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REVIEW ARTICLE

A comprehensive review on algal nutraceuticals as prospective therapeutic agent for different diseases

Asmita Kumari[1] · Garima[1] · Navneeta Bharadvaja[1]

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Abstract
Ongoing research in the food supplement sector provides insightful information regarding algae as a new-generation nutritional supplement and is also referred to as a superfood. Due to the diverse nutritional components, algae have documented numerous health benefits like fighting microbial diseases, hypertension, obesity, and diabetes. Therefore, algae-derived nutraceuticals account for a rapidly expanding market in the food supplements sector. The concept of algal prebiotics and their role in modulating gut microbiota have also been a chief contributor to this. This review evaluates the use of possible algal species and their specific bioactive compounds for the management of several chronic diseases. Proteins, peptides, polysaccharides, phenolics, and vitamins give an insight into the significance of algae in boosting the immune system and improving the body's nutritional makeup. In addition, phyco-compounds such as polysaccharides and polyphenols are also receiving a lot more interest in cosmeceutical applications for protecting skin from photodamage. The incorporation of algae in the diet for the management and prevention of chronic diseases like cancer, lung, and heart disease has been discussed in this review along with their action mechanism. This review provides a brief overview of several bioactive compounds present in micro and macroalgae and their therapeutic effect on lifestyle diseases, gastrointestinal diseases as well as neurodegenerative diseases.

Keywords Nutraceutical · Bioactive compounds · Phycocompounds · Prebiotics · Gut microbiota · Cosmeceutical

Introduction

Algae belong to the plant kingdom's lower phylogenetic tiers, possessing the unique feature of carrying out photosynthesis. The diversity ranges from the microscopic Cyanobacteria to enormous complex kelps. Macroalgae and microalgae are the two major sub-divisions of algae. Macroalgae also known as "seaweeds" are massive, multi-cellular marine organisms resembling big plants. It is further divided into three categories based on colour; Rhodophyta, Chlorophyta, and Phaeophyta also called red algae, green algae, and brown algae, respectively. Phytoplanktons are examples of microalgae and are single-celled photosynthetic organisms. Its two main groups are diatoms and dinoflagellates (Koyande et al. 2021; Radmer 1996). Algae form the basis of the food chain and cover more than 70% of the world's total living mass. Approximately 300,000 algal species have been discovered to date. Owing to their bioactive molecules and their effect on human health, algae are an extensively desired product for use in nutraceuticals. Protein, carbohydrates, and lipids are among the important substances derived from these algae for pharmacological and nutraceutical purposes. *Chlorella* was the first commercially cultivated microalgae for nutraceuticals, which began in Japan in 1960 (Nilesh Hemantkumar and Ilza Rahimbhai 2020). Because these microalgae grow at a rapid rate, they produce a substantial amount of protein-rich biomass and are a rich source of single-cell protein. Apart from its high-value food product algae can be used as additives, antioxidants, dyes, and feed for aquaculture. These are also used in cosmetics and the preparation of biofilm (Mendis and Kim 2011).

The exponential population surge threatens to reduce levels of food security as time progresses. Meeting the current demands of high nutritional value food is a challenge for the agricultural sector as well as the food industry. Because of the decreasing nutritional food quality, there has been a

✉ Navneeta Bharadvaja
navneetab@dce.ac.in

[1] Plant Biotechnology Laboratory, Department of Biotechnology, Delhi Technological University, Shahbad Daulatpur, Main Bawana Road, Delhi 110042, India

rise in lifestyle diseases and certain nutritional deficiency diseases. To attenuate this problem studies are being done on algae to be used as a nutritional supplement and have been widely accepted as a functional food. Microalgae *Spirulina* is regarded as a superfood as it contains 60–70% protein weight; it also contains vitamin B, phycocyanin, omega-6 fatty acid, vitamin E, and many minerals. It is highly effective in diabetes, hypertension, and weight loss. It helps to manage cholesterol metabolism by raising HDL levels which promotes better cardiovascular health. C-phycocyanin pigment found in *Spirulina* has anti-oxidant and anti-inflammatory properties (Bishop and Zubeck 2012). Another microalgae *Chlorella*was utilized as an ideal food in space journeys. It has detoxicant action and helps in the stimulation of the immune system (Nicoletti 2016). It consists of > 50% protein, ~ 5% chlorophyll, ~ 20% dietary fibre, carbohydrates, lipids, provitamin A, thiamin B1, riboflavin, niacin, vitamin E, B6, B12, biotin, folic acid, and pantothenic acid. It is known to regulate high blood pressure, and relieve fibromyalgia, and ulcerative colitis (Naguib 2000).

Chlorella is being marketed as a tablet by different companies. It also shows inhibitory action on aortic atheromatous lesions. *Haematococcus* is a unicellular green alga that is used for pharmaceuticals and cosmetics as well. It is the largest source of astaxanthin. Astaxanthin is a carotenoid that has 10 times the antioxidant potential than β-carotene and 1000 times the antioxidant potential of vitamin E (Naguib 2000). It shows important gastroprotective effects, neuroprotective, ocular protective, anticancer, and hepatoprotective effects and also helps in kidney function impairment (Yuan et al. 2011b). It also aids in some important metabolic functions like immune response, protection against UV radiation, reproductive behavior and anti-inflammatory effects. Astaxanthin extracted from *Haematococcus* was tested on humans for 8 weeks to study the efficacy as well as any toxicity of algal-derived astaxanthin. No significant toxicity was observed (Satoh et al. 2009). Moreover, it showed positive results for treating and preventing neurological damage relating to age-related macular degeneration.

Aphanizomenon is a prokaryotic cyanobacterium and is being used as a food source since ancient times. A significant amount of C-phycocyanin is present in *Aphanizomenon* and is known to promote liver function and boost bile output. Apart from this, it exhibits antioxidant, anti-inflammatory, and high hypo cholestrolemic activity. A large amount of omega 3 and omega 6 (i.e., polyunsaturated fatty acid) are also present in *Aphanizomenon* which helps in the prevention of immunosuppressive and cardiovascular diseases. Furthermore, it also helps to prevent mental health issues and dermatological problems (dos Santos et al. 2021). Recent studies have also found its ability to promote the activity of natural killer cells that trigger apoptosis in cancer or cells infected with the virus (Hart et al. 2007). *Dunaliella salina*is dominantly used in nutraceutical production. Protein, glycerol, and beta-carotene can be extracted in large amounts from its thin cell wall. A smaller amount of alpha-carotene can also be extracted. These beta carotenes are highly effective free radical scavengers that help restore enzyme activity by decreasing levels of lipid peroxidation and enzyme inactivation (Marino et al. 2020). This antioxidant activity of beta carotene also helps in slowing the ageing process and preventing cancer in various organs. *Dunaliella* also has hepatoprotective properties and reduces the incidence of liver lesions (Hsu et al. 2008; Al-obaidi et al. 2021).

Recent trends in the food industry demand a more sustainable switch in food products. This plant-based food supplement is preferred over animal-derived products and is considered to be more healthy. In comparison with terrestrial crops, algal biomass possesses more nutritional value and further its production is more sustainable. Food and herbs have been used as medicines in traditional Asian cultures. Therefore, the idea of incorporating seaweeds has been adopted in the modern approach. This not only meets the current demand for more sustainable and healthy food but also acts as a therapeutic agent for the treatment and prevention of certain deadly diseases (Shannon and Abu-Ghannam 2019; Katiyar and Arora 2020). In comparison with modern treatment methods such as radiotherapy or chemotherapy that have several side effects on the body, these phycocompounds are being used as a substitute by the pharmaceutical industries. Furthermore, worldwide availability, diversity, and productivity make it the best substitute for integral utilization where specifically refined phycocompounds are used or even whole alga can be used as a target product. Improvements in technical conditions and the development of advanced biorefineries have made it possible to exploit every fraction of algal biomass for beneficial byproducts. In addition, intensive research and current studies are making use of genetic engineering tools to increase the value of these phycocompounds (Domínguez 2013; Martins et al. 2018).

