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Seaweeds: A Comprehensive Review of Pharmacological Interests

Research Article

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Abstract

The global economic impact of the five leading chronic diseases - cancer, diabetes, mental illness, CVD, and respiratory disease - could reach $47 trillion over the next 20 years, according to a study by the World Economic Forum (WEF). According to the WHO, 80% of the world's population primarily those of developing countries rely on plant-derived medicines for the healthcare. The purported efficacies of seaweed derived phytochemicals showing great potential in obesity, T2DM, metabolic syndrome, CVD, IBD, sexual dysfunction and some cancers. Therefore, WHO, UN-FAO, UNICEF and governments have shown a growing interest in these unconventional food with health-promoting effects. Edible marine macro-algae (seaweed) are of interest because of their value in nutrition and medicine. Seaweeds contain several bioactive substances like polysaccharides, proteins, lipids, polyphenols, and pigments, all of which may have beneficial health properties. People consume seaweed as food in various forms: raw as salad and vegetable, pickle with sauce or with vinegar, relish or sweetened jellies and also cooked for vegetable soup. By cultivating seaweed, coastal people are getting an alternative livelihood as well as advancing their lives. In 2005, world seaweed production was totaled 14.7 million tons which more than double (30.4 million tons) in 2015. The present market value is nearly $6.5 billion and projected to reach some $9 billion seaweed global market by 2024. Aquaculture is recognized as the most sustainable means of seaweed production and accounts for approximately 27.3 million tons (more than 90%) of global seaweed production per annum. Asian countries produced 80% for world markets where China alone produces half of the total demand. The top six seaweed producing countries are China, Indonesia, Philippines, Korea, and Japan.

Keywords: Seaweeds; Cancer Prevention; Hyperglycemia Management; Microalgae; Neuroprotection; Alimentary Disorders.

Abbreviations: Monoisobutyl Phthalate (MiBP); Monoethyl Phthalate (MEP); The molar sum of MEHHP and MEOHP (∑DEHP); mono(2-ethylhexyl) phthalate (MEHP); mono(2-ethyl-5-oxohexyl) phthalate (MEOHP); World Economic Forum (WEF); Ischemic Heart Diseases (IHDs); Food and Agriculture Organization of the United Nations (UN-FAO); Gastric Emptying Breath Test (GEBT); Low and Middle Income Countries (LMICs); Conjugated Linoleic Acid (CLA); State of Food and Agriculture (SOFA); Uncoupling protein-1 (UCP-1); Hemoglobin A1c (HbA1c); extracellular signal–regulated kinases (ERK); Inflammatory bowel disease (IBD); Angiotensin Converting Enzyme (ACE); Osteoarthritis (OA); Cytochrome P450 1 (CYP1); Mitogen-Activated Protein Kinases (MAPK); Cyclooxygenase-2 (COX 2); Phosphatidylinositol 3-Kinase/Protein Kinase B (PI3K/Akt); Nuclear Factor Kappa-Light-Chain-Enhancer Of Activated B cells (NF-κB).

Obesity, Hypertension and Hyperglycemia Management

According to the WHO, 2.3 billion adults are overweight and the prevalence is higher in females of childbearing age than males [1]. In the US, the economic burden is estimated to be about $100 billion annually [2]. Worldwide obesity causes 2.8 million deaths per year and 35.8 million disability-adjusted life-years, some 45% of diabetes, 25% of IHDs and up to 41% of certain cancers [3]. Four major bioactive compounds from seaweeds which have the potential as anti-obesity agents are fucoxanthin, alginates, fucoidans and phlorotannins [4]. Alginates are amongst the seaweed fibers that are well-known for their anti-obesity effects. They have been shown to inhibit pepsin, pancreatic lipase [5], reduced body

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Figure 1. Seaweed Farming. According to FAO of the UN, a nearly 45% of the female workforce working in agriculture. Seaweed farming is surely a step toward gender equality (Source: SOFA Team and Cheryl Doss. The role of women in agriculture. ESA Working Paper No. 11-02, March 2011).

