 - 55	36 - 43	0.3 – 4.2
U. pertusa	20 - 26	-	-	47.0	0.6 – 1.6
U. rigida	18 - 19	28.6	38 - 41	43 - 56	0.9 – 2.0
U. reticulata	17 - 20	-	65.7	50 - 58	1.7 – 2.3
Rhodophyta (Red seaweed)					
Chondrus crispus	11 - 21	21	10 - 34	55 - 68	1 - 3.0
Gracilaria changii	6.9	22.7	24.7	-	3.3
G. chilensis	13.7	18.9	-	66.1	1.3
Palmaria palmata	8 - 35	12 - 37	29 - 46	46 - 56	0.7 - 3
Porphyra tenera	28 - 47	8 - 21	12 - 35	44.3	0.7 – 1.3
P. umbilicalis	29 - 39	12	29 - 35	43	0.3
P.yezoensis	31 - 44	7.8	30 - 59	44.4	2.1
Phaeophyceae (Brown seaweed)					
Alaria esculenta	9 – 20	-	42.86	46 - 51	1 - 2
Eisenia bicyclis	7.5	9.72	10 - 75	60.6	0.1
Fucus spiralis	10.77	-	63.88	-	-
F. vesiculosus	3 - 14	14 - 30	45 - 59	46.8	1.9
Himanthalia elongata	5 - 15	27 - 36	33 - 37	44 - 61	0.5 – 1.1
Laminaria digitata	8 - 15	38	36 - 37	48	1.0
L. ochroleuca	7.49	29.47	-	-	0.92
Saccharina japonica	7 - 8	27 - 33	10 - 41	51.9	1.0 – 1.9
S. latissima	6 - 26	34.78	30	52 - 61	0.5 – 1.1
Sargassum fusiforme	11.6	19.77	17 - 69	30.6	1.4
Undaria pinnatifida	12 - 23	26 - 40	16 - 51	45 - 51	1,05 - 4.5

Source : Pereira, L. (2011). A review of the nutrient composition of selected edible seaweeds. *Seaweed: Ecology, nutrient composition and medicinal uses*, *7*(4), 15-47.

Seaweed fibers consist of structural (cellulose, hemicellulose and xylans), and storage polysaccharides(carrageenan, alginate and agar), which are not nutritious due to human inability to metabolize them. However, they can be valuable dietary fibers in a balanced diet. Regular consumption of high-fiber seaweeds has been linked to Japan's low colon cancer prevalence [8]. Seaweeds contain both soluble and insoluble fibers. Soluble fiber content is higher in red seaweeds such as *Chondrus* and *Porphyra sp*. than in brown and green seaweeds, whereas brown seaweeds such as *Laminaria sp. Saccharina sp*. and *Fucus sp.* have higher insoluble fiber content. The different types of soluble fiber available in seaweed are given in Table 2.

Table 2.Different types of soluble fiber present in Seaweed

Soluble fiber (hydrocolloid)	Source
Agar	Red seaweeds (*Gracilaria*, *Gelidium*, *Pterocladia*)
Carrageenans	Red seaweeds (*Eucheuma*, *Chondrus*,*Hypnea*,*Gigartina*)
Alginate	Brown seaweeds (*Macrocystis, Laminaria,Ascophyllum*)
Fucoidan	Brown seaweeds (*Laminaria religiosa, Nemacystus decipiens*)
Laminarin	Brown seaweeds (*Laminaria japonica, Saccharina latissima*)
Porphyran	Red seaweeds (*Porphyra spp.*)
Ulvan	Green seaweeds (*Ulva lactuca, Enteromorpha spp*.)

Source: Rajapakse, N., & Kim, S. K. (2011). Nutritional and digestive health benefits of seaweed. Advances in food and nutrition research, 64, 17–28.

All the required amino acids are present in seaweed protein which is high in glycine, arginine, alanine, and glutamic acid, meets FAO/WHO dietary protein criteria. However, it lacks lysine and cystine compared to other protein sources. Red seaweed has a higher essential amino acid index and amino acid score than brown and green seaweeds in terms of protein content and composition.

Seaweed's mineral composition is similar to that of seawater, however it differs among species and is influenced by seasonal variations, salinity, pH, light, and nitrogen source. They are an excellent source of iodine; brown seaweeds contain the highest content of iodine, with some species exceeding the RDI (150 µg per day). Red and green seaweed species such as *Eucheuma cottoni, E. spinosum, Palmaria palmata, Porphyra sp., Ulva lactuca* also contain iodine but at lower concentrations [9]. The mineral composition of some edible seaweed is shown in Table 3.