Current challenges and market of Algal products

Although the potential of algal biomass is known and thousands of algal species have been identified to date, very few of them are being used at the industrial level production. Production of macroalgae is still limited to countries in Europe like France, Ireland and Spain contributing to 32% of macroalgae production, while the rest 68% of macroalgae harvesting is still done from wild stocks (Araújo et al. 2021). The small market size in certain countries, variability in annual biomass supply, and current technological development are responsible for the slow expansion of algal industries. Besides the lack of large-scale outdoor locations for the cultivation and processing of the algae, the ack of optimum growth conditions isa vital reason for a lower rate of expansion of algal products (Araújo et al. 2021). Cultivation of algae also requires precautionary measures such as prevention from contamination and predators. On a wider level of commercial production, insufficient utilization and recycling of resources add to high manufacturing costs. The lack of production of valuable co-products also adds to the high manufacturing cost of algal products (Sharma and Sharma 2017).

Steadfastly increasing interest in the use of algae in food industries and new improved technologies for hygienic cultivation limits the constraints of algae production (Kratzer and Murkovic 2021). In a study conducted by Araújo et al. (2021) about the current status of algae production, the results showed that algae-producing sectors in Europe account for 67% of macroalgae production and 33% of microalgae production at industrial levels. 222 Spirulina-producing companies are spread across 22 countries in Europe. In 2019 Norway has reported as the third largest seaweed harvesting company whereas France, Ireland, Portugal, the Faroe Islands, and Iceland were also significant producers (Kratzer and Murkovic 2021). In comparison to algae-producing companies in Europe in the last decade, there has been an increase of 150% in the number of new algae-producing companies. There is an ongoing increase in macroalgal production in a total of 13 countries in Europe (Araújo et al. 2021). Owing to the raising demands from the pharmaceuticals and nutraceutical industries, the global market for algae is targeted to reach USD 3318 million by 2022 (Balasubramaniam et al. 2021). Seaweed has been an integral part of Asian cuisine since ancient times and therefore Asia accounts for major seaweed production in the world (Balasubramaniam et al. 2021). In 2019, Asia contributed 97.4% of world seaweed production whereas America and Europe contributed 1.4% and 0.8%, respectively. In 2019, worldwide cultivation of brown seaweed reached 16.4 million tonnes and there has been an increase of 10.9% annual growth rate in its production since 1950–2019 (Cai et al. 2021). Red seaweed cultivation across the globe was estimated to be 18.3 million tonnes in 2019. In terms of quantity and value, red seaweed accounted for 52.6% and 47.6%, respectively, of worldwide seaweed cultivation. Production of green seaweed contrarily showed a stunted growth rate with 16,696 tonnes of global annual production. Production of microalgae accounts for 25,000 tonnes which has a current market value of 50 million Euros and is targeted to reach 70 million Euros by 2025 (Fernández et al. 2021). Since there is a rapid and consistent increase in world population, by 2050 food production and alternative dietary source needed to be increased by 60%The algal nutraceuticals and pharmaceutical industry is estimated to reach a market value of 1131 million Euros by 2027 (Mendes et al. 2022). Algae as meat substitute in the food industry raised its value to 223.65 million Euros. The use of algae in the form of dietary supplements and nutraceuticals has increased globally and it accounted for 30 billion Euros in 2020 and is also expected to grow at a rate of 50.6% by 2026. Sales of algal vitamins and nutraceuticals in the western market are threefolds to the eastern market and are expected to reach a value of 182 billion Euros by 2022 (Mendes et al. 2022). Table 1 describes a list of industries involved in the production of algal products.

Algae for lifestyle diseases

Diabetes mellitus

Diabetes mellitus is the most prevalent metabolic condition with the highest growth rate in the world, characterized by persistent hyperglycemia. Based on its causes it can be classified into two types, 1) insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus also called type 1 and type 2 respectively. In particular, type 2 diabetes mellitusis characterized by insulin resistance induced by an unbalanced diet, and low physical activity, with which obesity being the primary reason for its exponential rise worldwide. Due to insulin resistance, there is excess production of glucose by the liver but due to its insufficient utilization by muscle and adipose tissues, a condition of hyperglycemia arises and is characterized by polyuria, polydipsia, and polyphagia (Gunathilaka et al. 2020).

Bioactive compounds present in algal species include phlorotannins, polysaccharides such as fucoidans, alginates, laminarins, carotenoids such as fucoxanthin, sterol–fucosterol have proved to have high antidiabetic potential. Therapeutic targets for these bioactive compounds and their mechanisms are:

(i) Inhibitory activity of α-Amylase and α-Glucosidase enzymes: In the cell's metabolic pathway, α-amylase and α-glucosidase enzymes play a vital role in the formation of glucose. Inhibition of these enzymes helps in lowering postcibal blood glucose levels. The presence of several phlorotannins in marine algae such as eckol, phloroglucinol, dieckol, 7-phloroeckol and 6,6′-bieckol, phlorofucofuroeckol-A and methanol extracts have shown to have an inhibitory effect on these enzymes. Compared to regular acarbose, algal phlorotannins show strong antidiabetic activity (Lee and Jeon 2013).
(ii) Inhibitory activity of Aldose Reductase (AR): Aldose reductase is an enzyme that converts glucose to sorbitol, which is a key step in the polyol pathway. A high amount of this can cause diabetic neuropathy. Phlorotannins found in ethanol extract, hexane, and aque-

ous fractions extracted from the brown alga *Ecklonia stolonifera* exhibit inhibitory action on the enzyme AR (Jung et al. 2008). Jung et al. investigated the inhibitory action of algae on aldose reductase. Fucosterol, a substance derived from *Ecklonia stolonifera*, was found to block aldose reductase activity in rat lenses as well as human recombinant aldose reductase enzyme (Gunathilaka et al. 2020). Similar activity was also shown by dichloromethane fraction extracted from *Saccharina japonica* and fucoxanthin extracted from *Eisenia bicyclis*and *Undaria pinnatifida* (Jung et al. 2012).

(iii) Inhibitory activity of angiotensin-converting enzymes: Activation of rennin–angiotensin–aldosterone causes an increase in the blood pressure in diabetic patients that further leads to microvascular and macrovascular complications. Phlorotannins prevent this condition by having an inhibitory role on angiotensin-converting enzyme (ACE) (Paiva et al. 2017). *Ecklonia stolonifera* was examined for its anti-diabetic properties and was found to have significant amounts of phlorotannins, which inhibited the angiotensin-converting enzyme (ACE). These phlorotannins include eckol, phlorofucofuroeckol-A and dieckol, among which dieckol inhibited ACE non-competitively. Other seaweeds such as *Sargassum fusiforme, Sargassum horneri* and *Ecklonia cava* have been shown to have similar ACE (Jung et al. 2006).

(iv) Inhibitory activity of protein tyrosine phosphatase (PTP) 1B: Inhibition of the enzyme PTP 1B increases insulin sensitivity thus decreasing the blood glucose levels. Eckol, 7-phloroeckol, phlorofucofuroeckol-A isolated from several species of brown algae blocks the activity of PTP 1B enzyme through a non-competitive inhibitory mechanism (Lopes et al. 2017). Among these phlorofucofuroeckol-A possess the highest inhibitory efficiency. In a study by Ali et al. *Sargassum serratifolium* was explored for the inhibitory activity of the PTP 1B enzyme. The results showed the highest inhibitory effect with hexane fraction than ethanol extract.