weight, BMI, and the blood glucose level [6], ameliorate fat accumulation, TG and TC [7] in experimental animals. Koo et al., 2019 reported Fucoxanthin powder developed from microalga *Phaeodactylum tricornutum* plus CLA or Xanthigen improved lipid metabolism, reduced body weight gain and adipose tissue [8]. Individually, fucoxanthin lowers glycated hemoglobin, especially in in healthy subjectswith a certain UCP1 genotype [9]. Mendez et al., 2019 reported anti-obesogenic potential of seaweed dulse (*Palmaria palmata*) (Figure 2) in High-fat Fed mice [10]. Seca et al., 2018 suggested that small peptides from seaweed may possess bioactivity, for example, of relevance for BP regulation [11]. Yang et al., 2019 reported Fucoidan A2 from the brown seaweed *Ascophyllum nodosum* (Figure 3) lowers lipid by improving reverse cholesterol transport in mice [12]. Sørensen et al., 2019 reported improved HbA1C and lipid profile with *Saccharina latissima*or sugar kelp (Figure 4) in mice [13]. Fucoidan taken twice daily for a period of 90 days did not markedly affect insulin resistance in obese, nondiabetic cohort [14], but attenuates obesity-induced severe oxidative damage [15], show anticoagulant activity [16], suppress fat accumulation [17], may improve obesity-induced OA [18], antioxidant and lipolytic activities [19]. Catarino et al., 2019 and 2017 reported *Fucus vesiculosus* (Figure 5) phlorotannin-rich extracts have significant effect on α-glucosidase, α-amylase and pancreatic lipase [20]. Phlorotannins, farnesylacetones and other constituents from seaweeds have also been described for their potential use in hypertension due to their reported vasodilator effects [21]. Sun et al., 2019 reported the hydrogen bond and Zn (II) interactions between the peptides of Marine Macroalga Ulva intestinalisand ACE [22]. In similar studies, peptides from *Sargassum siliquosum, Sargassum polycystum* [23], *Fucus spiralis* L [24], *Palmaria palmata* [25], *Pyropia yezoensis, Undaria pinnatifida, Enteromorpha clathrate, Ulva rigida C, Gracilariopsis lemaneiformis, Pyropia columbina, Ecklonia cava Kjellman, Ecklonia stolonifera Okamura, Pelvetia canaliculate, Sargassum thunbergii* [26], *Porphyra yezoensis* [27], *Lomentaria catenata, Lithophyllum okamurae, Ahnfeltiopsis flabelliformis* [28] show potential ACE inhibitory activities. Besides the activation of Ag II, ACE plays a concomitant role in the regulation of hypertension via the inactivation of an endothelium-dependent vasodilatory peptide, bradykinin [28, 29]. Kammoun et al., 2018 reported hypolipidemic and cardioprotective effects of Ulva lactuca, which effectively counteracts cardiotoxic effects of hypercholesterolemic regime [30]. In several studies Ulva species showed hypotensive, hypoglycemic, hypolipaemic and antiatherogenic properties [31-40]. Moreover, studies also support seaweed induced effects of postprandial lipoproteinaemia [41-43] postprandial hyperglycemia [44-55], lipid metabolism and atherosclerosis [56-70], reduce body weight [71-80], HbA1c [13, 34, 52, 55, 81-90], reduce BP/episodes of hypertension [11, 26, 28, 46, 49, 53, 66, 80, 91-102] and prevent obesity induced oxidative damage [4, 8, 13, 34, 103-120]. Increased seaweed consumption may be linked to the lower incidence of metabolic syndrome in eastern Asia [28].

Cancer Prevention & Tumor Control

In 2019, 1,762,450 new cancer cases and 606,880 cancer deaths are projected to occur in the United States [121]. Globally, cancer responsible for at least 20% of all mortality [122], 18.1 million new cancer, 9.5 million deathin 2018 [123, 124], 5- year prevalence 43.8 million [125], is predicted to rise by 61.4% to 27.5 million in 2040 [126]. Approximately 70% of deaths from cancer occur in LMICs [127]. Asia, Africa, and Latin America are collectively home to more than 50% of cancer patients; with more than half of global cancer-related mortalities occurring in Asia alone [128]. Cancer causes 46 billion in productivity lost in major emerging economies [129] and economic costs of tobacco-related cancers exceed USD 200 billion each year [130]. Compounds from natural sources with anti-proliferative activity represent an important and novel alternative to treat several types of cancer. *Egregia menziesii* (brown seaweed) (Figure 6) [131], *Portieria hornemannii* [132], *Grateloupia elliptica* [133] *Sargassum serratifolium* [134], Chitosan alginate (polysaccharide from seaweeds) [135-143], xanthophylls (astaxanthin, fucoxanthin) and Phlorotannins (phloroglucinol) obtained from the microalgae [144-155], are reported in brain tumor (glioblastoma) studies. Astaxanthin and fucoxanthin are major marine carotenoids. Major seaweed sources of astaxanthinmono- and di- esters are green algae (*Haematococcus pluvialis*(Figure7), *Chlorella zofingiensis, Chlorococcum*) and red-pigmented fermenting yeastPhaffia rhodozyma [156, 157]. Fucoxanthin present in Chromophyta (*Heterokontophyta or Ochrophyta*), including brown seaweeds (*Phaeophyceae*) and diatoms (*Bacillariophyta*) [158]. Several 2019 reviews reveal fucoidans (sulfated polysaccharide mainly derived from brown seaweed) in lung cancer management. Brown algae like *Fucus vesiculosus*, *Turbinaria conoides*, *Laminaria japonica* (Figure 8) are reported in inhibition of tumor migration and invasion, apoptosis induction and inhibition lung cancer cell progression respectively [159]. *Fucus evanescens, Sargassum sp.* (Figure 9), *Saccharina Japonica*