Table 3. Mineral composition of edible seaweed (mg/100gm DW)

Species	Na	K	P	Ca	Mg	Fe	Zn	Mn	Cu	I
Chlorophyta (Green										

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seaweed)										
Caulerpa lentillifera	8917	700 - 1142	1030	780 - 1874	630 - 1650	9.3 - 21.4	2.6 - 3.5	7.9	0.11 – 2.2	-
C. racemosa	2574	318	29.71	1852	384 - 1610	30 - 81	1 - 7	4.91	0.6 – 0.8	-
Ulva lactuca	-	-	140	840	-	66	-	-	-	-
U. rigida	1595	1561	210	524	2094	283	0.6	1.6	0.5	-
Rhodophyta (Red seaweed)										
Chondrus crispus	1200 - 4270	1350 - 3184	135	420 - 1120	600 - 732	4 - 17	7.14	1.32	<0.5	24.5
Gracilaria spp.	5465	3417	-	402	565	3.65	4.35	-	-	-
Palmaria palmata	1600 - 2500	7000 - 9000	235	560 - 1200	170 - 610	50	2.86	1.14	0.376	10 - 100
Porphyra tenera	3627	3500	-	390	565	10 - 11	2 - 3	3	<0.63	1.7
P. umbilicalis	940	2030	235	330	370	23	-	-	-	17.3
P. yezoensis	570	2400	-	440	650	13	10	2	1.4 - 7	-
Phaeophyceae (Brown seaweed)										
Fucus vesiculosus	2450 - 5469	2500 - 4322	315	725 - 938	670 - 994	4 - 11	3.71	5.50	<0.5	14.5
Himanthalia elongata	4100	8250	240	720	435	59	-	-	-	14.7
Laminaria digitata	3818	11.5 - 79	-	1005	659	3.29	1.77	<0.5	<0.5	-
Saccharina japonica	2532 - 3260	4350 - 5951	150 - 300	225 - 910	550 - 757	1.19 - 43	0.89 – 1.63	0.13 – 0.65	0.25 – 0.4	130 - 690
S. latissima	2620	4330	165	810	715	-	-	-	-	15.9
Sargassum fusiforme	-	-	-	1860	687	88.6	1.35	-	-	43.6
Undaria	1600	5500	235 -	680 -	405 -	1.54	0.944	0.332	0.185	22 -

pinnatifida	-7000	-6810	450	1380	680	- 30				30

Source : Pereira, L. (2011). A review of the nutrient composition of selected edible seaweeds. Seaweed: Ecology, nutrient composition and medicinal uses, 7(4), 15-47.

Seaweed contains a very little amount of lipid content of 1% to 5%,and is rich in polyunsaturated fatty acids (PUFAs), particularly in mild climates while its lipid content is higher in warmer seasons, with Eicosapentaenoic acid (EPA) being the major PUFA. Seaweed is a balanced source of ω-3 and ω-6 acids, with red seaweed being particularly high in EPA and ω-6 fatty acids like arachidonic acid. Phospholipids make up 4-10% of the total lipid content [10]. Seaweed has variable amounts of numerous vitamins, including lipid-soluble ones like A and E and water-soluble ones like B and C. Vitamin E content of brown seaweed, *U. pinnatifida*, was 14.5 mg/100 g, significantly higher than that of peanuts (10 mg/100 g). The levels of carotenes, or provitamin A, and vitamin C found in red and brown seaweeds can vary from 20 to 170 ppm and 500 to 3000 ppm, respectively. They are also thought to be excellent providers of vitamin B12, which is scarce in most terrestrial plants but abundant in a few vegetables [9].

THERAPEUTIC PROPERTIES OF SEAWEED

1. Effect on glucose metabolism

Diabetes mellitus is a chronic condition in which the body either cannot properly utilize the insulin that the pancreas generates or fails to produce enough of it. An altered glucose metabolism is seen in diabetic people. An improper use of glucose leads to a series of increasingly complex problems with different body functions and impacts the body's mineral levels. Type-1 or Type-2 diabetes is the most common form of diabetes mellitus, with Type-2 diabetes making up 90% of cases that are documented. Since chronic cardiovascular issues, persistent renal failure, nerve damage, fainting, and diabetes coma can result from unusually high or low blood glucose levels [11].