(v) Inhibitory activity of dipeptidyl peptidase-4 Enzyme: The enzyme DPP-4 regulates glucose metabolism by lowering the GLP-1 levels thus leading to the hyperglycemic condition. Ethyl acetate fractions and sulfated polysaccharide fractions of algae have been shown to have an inhibitory effect on the DPP-4 enzyme (Yang et al. 2019). In a dose-dependent manner, *Turbinariaconoides, S. binderi* and *Padina sulcata* are known to have significant DPP-4 inhibitory action. *Turbinariaornata* possess a high content of sulphated polysaccharides which are known to block the DPP-4 enzyme (Sharifuddin et al. 2015). Figure 1 represent the target

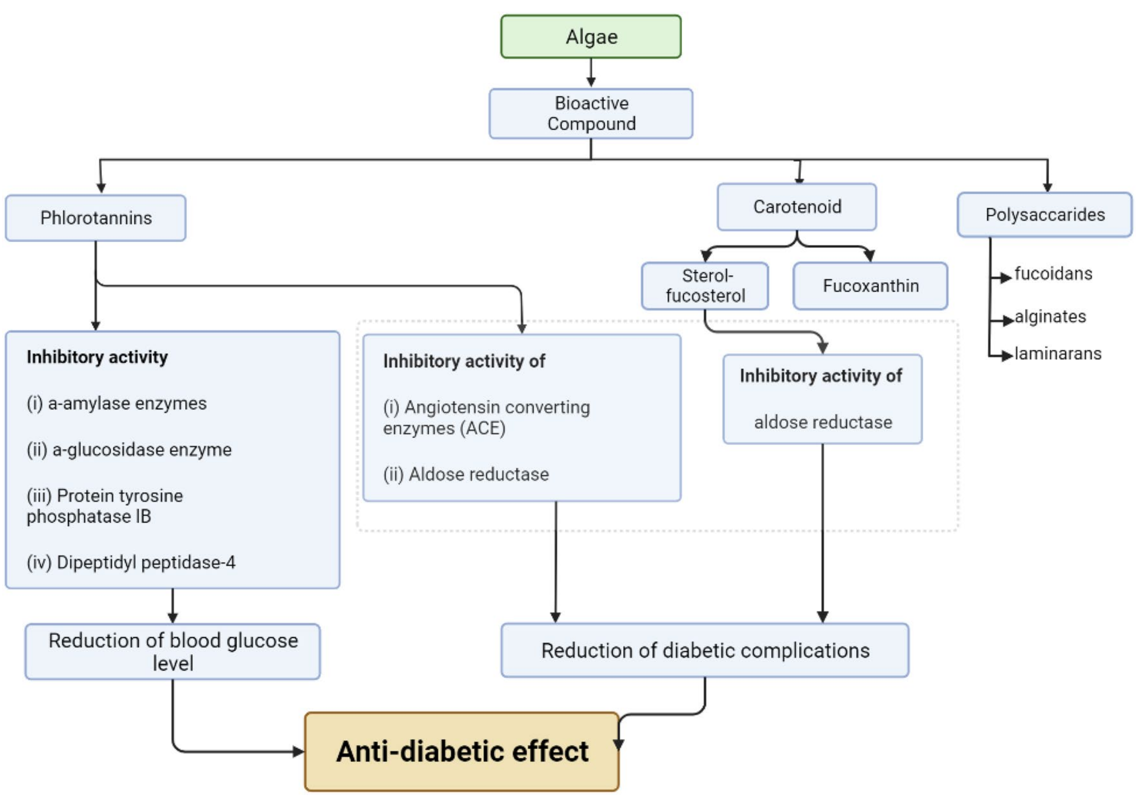

Fig. 1 Target mechanism of algal bioactive compounds for management of diabetes mellitus

mechanism of algal bioactive compounds for the management of diabetes mellitus.

Hypertension

Among the diverse functions of algae comes the anti-hypertensive effect. Apart from the abundance of bioactive compounds present in algae, it is also rich in dietary fibre and nitrate content which accounts for the hypotensive effect and leads to a decrease in blood pressure (Ismail et al. 2020). Certain peptides from macroalgae possess hypotensive potential on the human circulatory system and promote a healthy heart by preventing lethal illnesses including peripheral vascular disease and atherosclerosis (Fitzgerald et al. 2011). Nori-peptides a secondary metabolite extracted from seaweed *Porphyraye zoensis* show an important antihypertensive activity and also regulate blood cholesterol levels, inhibit hepatic cholesterol biosynthesis, and prevent hyperplasia (Toblli et al. 2002). Peptides, phlorotannins and polysaccharides are the chief bioactive compounds that target to regulate hypertension. Calcium channel blockers and diuretics are also some of the other common treatments for hypertension while, renin–angiotensin system inhibitors are the most widely used effective approach. In its working mechanism renin transforms angiotensinogen into activated angiotensin I, a potent vasodilator. Upon action of angiotensin-I converting enzyme, this angiotensin-I is further transformed to angiotensin II. This angiotensin II is a potent vasoconstrictor, that leads to hypertension. Therefore, blocking the reaction at the initial stage of the formation of angiotensin II or directly inhibiting angiotensin I synthesis are the two main approaches to lower blood pressure (Seca and Pinto 2018). ACE I inhibitors have a twofold mode of action. The first is they reduce the quantity of salt retained in the kidneys and the second is, they block the hormone angiotensin II from being produced (a hormone that causes blood vessels to narrow) (Reis et al. 2020). The reduced level of this hormone causes the blood to flow more efficiently through the arteries by helping the blood vessels to dilate and contract and thus regulating high blood pressure (Seca and Pinto 2018). Figure 2 represents a working mechanism of the anti-hypertensive effect of algal bioactive compounds.

Commercialized hypotensive peptides extracted from *Porphyrayezoensis, Pyropiayezoensis, Undaria pinnatifida, and Gracilariopsis lemaneiformis*are commonly available for consumption. Macroalgae *Ecklonia stolonifera and Ecklonia cava* are the largest sources of antihypertensive phlorotannins (Seca and Pinto 2018). In a study by Suetsuna et al., ten amino acids were extracted from the brown algae *Undaria pinnatifida*, which comprises 15% protein. These ten isolated amino acids were sequenced and studied for their hypotensive effect. It was found that these ten dipeptides followed the mechanism

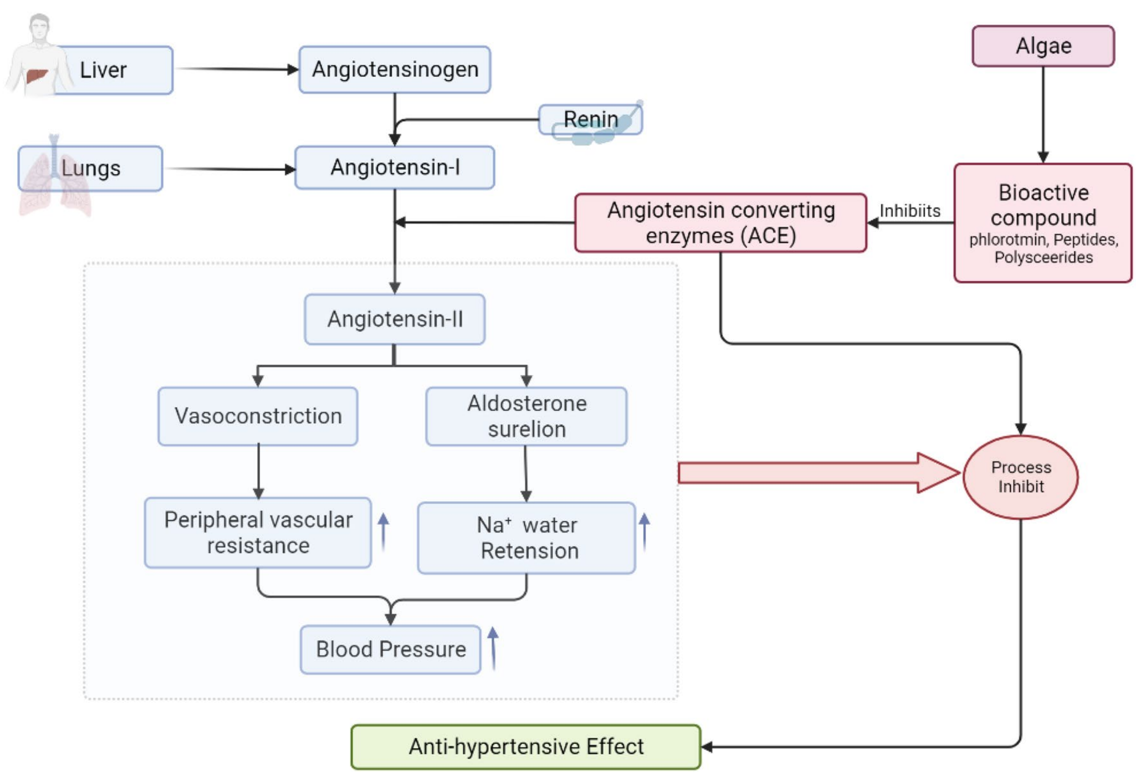

Fig. 2 Mechanism of anti-hypertensive effect of algal bioactive compounds

of ACE I inhibition to lower blood pressure (Seca and Pinto 2018). D-Polymannuronic sulphate is the prime polysaccharide isolated from *Pelvetiacanaliculata* (Linnaeus) and have been shown to possess acute and prophylactic hypotensive activity in vivo. It shows an antihypertensive effect by increasing the level of NO contents and lowering the levels of Angiotensin II and Endothelin 1 hormone (Seca and Pinto 2018).