Figure 2. *Palmaria palmata* (Source: What is Dulse Seaweed? Mara Seaweed October 17, 2017).

Figure 3. *Ascophyllum nodosum* (Source: Ascophyllum nodosum. Jiloca Industrial, S.A. Agronutrientes Blog).

Figure 4. *Saccharina latissima or sugar kelp* (Source: Nature Picture Library).

Figure 5. *Fucus vesiculosus* L. (Source: Seaweed Site of M.D. Guiry).

was reported to inhibit proliferation and metastasis, and inducing apoptosis *in vitro* [160]. *Undaria pinnatifida* acted on ERK1/2 MAPK and p38, PI3K/Akt signaling, *F. evanescens* increased metastatic activity of cyclophosphamide and showed cytolytic activity of natural killer cells in 2 different studies and *F. vesiculosus* decreased NF-κB in LLC [161]. *U. pinnatifida* was found to show average antitumor and superior efficacy against LLC in review of Misra et al., 2019 [162]. Sponge alkaloids from Aaptos showed potential in human lung adenocarcinoma A549, from *Fascaplysinopsis* exerted an anti-proliferative and pro-apoptotic effect in lung cancer, from blue sponge Xestospongia showed apoptosis as well as stimulate anoikis in H460 lung cancer cells in review by Ercolano et al., 2019 [163]. The most common breast cancer type is the invasive ductal carcinoma accounting for 70-80% of all breast cancers diagnosed [164]. Brown seaweed fucoidan inhibited human breast cancer progression by upregulating microRNA (miR)-29c and downregulating miR-17-5p, thereby suppressing their target genes [165]. *Lophocladia* sp (Lophocladines), *Fucus* sp (fucoidan), *Sargassum muticum* (polyphenol), *Porphyra dentata* (sterol fraction), *Cymopolia barbata* (CYP1 inhibitors), *Gracilaria* termistipitata was found to be effective in breast cancer studies [166]. High Urokinase-type plasminogen activator receptor (uPAR) expression predicts for more aggressive disease in several cancer types [167], dietary seaweed may help loweringbreast cancer incidence by diminishing levels of uPAR [168]. The tropical edible red seaweed *Eucheuma cottonii* L. (Figure 10) is rich in polyphenols that exhibited strong anticancer effect with enzyme modulating properties [169]. Jazzara et al., 2016 concluded that λ-carrageenan (sulfated galactans found in certain red seaweeds)could be a promising bioactive polymer [170], showed a remarkable inhibitory effect on MDA-MB-231(triple negative breast cancer cell line) cell migration [171]. Several studies support polyphenols [172-176], flavonoids [177-186], fucoidan [159, 160, 166, 187-195], lutein/zeaxanthin [196-200], other seaweed alkaloids, peptides, tannins and polysaccharides [132, 164, 201-210] in breast cancer management. The number of deaths from colorectal cancer in Japan continues to increase [211], it is the third most common diagnosis and second deadliest malignancy for both sexes combined [212]. It has been projected that there will be 140,250 new cases of colorectal cancer in 2018, with an estimated 50,630 people dying of this disease [213]. High intake of red and processed meat and alcohol increase the risk of colorectal cancer [214]. *U. pinnatifida* [159, 188, 215-221], *Saccharina latissimi* [222], *Fucus vesiculosus* [117, 160, 223, 224], *Sargassum hemiphyllum* [155, 225, 226] have proven efficacy in this situation. Also, Algae derived astaxanthin [150, 227-232], fucoxanthin [233-237], lutein and zeaxanthin [238-241], polyphenols [242-246] shown individual excellence.