In recent years, a plethora of novel medications have been developed to treat diabetes, such as insulin mimickers and oral hypoglycemic agents. Anti-type-2-diabetes bioactive substances from seaweed have been shown to be safe and effective in reversing the enzymes involved in the metabolism of carbohydrates. Alkaloids, flavonoids, carotenoids, polyphenols, and phlorotannins were found to have a hypoglycemic effect among the many seaweed bioactive compounds [12]. Antioxidant properties have been demonstrated by polyphenolic substances such as tannins, flavonoids, and phenolic acid, as well as pigments like fucoxanthin and astaxanthin. ROS can be scavenged by polyphenolic substances. Nonetheless, there are significant differences between the polyphenols made by terrestrial plants and their marine counterparts. Because of this, marine-derived polyphenols present a viable new target source for phenolic chemicals that the pharmaceutical industry could use to develop lead drugs[13]. A study including samples of *Alaria esculenta, P. palmata,* and *A. nodosum* (Phaeophyceae) revealed that the extracts from *A. nodosum* were the most active among the three seaweeds. At low doses, the α-glucosidase activity was also inhibited by the same extracts. High α-glucosidase inhibitory activity was observed in two bromophenols

(2,4,6-tribromophenol and 2,4-dibromophenol), which were isolated and purified from the red seaweed *Grateloupia elliptica* (Rhodophyta) [14].

2. Obesity and Metabolic Disorder

In developed nations, obesity is prevalent, and in emerging nations, it is on the rise. Obesity increases the risk of osteoarthritis and congestive heart failure (CHD) and other diseases, such as type 2 diabetes, hypertension, and dyslipidemia, greatly [15]. Up until recently, there hasn't been many research examining the impact of marine fiber from whole seaweed on hunger and related markers. Seaweed contains a good source of dietary fiber, and there's emerging evidence that seaweed isolates, specifically alginate, may reduce appetite [16]. An alginic acid-derived medication was used in a study to treat participants who were 25–30% overweight, and the results showed a considerable reduction in body weight [17]. The polyphenols in the seaweed extracts of Ascophyllum and *Ascophyllum nodosum* inhibited the activities of a-amylase and a-glucosidase in addition to dietary fiber. Fucoxanthin, which possesses anti-obesity qualities, is found in various microalgae and brown seaweeds. In a 2017 study, Hitoe and Shimoda investigated the effects of fucoxanthin on 50 individuals, aged 20 to 59, with a body mass index (BMI) greater than 26–30 kg m^2 and a waist circumference ≥90 cm for women and ≥85 cm for men. Subjects were healthy except for having a BMI that was higher than the advised range of 18–25 kg m^2. For a duration of four weeks, either fucoxanthin capsules or placebos were administered at a dosage of 1 mg or 3 mg daily [18].

The role of alginate, a marine source of fiber that is separated from the cell wall of brown algae, and its possible mechanisms of action in managing weight have been studied. When compared to the consumption of a high-fiber control drink, the consumption of an alginate-based drink over a 4-week period was found to significantly reduce energy intake in apparently healthy obese, overweight, and normal-weight individuals. However, because the intervention period was short (68 individuals), conclusions regarding long-term effects on weight loss were not possible [19]. Seaweed and its extracts may help treat obesity when combined with other lifestyle modifications like exercise and diet modifications.

3. Role in Cardiovascular diseases

Heart disease and stroke are two examples of the many conditions known as cardiovascular diseases (CVD), which impact the circulatory system of mammals. Collectively, CVDs rank as the leading cause of death for people globally. In 2008, cardiovascular diseases accounted for 30% of all deaths. While there are numerous known risk factors for CVDs, the four most significant ones are abdominal obesity, hypertension, hyperlipidemia, and hyperglycemia [20]. One of the main polysaccharides found in brown seaweeds is potassium alginate. It is well known that alginates can bind to ions of sodium, potassium, and calcium. This lowers blood pressure by preventing the intestines from absorbing sodium. In this sense, individuals with high blood pressure may utilize dried seaweed flakes containing potassium alginate in place of table salt [21].

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Due to the persistent endothelial dysfunction and vascular inflammation it causes, hyperlipidemia is a primary cause of CVDs. Plasma cholesterol levels in test subjects who administered dietary cholesterol supplements were lowered by a diet of restructured pork enriched with *Himanthalia elongata* fed to rats [22]. Seaweed's docosahexaenoic and eicosapentaenoic acids may also contribute to the mechanism of heart disease risk reduction. By influencing ionic channels and maintaining intracellular calcium homeostasis, these n-3 fatty acids can have an antiarrhythmic impact within the phospholipids that make up the membrane of the cardiac cell [23]. Since CVD is the leading cause of mortality and morbidity globally, and the dietary benefits of macroalgae have clearly been suggested, further research in humans is required to elucidate the effects of marine bioactive compounds with potentially cardioprotective properties.