Obesity

Obesity refers to the building-up of extra fat in the body and is linked to having adverse effects on the body such as hypertension, cardiovascular complications, and diabetes. Macro and microalgae have shown positive results for obesity treatment pressure (Ismail et al. 2020). Key bioactive compounds found in algae such as alginates, fucoidan, phlorotannins, fucoxanthin, fucosterol, and indole derivatives have been shown to have a role in digestion and are regarded as potential agents for obesity treatment. Changes in lipoprotein breakdown, repression of inflammation, reduction of adipogenesis, and a delay in stomach emptying are all part of these drugs' mechanisms of action (Wan-Loy and Siew-Moi 2016).

Fucoxanthin is abundantly found in *Undaria pinnatifida, Laminaria digitata, Hijikia fusiformis, tricornutum,* and *Isochrysisgalbana.* It increases β-oxidation and decreases lipogenesis in epididymal adipose tissue as well as enhances the activity of 5′ adenosine monophosphate-activated protein kinase along with acetyl-coenzyme A carboxylase (Hu et al. 2012). Alginates present in seaweed improve satiety and assist intestinal transit through their bulking capacity, providing an anti-obesity effect. These are commonly extracted from the genera *Lessonia, Macrocystis, Laminaria* and *Ascophyllum. Laminaria* and *Lessonia* are the primary sources. The mechanisms by which they exert their effect include delay in stomach clearance, activation of gastric stretch receptors, and restricted nutrient absorption by the cells (El Khoury et al. 2014). Phlorotannins such as phloroglucinol, and dioxinodehydroeckol extracted from brown algae *Ecklonia stolonifera* works as anti-obesity agents by preventing the differentiation of adipocytes. 1*H*-indole—carbaldehyde and 6-Formylindole are the chief indole derivative compounds that show adipogenesis inhibition. Another compound isolated from *Ecklonia stolonifera* that acts as an anti-obesity agent is sterols. Sterols block the expression of PPARγ and CCAAT proteins which are marker proteins of adipocyte expression (Seca and Pinto 2018).

Algae for cardiovascular diseases

Hypertension, hyperglycemia, and hyperlipidemia further give rise to achronic risk of cardiovascular disease (CVD). CVD includes conditions such as atherosclerosis, arteriosclerosis, thrombosis, myocardial infarction, and stroke in some cases. Damage to cells by free radicals is a crucial factor underlying CVD and stroke. Algal carotenoids have proved to have a beneficial role in treating CVD. This effect is attributed to the antioxidant activity of carotenoids. Carotenoids protect against oxidative stress by activating genes that regulate enzymes including superoxide dismutase (SOD), and catalase which protect against oxidative degradation of lipids and consequent damage to nucleic acid and proteins. Beta-carotene also helps to prevent oxidative stress by inhibiting lipid free radicals, scavenging reactive oxygen species, and absorbing UV radiation. *Dunaliella* being a rich source of Beta-carotene helps in the reduction of lipid peroxidation thus lowering plasma cholesterol levels (Raposo and De Morais 2015). A study by Hussein et al. (2005) showed the correlation between astaxanthin and low-density lipoprotein (LDL). It showed the inhibitory action of astaxanthin on low-density lipoprotein and thereby lowering the risk of atherosclerosis. Clinical trials on astaxanthin oral administration for 14 days showed positive results in regulating hypertension and a long-term dose of 5 weeks could reduce the risk of stroke (Sathasivam and Ki 2018). In humans, astaxanthin helps to increase adiponectin levels in the body and improve triglyceride levels along with high-density lipoprotein cholesterol (Ambati et al. 2014).

Genera *Haematococcus* is the largest producer of carotenoids, producing ~ 3.8% of astaxanthin of its dry weight. Other algal species include *Ulva lacuta*, and *Catenella repens* (O'Sullivan et al. 2010). Microalgae *Arthrospira* was studied by Miranda et al. for its effect on cardiovascular diseases. It was found that extracts from *Arthrospira* mainly phenolic components showed antioxidant effects and inhibited LDL cholesterol peroxidation. Microalgae are a rich source of vitamin C, B complex and provitamin A. These vitamins can counteract endothelial dysfunction that is mainly caused by the formation of free radicals and also prevent stroke in patients with cardiovascular disease (Raposo and De Morais 2015).

Algae for gastrointestinal diseases

The algal prebiotic concept has proved to be beneficial for the modulation of intestinal microbiota. Polysaccharides are major constituents of seaweeds and microalgae and act as prebiotics. These algal polysaccharide compounds that act as prebiotics include alginates, fucoidans, laminarin, and carrageenan. They act as roughage as they do not get metabolized in the upper gastrointestinal system. These dietary fibres delay stomach emptying due to their viscosity and regulate the transit time, thus improving nutrient and mineral absorption. The colon is heavily colonized with genera "*Bacteroides, Prevotella, Eubacterium, Clostridium* *and Bifidobacterium, Lactobacillus, Staphylococcus, Enterococcus, Streptococcus, Enterobacter and Escherichia*" (Besednova et al. 2020). These prebiotics provide a selective fermentation substrate for beneficial microbes to flourish thus changing the microflora profile of the human gut thus aiding in better digestion and preventing diseases caused by harmful bacteria (Besednova et al. 2020; Zheng et al. 2020).

Inflammatory bowel disease (IBD) are chronic inflammatory intestinal conditions that occur majorly due to an imbalanced immune system and interaction with microbes. The two most prevalent kinds of IBD are Crohn's disease and ulcerative colitis which are characterized by persistent diarrhoea, abdominal pain, and rectal bleeding. Furthermore, immunological dysregulation also occurs in IBD, when regulatory cells of innate acquired immunity fail to function properly, resulting in T-cell activation. As a result, soluble inflammatory mediators are released (Besednova et al. 2020). Immunosuppressants, antibiotics, and anti-inflammatory drugs are the current recommendations for the treatment of IBD. However, their usage is frequently harmful to the body and can also cause negative side effects. Some common side effects include osteoporosis, hypertension, and gastrointestinal ulcer aggravation from corticosteroids. Headache and nausea might occur due to amino salicylates. As a result, novel therapy options are being developed that target therapeutic targets which include potent natural compounds that can inhibit leukocyte adherence and migration into inflamed gut walls and inhibit the activity of cytokines and restore gut microflora, thus stimulating the healing of gastric mucosal layer. Algal polysaccharides such as alginates, fucoidans, carrageenans, agars, porphyrin, xylan, and ulvan are being used as nutraceuticals for the treatment of IBD (Besednova et al. 2020; Christaki et al. 2013). *Helicobacter pylori* colonize the gastric mucosa affecting the microbiota of the gut and can cause gastritis and peptic ulcer. Algal polysaccharides mainly fucoidans are used for the eradication of *H. pylori* by targeting the cell receptors of gastric mucosa and thus preventing its binding to the intestinal wall. Fucoidans possess potent anti-inflammatory and immunomodulatory effects which further enhance with increasing degree of sulfation in its structure. Therefore, besides protecting intestinal mucosa, fucoidans also protect against stomach infection and gastric cancers (Zheng et al. 2020).

Algae for microbial diseases

Antibacterial effects

Brown algae *Ecklonia kurome* are a rich source of phlorotannins and has antibacterial effects by interacting with bacterial proteins which results in bactericidal effect. It shows bactericidal action on multiresistant Gram-negative and Gram-positive bacteria. *S. enteritidis, S. typhimurium*, and *V. parahaemolyticus* are some of the Gram-negative strains while *S. aureus*, and *B. cereus* are the Gram-positive strains. Bromoditerpenes extracted from red algae *Sphaerococcus coronopifolius* exhibit antibacterial action on Gram-positive bacteria. Other marine seaweed having antibacterial effects include *Ulva fasciata*, and *Hypneamusci formis* (Ismail, Alotaibi and EL-Sheekh 2020). Bioactive compounds in these algae modify the cell porousness of the pathogen, disrupting the function of the membrane and finally leading to the destruction of pathogen cells. Red algae *Laurencia luzonesis* contain sesquiterpenes which have a strong bactericidal effect. *Bacillus megaterium* also acts as an antifungal agent (Arvinda Swamy 2011). Elatol and iso-obtusol are halogenated furanones which can be extracted from *Laurencia majuscule.* The human pathogenic bacterium *Staphylococcus epidermis* is susceptible to elatol, while iso-obtusol works against *Salmonella* species. Both of these halogenated compounds work by interfering with the biosynthetic pathway AI-2 of bacteria. They bind covalently with the LuxS enzyme which leads to the production of autoinducers-2 which in turn has bactericidal action (Arvinda Swamy 2011). In humans, urinary tract infection (UTI) is most of the most frequent and concerning infection caused by bacteria, and methanol extracts of seaweeds effectively kill bacterial pathogens *E. coli* and *S. aureus* causing UTI (Arvinda Swamy 2011).