Neuroprotection in Stroke, Alzheimer's and Parkinsonism

Stroke is a leading cause for disability and morbidity associated with increased economic burden due to treatment and post-stroke care. Acute ischemic stroke has enormous societal and financial costs due to rehabilitation, long-term care, and lost productivity. Between 2010 and 2030, stroke is expected to increase by more or less 60% in men and 40% in women [248]. Several studies reported neuroprotective role of astaxanthin and fucoxanthin [145, 248-268] in stroke prevention, Alzheimer's, Parkinsonism and other neurodegenerative diseases. Barbalace et al., 2019 reported that marine algae inhibit pro-inflammatory enzymes such as COX-2 and iNOS, modulate MAPK pathways, and activate NK-kB [269]. *Neorhodomelaaculeate, Rhodomela confervoides* [26, 270], *Ecklonia cava* (Figure 11) [271-275], *Laminaria japonica* [276-281], *Fucus vesiculosus* [282-287], *Sargassum* spp. [288-295], *Saccorhiza polyschide* [283], *Codium tomentosum* [296], *Ulva* spp [256, 267, 293, 297-300], *Ecklonia maxima* [256, 301-303], *Gracilaria* spp. (Figure 12) [296, 304-311], *Gelidium pristoides* [312, 313], *Halimeda incrassate* [314, 315], *Bryothamniom triquetrum* [316-318], *Chondrus crispus* (Figure 13) [319, 320], *Hypnea valentiae* (Figure 14) [298], *Ecklonia stolonifera* [321-323] were reported in several studies as neuro-protectives and suggested in neurodegenerative situations or already in use in as such conditions.

Alimentary Disorders

In the USA, the sales of prescription GI therapeutic drugs were $25 billion, the 10th leading therapeutic class in terms of sales [324], spend $135.9 billion for GI diseases in 2015 [325].Urbanization, western diet, hygiene, and childhood immunological factors are associated with IBD in Asia [326]. On the other hand, 14% of the global population is affected by IBS and 30% by con-

Figure 6. ***Egregia menziesii*** **brown seaweed (Source: University of British Columbia Garden).**

Figure 7. ***Haematococcus Pluvialis*** **(Source: VERYMWL, Thailand).**

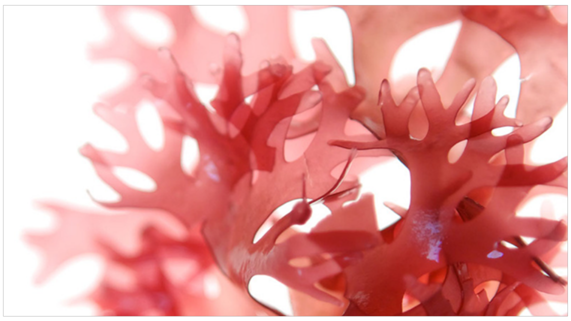


Figure 8. ***Laminaria japonica*** **(Source: TCM Herbs).**

Figure 9. ***Sargassum*** **sp. (Source: POND5).**

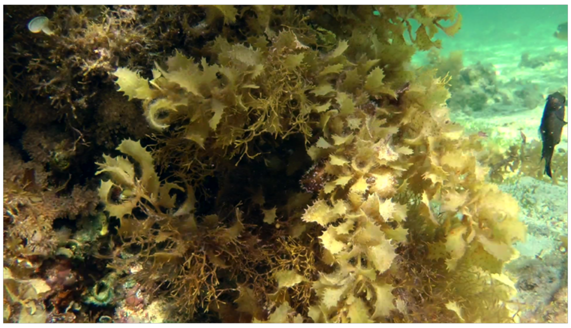
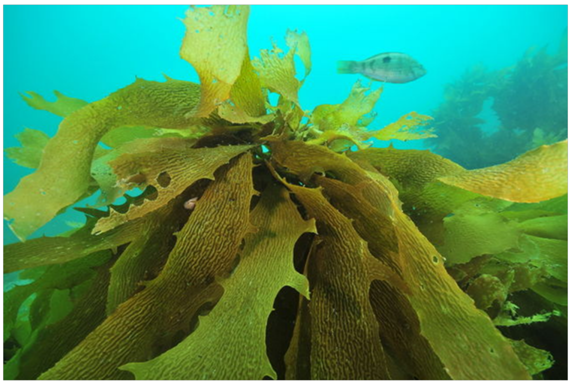