4. Anti-cancer activity

For a considerable time, there has been a hypothesis that eating seaweed helps prevent cancer. This theory is mostly based on the observation that communities that consume a diet high in seaweed, like those in Asia, have lower cancer incidence than cultures that consume a diet high in Western foods [24]. Research indicates that fucoidan may modulate the human immune system to have anti-cancer effects. Dendritic cell maturation has been observed to be induced by fucoidan, which also shapes T-cell-mediated immune responses when associated with other cytokines [25]. There is a clear correlation between consuming a lot of seaweed and a decreased risk of diet-related diseases like cancer. Park et al. (2016) evaluated the food habits of 923 individuals, average age 56, who had undergone colon cancer surgery at the National Cancer Centre of South Korea (including 1846 control subjects). The conservative diet group, which consumed the most vegetables and seaweed, had a highly significant reduction in risk factors for colorectal cancer. The traditional diet group, which consumed slightly less seaweed, was next in line, with the Westernized diet group, which consumed the highest amounts of processed foods, and red meat [26]. Seaweeds have been found to trigger apoptosis in cancer cells by a variety of mechanisms, which include the following: fucoxanthin, polyphenols, and other antioxidants, iodine, phlorotannins, and sulphated polysaccharides like fucoidan.

5. Anti-oxidant activity

Chronic illnesses are associated with damage by free radicals to live cells. Imbalances persist despite human defense mechanisms, particularly in people who have high-stress levels and low antioxidant diets. Phlorotannins and fucoxanthin are two dietary chemicals that have been shown to lower the chance of developing metabolic syndrome, cancer, cardiovascular disease, osteoporosis, renal disease, Parkinson's, Alzheimer's, and neurodegenerative illnesses [27]. One potent dietary antioxidant that has been reported to be a tetraterpenoid carotenoid is fucoxanthin. Instead of giving up a proton as most antioxidants like ascorbic acid or β-carotene do, fucoxanthin gives an electron to quench reactive oxygen species because of its unique molecular composition. In contrast to most antioxidants, fucoxanthin has antioxidant properties in anoxic environments. Because the oxygen content of physiological tissues is low, this is beneficial for humans [28]. The antioxidant action of the brown seaweed *Sargassum wightii* is attributed to its abundance of phytochemicals, including steroids, alkaloids, phenolic compounds, saponins, flavonoids, and anthroquinones [29].

6. Anti-microbial and Anti-fungal activity

Naturally occurring seaweed contains a number of chemicals that have shown antibacterial activity comparable to that of pharmaceutical medications. Polysaccharides, fatty acids, terpenes, peptides, lactones, pigments, and chrysophaentins are a few of them [30]. *Turbinaria ornate* and *Sargassum wightii*, two brown seaweeds, have antibacterial properties in their methanolic extracts. Nine pathogens, including *Aeromonas hydrophila*, *Bacillus subtilis*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Shigella flexneri*, and *Staphylococcus aureus*, were tested for antibacterial activities using exanimate methods. The activity suggests that *T. ornate* methanol extracts could be the best source of antimicrobial agents because phenolic compounds and polyphenols affect the growth and metabolism of bacteria [31].

CONCLUSION

For an ever-increasing proportion of the population worldwide, managing a chronic condition on a daily basis is an inevitable part of life. This is an unfortunate side effect of longer lifespans for humans and a lower prevalence of infectious illness incidence. The most significant preventative action one can take to ward off the onset of chronic, non-communicable disease is by modifying dietary and lifestyle changes. Over 70% of the Earth's surface is made up of water, and the planet's marine environments (lakes, rivers, and oceans) are home to a vast amount of biological diversity that has yet to be fully explored. Seaweeds are a typical sight all throughout the world's coasts. These marine plants have been used for ages in traditional medicine and food preparation, giving mankind a rich history of varied uses. Bioactive substances for human health and functional food uses can be obtained sustainably from seaweeds. The cost and availability of health services in impacted nations are severely strained by the worldwide burden of non-communicable, lifestyle-related diseases such as Type 2 diabetes, hypertension, obesity, cancer, antibiotic resistance, and heart disease. Incorporating seaweed and seaweed isolates in the diet as part of an improved lifestyle may help with this. Seaweeds are a major source of proteins, lipids, polysaccharides, enzymes, minerals, and trace elements. Even though seaweed and its products are widely used in the clinical, industrial, and pharmaceutical sectors, frequent consumption of seaweed may not be safe due to the possibility of heavy metal contamination.

It can be concluded that seaweeds are a desirable natural resource for the creation of innovative nutraceuticals and other functional food supplements because of the many health advantages of biomolecules. The rising consciousness among consumers regarding the health benefits of seaweeds also contributes to their growing allure as a dietary option. However, further studies are required to elucidate the effects and mechanisms of actions of seaweeds, enabling the

exploitation of bioactive marine-derived substances such as micro- and macroalgae in the development of therapies and foods.

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