Antiviral effects

Macroalgal polysaccharides are a potent source for treating viral diseases, such as HIV, hepatitis C, herpes simplex virus, and genital warts. Sulphated polysaccharides are found abundantly in algal cell walls and these include carrageenan, agar, ulvan, fucoidan, laminarin. By interfering with distinct phases of viral infection, these polysaccharides have antiviral efficacy against a wide range of viruses (Hans et al. 2021; Besednova et al. 2021). Sulfated polysaccharides have a distinctive structure that disrupts the virus life cycle at various stages. They either cause the inactivation of virions before infection or block their replication inside the host cell. They are also capable of attaching to immunomodulators that stimulate Natural Killer cells and trigger immunological responses. Polyphenolic compounds derived from algae also resist the replication of enveloped as well as non-enveloped viruses (Sami et al. 2021). Figure 3 describes the possible antiviral mechanism exhibited by algal nutraceuticals.

Algae as a novel approach have been developed to treat the present outburst of acute respiratory disease coronavirus disease 19 (COVID-19). The spike (S) proteins of the SARS-CoV-2 virus are the structural proteins that contain recombinant receptor-binding domain (RBD) which binds to ACE2 protein and help in viral invasion into the host cell (Sami et al. 2021). Currently, studies are being done to combat the spread of the SARS-CoV-2 virus by developing effective and harmless drugs using algal bioactive compounds. Coronavirus proteins are translated from a single polyprotein, simultaneously releasing two proteases: major proteases (Mpro) and papain-like protease (PLpro). The protein's active site contains a dyad of Cys145 and His41 which are promising targets for the inhibitory drugs. Besides polysaccharides, algal polyphenols are potential therapeutic compounds that exhibit antiviral activity. They inhibit the activity of PLpro and S protein of coronavirus, thus blocking viral entry. Phlorotannins extracted from *E. cava* block the activity of PLpro of the SARS-CoV virus (Sami et al. 2021; Vo and Kim 2010). Griffithsin and cyanovirin-n are the most studied algal lectins for antiviral application. They are widely used to counteract HIV infection besides the SARS-CoV-2 virus (Pagarete et al. 2021). Table 2 summarizes the different bioactive compounds targeting different diseases.

Neuroprotective effects of algae

Neurodegeneration is defined as damage or reduction in the count of neurons in certain areas of the central nervous system over time. The term neuroinflammation refers to the activation of glial cells mostly microglia and astrocytes into a provocative inflammatory condition which is an efficient innate defense mechanism that protects the nervous system and also maintains homeostasis (Barbalace et al. 2019). The long-term inflammatory events in the neuronal cells, on the other hand, can trigger a cascade of events that culminate in the gradual destruction of nerve cells, as seen in Alzheimer's disease, multiple sclerosis, Parkinson's and Huntington's disease (Barbalace et al. 2019; Glass et al. 2010). Overstimulation of glial cells leads to the production of cytokines and oxygen radicals which cause synaptic impairment and neuronal death culminating in CNS damage (Barbalace et al. 2019). An increasing number of studies have emphasized the critical role of the immune system in the onset and development of neurodegeneration activity. Immune cell growth and migration are caused by alterations in cytokine signalling, further, impaired phagocytosis and nonspecific reactive change in glial cells are also typical characteristics of neurodegeneration (Tarozzi et al. 2013). The main molecular events that trigger the development of Alzheimer's disease are oxidative stress and protein deposition. Marine algae prevent neuroinflammation by blocking the action of pro-inflammatory enzymes such as cyclooxygenase-2 and inducible nitric oxide synthase, regulating mitogen-activated protein kinase (MAPK) or ERK pathways and activating NF-κB (Yu et al. 2015). Figure 4 describes the bioactivities of algal compounds to prevent neurodegeneration.

Alzheimer's disease (AD)

AD was originally recognized and reported in 1906 by Dr Alois Alzheimer and is the most prevalent type of neurodegenerative disease. This is marked by the gradual loss of nerve cells, resulting in brain atrophy, particularly in cognition centers. It is the most prevalent cause of dementia which

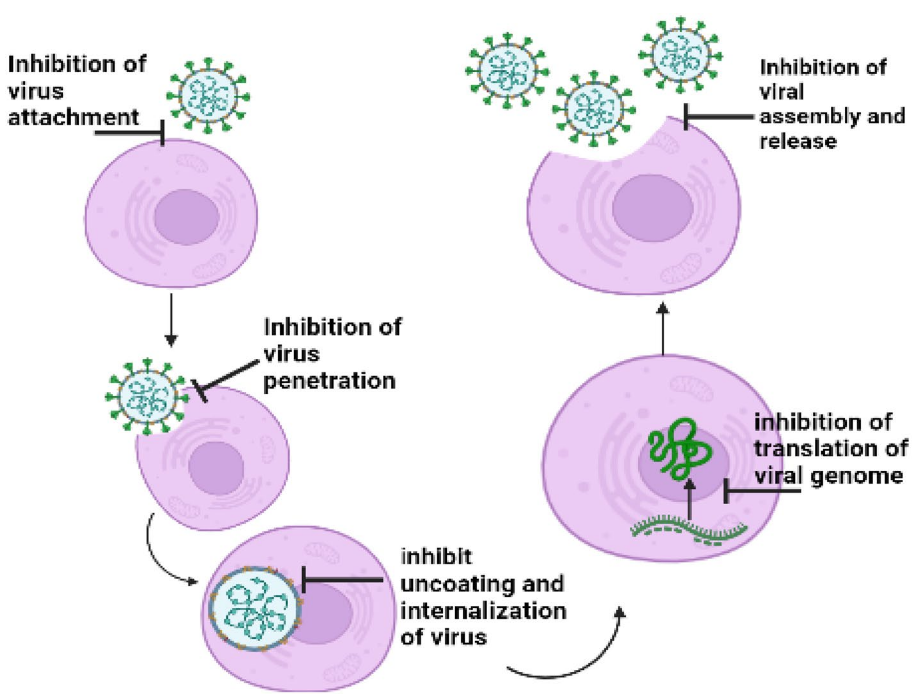

Fig. 3 Possible antiviral mechanism exhibited by algal nutraceuticals

is a progressive mental condition that leads to impairment of critical brain processes and leads to memory loss and cognitive deficit (Silva et al. 2021). The characteristic feature of AD is the dysregulation in the levels of beta-amyloid (Aβ), neurofibrillary tangles, and high concentration of unubiquitinated tau. AD is often referred to as tauopathy due to the presence of a greater percentage of misfolded and insoluble tau protein. The misfolding of Aβ leads to the appearance of senile plaques and misfolding of tau protein makes it insoluble and leads to its build-up due to the prevention of its release by the blood–brain barrier (Bauer et al. 2021; Bertsch et al. 2021). The involvement of reactive oxygen species also adds to neuronal damage. These subsequent events lead to altered levels of neuromodulators such as acetylcholine (ACh) and butyrylcholine (BCh). Principle therapeutic strategy against AD is the blocking of the binding of acetylcholinesterase enzyme (AChE) and butyrylcholinesterase enzyme (BuChE). Both of these enzymes are responsible for the hydrolysis of Ach and BCh (Pangestuti and Kim 2011; Silva et al. 2021). Seaweed being the recently discovered potent inhibitor of AChE and BuChE also improves the cholinergic deficit in patients. *Ochtodessecundiramea, Hypneamusciformis, Pterocladiacapillacea, Gelidiumpristoides*, and *Gracilariacorticata* exhibit inhibitory potency of these enzymes (Alghazwi et al. 2020). Besides this fucoidan extracts inhibit the aggregation of amyloid-beta and the production of ROS and significantly improve hydrogen peroxide toxicity (Li et al. 2017a). Seaweed polysaccharides inhibit lipid peroxidation and erythrocyte hemolysis leading to the control of neuroinflammation that prevents neuronal damage and helps in the repair of brain tissue (Silva et al. 2019).