Figure 10. ***Eucheuma cottonii*** **L (Source: Blog at WordPress.com).**

Figure 11. ***Ecklonia cava*** **(Source: Predator Nutrition).**



stipation [327, 328]. Na- alginate, has been used in the treatment of heartburn and GERD, although ESPGHAN/NASPGHAN Guidelinesdo not recommend it's use in chronic GERD [329, 330]. The [13C]-Spirulina platensis GEBT is an easy to measure of gastric emptying with accuracy [331-333]. *Laminaria japonica* (vomiting, hemorrhoids, IBD, probiotic synergist) [334, 335], *Eucheuma cottonii* (IBD, hepatoprotective, anti-food allergy) [336-338], *Caulerpa Mexicana* (Figure 15)(Gastroprotective, IBD)[339-341], *Hypnea musciformis* (IBD) [336, 342], *Fucus vesicolosus* (gastroprotective, ulcerative colitis) [117, 343], *Laminaria hyperborean, Laminaria digitate* (IBD) [344, 345], *Undaria pinnatifida* (Figure 16) (improves gut health) are reported in gut health modulation [346]. In addition, seaweed polysaccharides are atypical in structure to terrestrial glycans, and were found to resist gastric acidity, host digestive enzymes, and GI absorption [347]. Maternal seaweed extract supplementation can reduce both sow fecal *Enterobacteriaceae* populations at parturition and piglet *E. coli* populations at weaning [348]. Also, seaweeds are good source of prebiotics that improve intestinal microbiota and may exert positive effects on IBD and IBS [349, 350].

Figure 12. *Gracilaria tikvahiae* Red Seaweed (Source: Flickr).

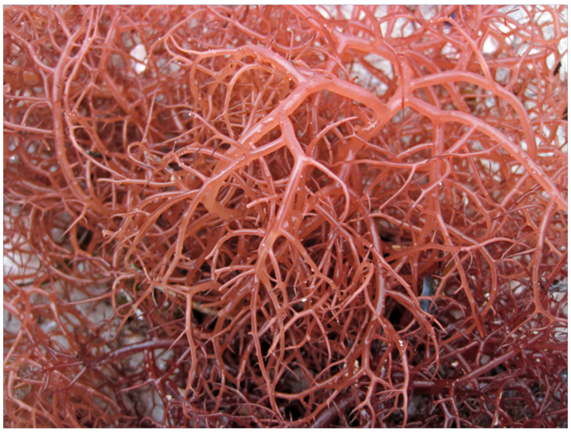
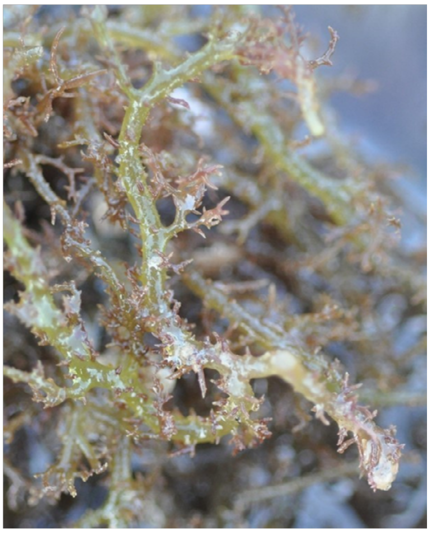


Figure 13. *Chondrus crispus* - Carragheen or Irish Moss (Source: APHOTOMARINE).

Figure 14. *Hypnea valentiae* (Source:iNaturalist).



Thyroid Function

Seaweeds are rich source of Iodine and Tyrosine [351], palatable and acceptable to consumers as a whole food or as a food ingredient and effective as a source of iodine in an iodine-insufficient population [352]. In addition, daily diet should include thyroid boosting foods like those rich in iodine, amino acid tyrosine, minerals like selenium, zinc, copper, iron, various vitamins including, B2, B3, B6, C and E [353]. Edible seaweeds are rich in these vitamins and minerals [95]. Although high iodine intakes are well tolerated by most healthy individuals, but in some people, it may precipitate hyperthyroidism, hypothyroidism, goiter, and/or thyroid autoimmunity [354]. Excess intake of iodine through seafood consumption is a suspected risk factor for thyroid cancer [355]. Also, some seaweeds are contaminated with arsenic, mercury, cadmium and other heavy metals that have positive association with thyroid hormones in adults [356-360].