Parkinson's disease (PD)

It is a type of neurological illness that impairs the mobility of the elderly. It is marked by the formation of Lewy bodies (deposits of a protein named alpha-synuclein), loss of dopaminergic (DAergic) neuronsin the "*substantia nigra* of *pars compacta* (SNpc)" and decline in the levels of dopamine (Ramkumar et al. 2017; Alves et al. 2016). Nerve cells and black substance which is a portion of the basal ganglia deteriorate. Though the basal ganglia do not convey connections directly to the CNS, they are essential structures connected to movement. Some other distinguishable symptoms of Parkinson's disease include resting tremors of muscles, muscular stiffness, and postural instability. Alves et al. verified the antioxidant potential of *Bifurcaria bifurcata.* Its methanolic and dichloromethane extracts work by scavenging the free radicals and protecting against neuronal damage (Li et al. 2017a; Hannan et al. 2020). Several extracts of macroalgae showed neuroprotective effects in human neuroblastoma cells from 6-hydroxydopamine (6-OHDA). *Laminaria japonica, Ecklonia cava, Fucus vesiculosus, Saccharina japonica, Turbinaria*, and *decurrens* are the other algal species used to produce dichloromethane extracts to cure PD (Rodriguez-Pallares et al. 2007). The other possible mechanisms associated with the treatment of PD include the prevention of alteration in mitochondrial membrane potential thus regulating oxidative phosphorylation. Decrease in level of H_2O_2 thus preventing oxidative stress (Valado et al. 2017). Decrease in the activity of Caspase-3 that mediate cell death by apoptosis. DNA staining with DAPI (4′,6-diamidino-2-phenylindole) probe unveiled that treatment with algal bioactive compounds decreased karyopyknosis and fragmentation of chromatin which are hallmarks of apoptosis (Pereira and Valado 2021).

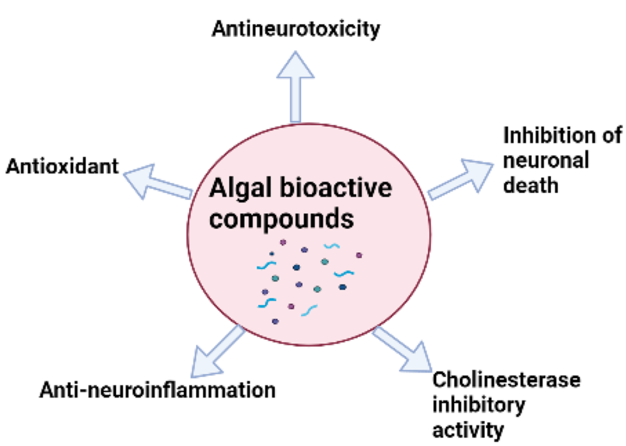

Fig. 4 Bioactivities of algal compounds to prevent neurodegeneration

Multiple sclerosis (MS)

It is an autoimmune-related neurological demyelination disorder of the CNS. Common symptoms of MS include muscular weakness, the disturbed balance of motor coordination, fatigue, joint ache, depression, and changes in visual acuity. Since this disease cannot be cured, algal compounds are employed to reduce the symptoms of this disease (Wahls et al. 2019; Saadaoui et al. 2020). Since lifestyle factors and food quality affects the course and seriousness of the disease, dietary recommendations for people diagnosed with MS can minimize the symptoms of the disease. Algal bioactive compounds induce epigenetic alteration in gene transcription and improve the composition of gut microbiota, which further results in decreased inflammation. This also provides for nutrient sufficiency needed for neuronal structure (Larsen and Minna 2011). PUFAs form a significant component of algal cell membranes and are pioneers of eicosanoids which are crucial bioregulators of a variety of cellular processes. PUFAs have been shown to effectively lower the risk of MS development (Saadaoui et al. 2020). Furthermore, vitamin deficiencies add to the severity of the multiple sclerosis symptoms, the most significant of which are vitamins A and D which act as response modifiers of the immune system. Vitamin C, E and B_{12} play a vital role in myelinogenesis and some of the algal species rich in these vitamins are *Porphyra* spp., *Ulva* spp., and *Laminaria* spp. (Pereira and Valado 2021).

Algae for treatment of cancer

Cancer is a worldwide critical health challenge. Mutations, tumor suppressor gene inactivation, and overexpression of growth-promoting oncogenes are among the genetic and epigenetic changes that cause cancer. The overstimulated oncogenes include EGFR, ERBB2, KRAS, CDK4, BCL2 (Hanahan and Weinberg 2011; Morgillo et al. 2016). Multiple molecular anomalies have been linked to the pathogenesis of human cancer, leading to increased angiogenesis, resistance to apoptosis, sustained proliferative signalling, inactivation of tumour suppressor genes, and stimulation of metastasis of cancer cells (Fan et al. 2014). Among the proposed mechanisms for cancer progression resistance to EGFR inhibitors is the most prevalent cause. Algal compounds are effective in different types of cancer such as breast cancer, colorectal cancer, and lung cancer (Gantar et al. 2012). Owing to their effectiveness and low toxicity, phycobiliproteins extracted from Rhodophyta species play an essential role as antitumor drugs. They can boost the effectiveness of traditional anticancer drugs while reducing their negative effects. Phycocyanin in particular has an antitumor effect, preventing cancer cells from multiplying and killing infected cells, these are some of its effects making it a viable source for anticancer drugs (Ismail et al. 2020). Inhibition of tumors via xenobiotic metabolism, which lowers the rate of carcinogenesis, or disruption of mitosis at the telophase stage of cell division are two ways macroalgal phenolic chemicals inhibit tumor progression. They also reduce the levels of cellular proteins and certain flavonoids can even block the activity of aromatase, which helps in the progression of cancer cells (Ismail et al. 2020).

The algal bioactive compounds that exhibit anti-inflammatory and anti-tumor activity include peptides from *Chlorella vulgaris*, *Chlorella pyrenoidosa* (Guedes et al. 2013), phycobiliproteins extracted from red microalgae (Somasekharan et al. 2016), polysaccharides such as carrageenan from *Betaphycusgelatinum, Eucheuma denticulatum, K. alvarezii, Kappaphycus striatus*, fucoidan from *F. vesiculosus, U. pinnatifida, S. cichorioides* and laminarin from brown algae such as *Saccharina* species and *Laminaria* (Vishchuk et al. 2013; Zainal Ariffin et al. 2014; Ouyang et al. 2012). Among other tetraterpenoids such as canthaxanthin and β-carotene, astaxanthin extracted from *H. pulvialis* exhibits mitotic arrest and promotes apoptosis thus, inhibiting tumor cells in human colon cancer (Ambati et al. 2014). Figure 5 describes the action of phenolic compounds in the treatment of cancer.