Analgesic and Anti-inflammatory Potential

Neuropathic pain estimates of 60% among those with chronic pain. Mild -to-moderate pain may be relieved by non-drug techniques alone [128]. 1g of brown seaweed extract (85% *F. vesiculosus* fucoidan) daily could reduce joint pain and stiffness by more than

Figure 15. *Caulerpa Mexicana* (Source: Reefs.com).

Figure 16. *Undaria pinnatifida* (Source: The Marine Life Information Network).

Figure 17. *Dichotomaria obtusata*, Tubular Thicket Algae (reefguide.org).

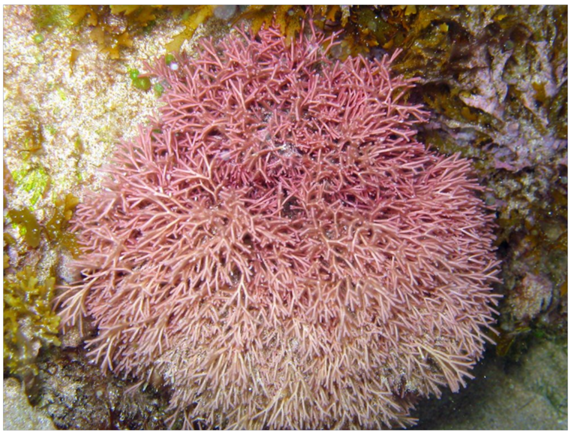


Figure 18. *Padina pavonica* (Source: Alchetron).

Figure 19. ***Dictyota menstrualis*** **(Source: flowergarden.noaa.gov).**

Figure 20. ***Ulva lactuca*****, Sea Lettuce (Source: Addictive Reef Keeping).**

50% [361, 362]. Association between algae consumption and a lower incidence of chronic degenerative diseases is also reported for The Japanese [363]. Carrageenan has been widely used as a tool in the screening of novel anti-inflammatory drugs [364]. Among others, *Porphyra vietnamensis* [365, 366], *Eucheuma Cottonii* [367], *Dichotomaria obtusata* (Figure 17) [368], *Cystoseira sedoides, Cladostephus spongiosis, Padina pavonica* (Figure 18) [369], *Ecklonia cava* (due to phlorotannins) [370-372], *Caulerpa racemose* [373], *Sarcodia ceylanica* [374], *actinotrichia fragilis* [375], *Dictyota menstrualis* (Figure 19) [376], *Gracilaria cornea* [377], *Gracilaria* birdiae [378], Class Phaeophyceae, Rhodophyceae and Chlorophyceae [379], *Caulerpa curpressoides* [380, 381], *Ulva lactuca* (Figure 20) [382], *Sargassum wightii and Halophila ovalis* [383], *Grateloupia lanceolate* [384], *Sargassum fulvellum and Sargassum thunbergii* [385], *Briareum excavatum* [386], *Caulerpa racemose* [387], *Sargassum hemiphyllum* [388], *Laurencia obtusa* [389], *Caulerpa kempfii* [390] *Caulerpa cupressoides* [391] are reported for their analgesic and anti-inflammatory properties.

Antimicrobial Properties

Rising antimicrobial resistance is a threat to modern medicine. Infections with resistant organisms have higher morbidity and mortality, are costlier to treat andestimated to cause 10 million deaths annually by 2050 with global economic loss US$100 trillion [392-394]. Lu et al., 2019 reported *Laminaria japonica*, *Sargassum, Gracilaria* sp. and *Porphyra dentata* potentiated the activities of macrolides against *E. coli* [394]. Carragelose® (first marketed product from algae) in the has ability to block viral attachment to the host cells being effective against a broad spectrum of respiratory viruses [395]. Besednova et al., 2019 reported that fucoidans, carrageenans, ulvans, lectins, and polyphenols are biologically active compounds from seaweeds that target proteins or genes of the influenza virus and host components [396].