Mechanism of anti-tumor activity

I. Apoptosis

Apoptosis causes cell cycle block and ultimately leads to cell death. The anticancer effect of the medications is centered on the interruption of these two phenomena. The concept of cell death caused by a cell cycle block has gotten a lot of interest since it might be utilized to minimize pharmacological resistance and reduce mutagenesis and toxicity. Upon treatment of tumor cells, Caco-2 and HepG2 with degraded κ-carrageenans at adequate concentrations, hallmarks of apoptosis such as detachment of adherent cells, externalization of phosphatidylserine, karyopyknosis, and formation of apoptotic bodies (ApoBDs) were observed. Furthermore, transcription of cell proliferation markers like PCNA, and MKI67 decreased in apoptotic cancer cells (Kim et al. 2010; Katoh 2017). Fucoidans increase the activation of Caspase-3 that are central effector of apoptosis. Fucoidans increase the porosity of the mitochondrial inner membrane and secretion of cytochrome c and Smac/Diablo

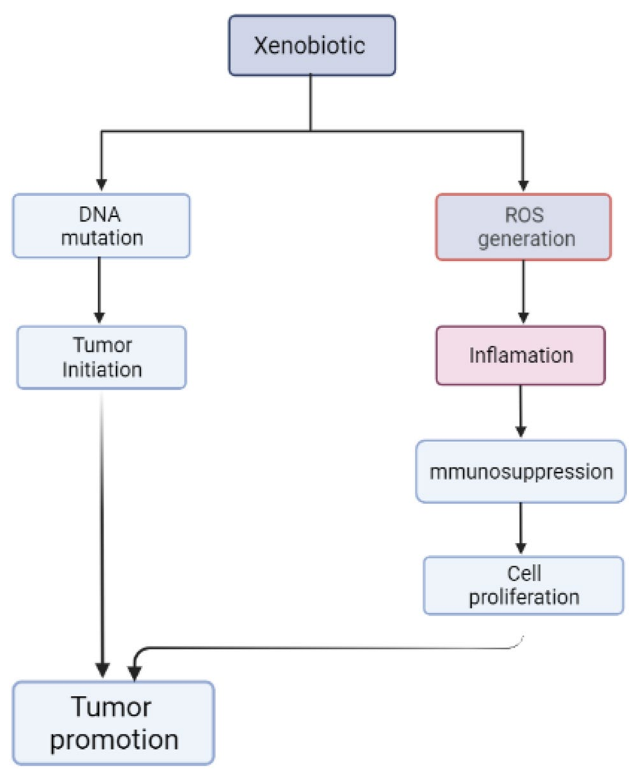

Fig. 5 Action of phenolic compounds in treatment of cancer

that promotes the activation of caspases (Dijksterhuis et al. 2014; Khotimchenko et al. 2020).

II. Wnt-cascade role in antiproliferation

The Wnt-cascade is one of the most essential cellular signalling pathways which is also involved in embryonic development and stem cell phenotypic maintenance. Mutation in this pathway leads to the formation of malignant tumors. Wnt comprises secreted glycolipoproteins that activate the signalling pathway that controls cell differentiation and the mitotic rate of cells. If the activity of Wnt is blocked, Axin, casein kinase 1 (CK1) and glycogen synthase 3β kinase (GSK3β) form a complex with cytoplasm β-catenin (Tabatabai et al. 2017). After the formation of this complex, CK1 and GSK3β then collectively phosphorylate β-catenin, which is subsequently identified and ubiquitinated followed by proteasome degradation (Yuan et al. 2011a; Li et al. 2017b). In the activated state, Wnt binds to its target Frizzleds (Fr) receptors which further activates the Dishevelled (Dvl) protein. The Dishevelled protein stabilizes a "destructing complex-Wnt/Fr/LRP/Dvl/Axin" and also inhibits GSK3 thus maintaining the levels of β-catenin (Khotimchenko et al. 2020).

III. Immune mechanism

Humoral and cell-mediated immunity inhibits tumour growth through activation of the complement system, proliferation of immune cells, and synthesis of immune cell factors. Enhanced NK cell activity and macrophage phagocytosis are observed in oligo-carrageenan-treated cancer cells (Yao et al. 2014). It also accelerated the maturation of Dendritic cells (DC) stimulating MHCII expression on DC. This stimulates the secretion of cytokines IL-12, IL-1β, and TNF-α. In a study by Li et al. (2017b), it was discovered that λ-carrageenan aids in DC maturation and cytokine production leading to the death of cancer cells by using the inhibitor for Toll-like receptors-TAK-242 and determining the phosphorylation status of components in the MAPK and NF-κB signalling pathways. Furthermore, the anticancer effects of λ-carrageenan have been linked to the suppression of Tregs (regulatory T-cells) and myeloid-derived suppressor cells (MDSC), both of which reduce the immune response to a foreign antigen (Khotimchenko et al. 2020).

IV. Anti-angiogenic mechanism

The term angiogenesis refers to the building up of new blood vessels on the foundation of preexisting blood vessels that aid in the progression of solid tumors by supplying nutrients to these cells. Since cancer is marked by increased vessel permeability, it also contributes to the greater metastatic potential of cancer cells. Algae-derived oligosaccharides possess the capability to hinder angiogenesis and reduce the levels of intracellular matrix metalloproteinase production inside endothelial cells further limiting endothelial cell invasion and migration. Yao et al. studied dose-dependent inhibition of vein endothelial cell proliferation by κ-carrageenan. It was found that under in vitro circumstances, it also decreased ECV304 cell migration triggered by human breast cancer cells (MCF-7) and fully blocked the development of capillaries in collagen gel at a dosage of 200 g/mL (Li et al. 2017b). Anti-angiogenic effects are induced by inhibiting cytokine mRNA production and receptors for vascular endothelium growth factor 1 (VEGF 1), basic fibroblast growth factor (bFGF), and CD105 (Khotimchenko et al. 2020). Figure 6 describes a detailed mechanism for the anti-cancer effect of algal bioactive compounds.

Algae for skin photoprotection

Ultraviolet radiation (UVR) wavelength ranges from 200 to 400 nm and is a part of the electromagnetic spectrum of solar radiation. UV-A and UV-B a component of UVR having a wavelength above 290 nm cause skin damage (Conde et al. 2000; Oren and Gunde-Cimerman 2007). Mycosporine-like amino acids (MAAs) commonly called "microbial sunscreens" are aromatic amino acids involved in photoprotection. The capacity of these chemicals to disperse hazardous UV radiations into heat energy that scatters into the environment without producing reactive photoproducts protects the cell (Misonou et al. 2003). In vitro, MAAs can also prevent UVR-induced thymine dimer formation (Chrapusta et al. 2017). Other phycocomponents such as carbohydrates, phenolic compounds, terpenoids, and carotenoids also show anti-oxidative photoprotection (Oren and Gunde-Cimerman 2007). Brown algae phycocomponents have a strong inhibitory action on the expression of UV-induced MMP-1 (Matrix-metalloprotein complex) resulting in photodamage. Dieckol and eckolare the two compounds from *Ecklonia stolonifera* that can suppress the expression of MMP-1 in the human dermal fibroblast cell line (Kalasariya et al. 2020). Furthermore, phlorotannins which are found in many algal species promote the expression of NF-κB and AP-1 (activator protein-1) which decreases the activity of MMP-1. A high level of expression of MMP can cause extracellular deterioration and algal polysaccharides can reduce the threat of photodamage by interacting with fibroblast growth factors (FGF) produced by macrophages and protecting them from proteolysis (Kalasariya et al. 2020; Joe et al. 2006).

Besides photoprotection, phycocomponents are also helpful in skin curation, and treating dehydration. Natural humectants containing MAAs, and polysaccharides improve the water-holding capacity of the stratum corneum preventing skin dryness and dehydration and maintaining the elasticity of the skin (Kalasariya et al. 2020).