Other Health Issues

Walsh et al., 2019 reported osteogenic potential of brown seaweeds *Laminaria digitata* and *Ascophyllum nodosum* [398]. Seaweed contains several compounds with antioxidant properties (phlorotannins, pigments, tocopherols, flavonoids, polyphenols and polysaccharides) [399]. Antioxidant properties of *Fucus vesiculosus* and *Ascophyllum nodosum*(due to phlorotannins) [399], *Turbinaria conoides* (2H-pyranoids) [400], *Ulva clathrate* (phenolics and flavonoid contents) [401], *Bifurcaria bifurcate* (Figure 21) (diterpenes eleganolone and eleganonal) [402], *Cystoseira* spp. (phenolic constituents) [119], *Sargassum siliquastrum* (phenolic compounds, ascorbic acid) [403], *Ulva compressa* (phenolic contents) [404], *Saccharina japonica* (polysaccharides) and *Sargassum horneri* (phenolic contents) [405, 406], *Halophila ovalis* (Figure 22) and *Halophila beccarii* (flavonoids) [407, 408], *Cystoseira sedoides* (mannuronic acid than guluronic acid) [369, 409, 410], *Caulerpa peltata, Gelidiella acerosa, Padina gymnospora*, and *Sargassum wightii* (phenols and flavonoids) [411], *Ecklonia cava Kjellman* (polyphenols) [412, 413], *Undaria pinnatifida* (phlorotannins) [414] are well reported. Most other medicinal effects are mainly due to presence of these antioxidants. Mesripour et al., 2019 reported antidepressant effects of *Sargassum plagyophylum* [415]. *Ecklonia bicyclis*, *Tribulus terrestris* improved sexual and ejaculation function and sexual QoL [416]. Chronic pain is often associated with sexual dysfunction, suggesting that pain can reduce libido [416]. However, red algae (especially sea moss/*Gracilaria* spp.), *Hypnea musciformis* (Vermifuge), *Porphyra crispata* are known to have aphrodisiac properties [417-419]. Thrombotic diseases are reported to contribute to 30% early deaths globally [420]. *Ulva rigida* [421], Udotea flabellum (Figure 23) [422], ulvans, and their oligosaccharides [380], Nemacystus decipieus, *Undaria pinnatifida* [423], *Porphyra yezoensis, Coscinoderma mathewsi, Sargassum micranthum, Sargassum yezoense, Canistrocarpus cervicornis* (Figure 24), *Dictyota menstrualis,*

Table 1. Antimicrobial activity of different solvent extracts from seaweeds [397].

Red Seaweed	Organisms
Alsidium corallinum	*Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus*
Ceramium rubrum	*E. coli, Enterococcus faecalis, S. aureus*
Ceramium virgatum	*Salmonella enteritidis, E.coli, Listeria monocytogenes, Bacillus cereus*
Chondrocanthus acicularis	*E. coli, K. pneumoniae, E. faecalis, S. aureus*
Chondracanthus canaliculatus	*S. aureus, Streptococcus pyogenes*
Chondrus crispus	*L. monocytogenes, Salmonella abony, E. faecalis, P. aeruginosa*
C. crispus	*Pseudoalteromonas elyakovii, Vibrio aestuarianus, Polaribacter irgensii, Halomonas marina, Shewanella putrefaciens*
Corallina elongata	*B. subtilis, S. aureus, E. coli, Salmonella typhi, K. pneumoniae, Candida albicans*
Gelidium attenatum	*E. coli, K. pneumoniae, E. faecalis, S. aureus*
Gelidium micropterum	*V. parahaemolyticus, V. alcaligenes*
Gelidium pulchellum	*E. coli, E. faecalis, S. aureus*
Gelidium robustum	*S. aureus, S. pyogenes*
Gelidium spinulosum	*E. coli, E. faecalis, S. aureus*
Gracilaria dura	*V. ordalii, V. alginolyticus*
Gracilaria gracilis	*V. salmonicida*
Grateloupia livida	*S. aureus, E. coli, P. aeruginosa*
Gracilaria ornata	*E. coli*
Gracilaria subsecundata	*S. aureus, S. pyogenes*
Green Seaweed	
Boodlea composita	*V. harveyi, V. alginolyticus, V. vulnificus, V. parahaemolyticus, V. alcaligenes*
Bryopsis pennata	*V. vulnificus, V. parahaemolyticus*
Caulerpa lentillifera	*E. coli, Staphylococcus aureus, Streptococcus sp., Salmonella sp.*
Caulerpa parvula	*V. vulnificus, V. alcaligenes*
Caulerpa racemosa	*E. coli, S. aureus, Streptococcus sp., Salmonella sp.*
Chaetomorpha aerea	*Bacilus subtilis, Micrococcus luteus, S. aureus*
Chaetomorpha linum	*V. ordalii, V. vulnificus*
Cladophora albida	*V. harveyi, V. alginolyticus, V. vulnificus, V. parahaemolyticus, V. alcaligenes*
Cladophora glomerata	*V. fischeri, V. vulnificus, V. anguillarum, V. parahaemolyticus*
Brown Seaweed	
Chnoospora implexa	*S. aureus, S. pyogenes*
Cladophora rupestris	*E. coli, S. aureus, P. aeruginosa, V. harveyii, V. parahaemolyticus, V. alginolyticus*
C. rupestris	*E. coli, S. aureus, P. aeruginosa, V. harveyii, V. parahaemolyticus, V. alginolyticus*
C. rupestris	*E. coli, S. aureus, P. aeruginosa, V. harveyii, V. parahaemolyticus*
Colpomenia sinuosa	*S. aureus, S. pyogenes, B. subtilis, S. aureus, E. coli, S. typhi, K. pneumoniae, C. albicans*
Colpomenia tuberculata	*S. aureus, Sreptococcus pyogenes*
Cystoseira osmundacea	*S. pyogenes*
Cystoseira trinodis	*S. aureus, B. subtilis, E. coli, P. aeruginosa*
Dictyopteris delicatula	*S. aureus, S. pyogenes*
Dictyopteris undulata	*S. aureus, S. pyogenes*
Dictyota dichotoma	*S. aureus, B. subtilis, E. coli, P. aeruginosa*
Dictyota flabellata	*S. aureus, S. pyogenes*
Dictyota indica	*S. aureus, B. subtilis, E. coli, P. aeruginosa*
Dictyota sp.	*S. aureus, Enterococcus faecalis, P. aeruginosa*
Eisenia bicyclis	*S. aureus, S. epidermidis, Propionibacterium acnes*

Figure 21. ***Bifurcaria bifurcate*** **(Source: APHOTOMARINE).**

Figure 22. ***Halophila ovalis*****, Spoon Seagrass (Source: CoMBINe).**

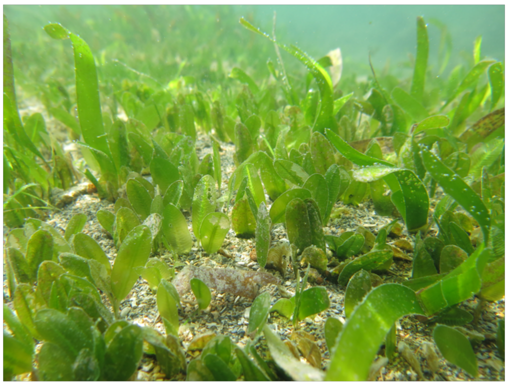


Figure 23. ***Udotea flabellum*** **(Source: Insta Phenomenons).**

Figure 24. ***Canistrocarpus cervicornis*** **(Source: Backyard Nature).**

Figure 25. ***Grateloupia elliptica*** **(Source: Papago.naver.com).**

Ecklonia Kurome, Ecklonia spp. [424] have shown anticoagulant and anti-thrombotic properties. He et al., 2019 reported that seaweed consumption may be a dietary predictor of elevated MEP, MiBP, and ∑DEHP concentrations among pregnant women [425]. Urolithiasis affects approximately 10% of the world population and is strongly associated with calcium oxalate (CaOx) crystals. Gomes et al., 2019 reported anti-urolithic effect ofgreen seaweed *Caulerpa cupressoides* [426]. *Grateloupia elliptica*has the potential to treat alopecia via inhibitory activity against *Pityrosporum ovale* [427]. Strong fungus-inhibitory effects of *Ochtodes secundiramea* and *Laurencia dendroidea* extracts were observed Banana and papaya during storage [428]. Marine macroalgae are a promising source of diverse bioactive compounds with applications in the biocontrol of harmful cyanobacteria blooms [429].

Conclusion

Seaweeds are well-known for their exceptional capacity to accumulate essential minerals and trace elements needed for human nutrition, although their levels are commonly very variable depending on their morphological features, environmental conditions, and geographic location. Food security, legislative measures to ensure monitoring and labeling of food products are needed. Being subject to environmental influences from its habitat, seaweeds also entail water-borne health risks such as organic pollutants, toxins, parasites, and heavy metals. Having in mind the serious environmental problems raised in coastal areas by urbanization and industrialization, the concentration of toxic elements in edible macroalgae is now a growing concern, mainly considering their increment in Western diet. Although many studies demonstrated their therapeutic value in various ailments but most of them performed on experimental animals. Proper labelling is necessary along with instruction of content, source and use. Furthermore, controlled human intervention studies with health-related end points to elucidate therapeutic efficacy are required.

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