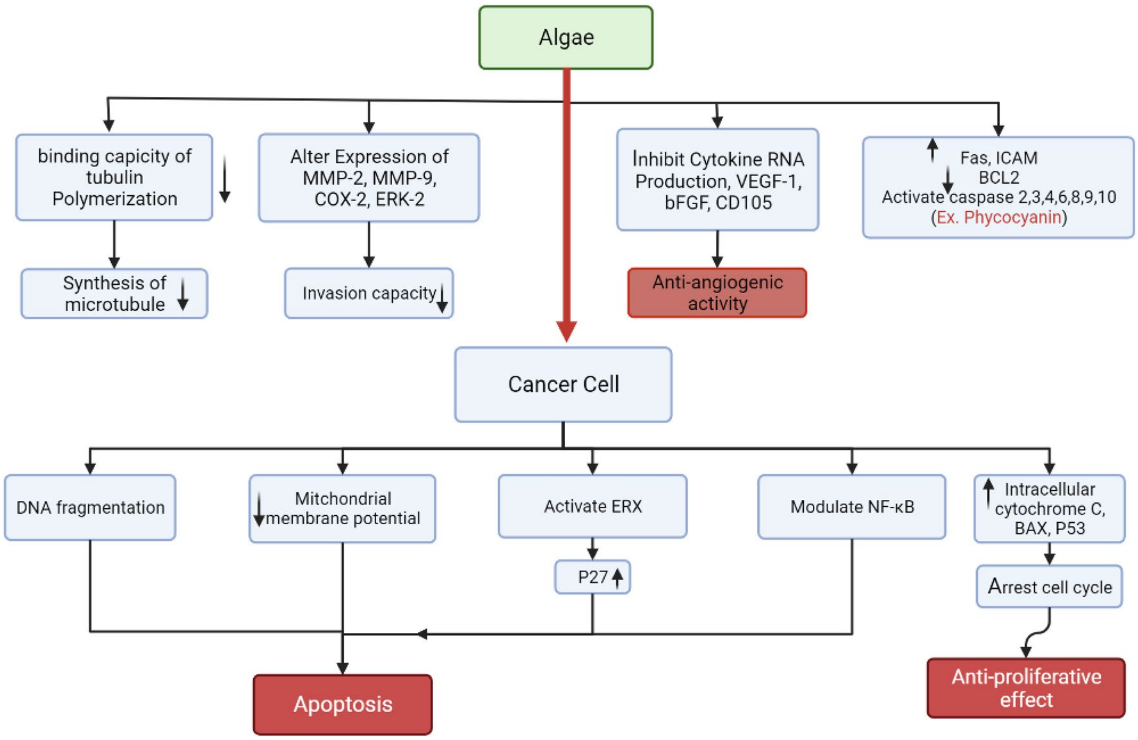

Fig. 6 Detailed mechanism for anti-cancer effect of algal bioactive compounds

Table 1 List of manufacturing companies involved in production of algal products

Company	Country	Algal species used	Key products	Annual revenue in 2021	References
Earthrise Nutritionals, LLC	California, USA	*Spirulina*	*Spirulina* based products	$ 22 million	Sharma and Sharma (2017), Araújo et al. (2021)
Cyanotech Corporation	Hawaii, USA	*Haematococcus pluvialis, Spirulina*	Bioastin astaxanthin and spirulina products	$ 32.3 million	Sharma and Sharma (2017)
BlueBioTech Int. GmbH	Germany	*Spirulina platensis, Haematococcus Pluvialis*	phycocyanin, astaxanthin, and microalgae powder	$ 5.9 million	Mehta et al. (2018)
Algatechnologies Ltd	Israel, USA	*Haematococcus pluvialis*	AstaPure, a natural astaxanthin	$ 15 million	Balasubramaniam et al. (2021)
E.I.D.—Parry (India) Limited	India	*Chlorella*, *Spirulina*	Nutraceuticals from micro algae	$ 22.7 million	Ratledge (2013), Kratzer and Murkovic (2021)

Conclusion

This review summarizes the medicinal importance of some algal-derived nutraceuticals. These bioactive compounds are not only potentially effective but also eco-friendly and safe. Furthermore, the cultivation of algae is sustainable as it has the ability for carbon dioxide sequestration. These algal bioactive compounds are being employed in food as stabilizers, thickening agents, emulsifiers, and texture modifiers. They serve in fulfilling various human dietary requirements and also have a significant role in combating serious health problems like cardiovascular, and neurodegenerative diseases, immune disorders, atherosclerosis, stroke, and carcinomas. Owing to the greater diversity in the biochemical composition of algae, it is now considered a potential functional food or superfood. Algal biomass possesses a significant variability in terms of biochemical composition and technological improvements about its incorporation as a food supplement has favored its

Table 2 Algal species and their bioactive compounds for different diseases

Algal species	Type of nutraceutical	Bioactive compounds	Target disease	References
Ecklonia cava, Fucus spp., *Ascophyllum*	Polyphenols	Phlorotannins	HIV	Vo and Kim (2010)
Porphyridum cruentum	Polysachharides	Lectins	Myeloid tumor	Gardeva et al. (2009)
Chlorella zofingiensis, Muriellopsis	Carotenoid	Lutein	Stroke and Cardiovascular disease	Liu et al. (2017), Ku et al. (2013)
Skeletonema costatum, Crypthecodinium cohnii	PUFA	Omega 3- fatty acid	Coronary heart disease, inflammatory disease	Shahidi (2012)
Saccharina latissima, Porphyra tenera	Amino acid, carotenoid	Taurine, Fucoxanthin	Obesity, hypocholes-trolemic effect	Maeda (2015)
Gracilaria blodget-tii, Gracilaria lemaneiformis,Ulva lacuta	Polyphenols, polysach-haride	Phlorotannins, porphyran, alginic acid	Allergy, asthama, inflam-matory diseases	Cheong et al. (2021), Jaswir and Monsur (2011)
Aphanizomenon	Carotenoid	c-Phycocyanin	Artheritis, dermatological problems	Bishop and Zubeck (2012)
Hematococcus	Carotenoid	Astaxanthanin	Age related muscular degeneration	Bishop and Zubeck (2012)
Chondrus crispus, Gelid-ium cartilagrinum	Carbohydrates	Carrageenan	STD (genital warts, gonor-rhea, herpes,simplex virus)	Mendis and Kim (2011)
Laminaria digitata, Lami-naria phyperborea	Polysaccharides	Alginic acid	Gastritis, gastroduodenal ulcers	Besednova et al. (2020)
Laminaria japonica	Vitamins	Iodine	Goiter	Mendis and Kim (2011)
Spirulina, Porphyra yezoensis, Chlorella vulgaris	Protein	Nori-peptides	Cardiovascular diseases, hypertension	Ambati et al. (2014), Toblli et al. (2002)
Wollea saccata, Phorme-dium fragile, Spirulina plantensis	Phenols, alkaloids	Alginates	Plant fungal diseases	Righini et al. (2019)
Laurencia spp.	Phytochemicals	Halogenated compounds	Tuberculosis, antimicro-bial	Cabrita et al. (2010)
Gracilaria spp., *Microcys-tis aeruginosa*	Protein	MAAs	Skin cancer	Lawrence et al. (2017)
Ecklonia kurome, Ulva fasciata, Hypnea musci-formis	Pigments, phenols	Astanxanthin, Phlorotan-nins,	Bacterial diseases	Arvinda Swamy (2011)
Ecklonia cava	Sulfated polysaccharides	Ulvan, fucoidan	Viral diseases	Pujol et al. (2012)
Sargassum polycystum *Ecklonia stolonifera,* Ishige okamurae	Phlorotannins, polysach-hacrides sterol	Fucoidans, alginates, lami-narans, fucosterol	Diabetes mellitus	Shimada et al. (2016)
Pterocladia capillacea, Gelidium pristoides, Gracilaria corticata	Polysaccharides, phenols	Fucoidan, phlorotannins	Alzheimer's disease	Silva et al. (2019)
Laminaria japonica, Ecklonia cava, Fucus vesiculosus, Saccharina japonica, Turbinaria, decurrens	Polysaccharides, phenolic compounds	Fucoidan, dieckol	Parkinson's disease	Jha et al. (2017)
Palmaria palmate, Sac-charina latissima, Sac-corhiza polyschides	PUFAs, phenols	Omega 3-fatty acids, bromophenol	Multiple sclerosis	Yuan et al. (2011a, b)
Haematococcus pluvialis	Carotenoid	Astanxanthin	Kidney function impair-ment	Bajpai et al. (2014)
Sarcothalia crispata, Mazzaella laminarioides, Chondrus crispus	Polyphenols, carotenoids, polysaccharides	Astanxanthin, carrageenan, laminarin, fucoidan	Cancer	Fan et al. (2014)

commercial production. Multinational food companies and pharmaceutical industries are bringing these nutritional innovations to customer consumption products (like breakfast cereals, probiotics, and soft drinks). Due to the increasing rate of inflation in recent years, the future seems more promising for the commercial application of algae in the food, cosmetic, and pharmaceutical industries as well as feedstock for energy. The challenge yet remains to modify seaweeds into more palatable functional food for increasing the consumption demand. Apart from these basic aspects, the amount of production must be increased so that raw seaweed demands may be satisfied at competitive costs and more attempts must be made to discover new sources of algae that have previously been overlooked.

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Author contributions The authors have equally contributed. All the authors have read the final manuscript.

Data availability The authors confirm that the data supporting the findings of this study are available within the article.

Declarations

Conflict of interest The authors declare that they have no conflict of interest in the publication.

Research involving human participants and/or animals No.

Informed consent Yes, we know every aspect of our participation.

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