Review Article

A Comprehensive Review on the Medicinal Uses of Algae Belonging to Rodophyta Family

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ABSTRACT

The seaweed family known as Rhodophyta is among the largest and most diverse. It encompasses a range of eukaryotic cells with characteristics such as the absence of flagella, floridenic starch, phycobiliprotein pigments, unstratified thylakoids, and chloroplasts that lack an outer endoplasmic reticulum. This group of algae is rich in beneficial compounds like omega-3 fatty acids, amino acids, polysaccharides, vitamins A, B, D, E, and minerals all of which have significant medicinal and nutritional value. Furthermore, certain phytochemicals found in Rodophyta algae including polysaccharides (such as agar, carrageenan, porphyran), fatty acids, phenolic compounds, and pigments (such as phycobiliproteins, phycoerythrin, phycocytenoids) are responsible for their potent healing properties. As a result, the pharmaceutical and neutraceutical industries are increasingly turning to red algae as a source of valuable ingredients. This article delves into the various phytoconstituents present in Rodophyta algae and their wide-ranging uses.

Keywords: Algae, Rhodophyta, phytoconstituents, pharmaceutical uses.

INTRODUCTION

Marine microalgae renowned for their rich abundance of unique and biologically active compounds with distinct chemical structures and properties have long been recognized as valuable sources of natural remedies.[1] These marine plants commonly known as seaweeds are particularly rich in bioactive substances that have proven effective in treating various human diseases. In light of the growing demand for feed supplements containing innovative and unconventional protein sources there has been a surge in research focused on discovering novel bioactive compounds derived from microalgae in marine environments.[1, 2] A recent trend has emerged in utilizing algae from the Rhodophyta family which boasts an impressive 5000-6000 species making it one of the largest families of marine algae.[2] This increased interest can be attributed to the presence of several phytochemicals with nutraceutical and medicinal properties including omega-3 fatty acids, amino acids, polysaccharides, vitamins A, B, D, E, minerals, and more.[3] Morphologically red algae vary greatly ranging from single-celled to complex thallus with parenchymatous and non-parenchymatous structures. They consist of various combined characteristics such as eukaryotic cells, a lack of flagella, floriden starch, phycobiliprotein pigments, unstacked thylakoids, and chloroplasts without an external endoplasmic reticulum. [2, 3] Their cellular composition includes double cell walls consisting of an outer layer composed of Agarose and Agaropectin and an inner layer primarily made of cellulose.[3] The unique cell structure of red algae includes normal spindle fibres, microtubules, and unstacked photosynthetic membranes, as well as the presence of phycobillin pigment granules and the absence of chloroplasts and endoplasmic reticulum. Flagella and centrioles are absent throughout their entire lifespan.[3,4] Furthermore the diverse chemical components found in algae are responsible for their notable medicinal properties.

Polysaccharides:

They are complex macromolecules consisting of monosaccharide units linked together by glycosidic bonds. Their primary functions include energy storage and providing structural support making them the most plentiful natural biopolymers found everywhere. Marine microalgae contain a diverse range of polysaccharides including cell wall polysaccharides, mucopolysaccharides, and storage polysaccharides.[4] Among these red algae are considered the richest source of polysaccharides and are renowned for their unique sulfated galactans such as agar agarose and carrageenan which make up 40%-50% of their dry weight. These sulphonated polysaccharides act as a protective barrier against pathogens and have been used for their antioxidant, anti-tumor, and antihypertensive properties.

Agar:

Agars also known as sulfated galactans are naturally found in various types of red seaweed and are soluble in water. These compounds consist of alpha (1-4)-3 6-anhydro-L-galactose and beta 9 (1-3)-D-galactose residues.[4] Acting as thermo reversible gelling agents agars are composed of two polysaccharides - agarose and agaropectin. This

versatile substance originated in Japan in 1658 and was later introduced to Europe in 1859.[4,5]

The production of agar involves drying a gelatinous extract obtained from *Gellidium amansii* a member of the Gelidiaceae family as well as other red algae species such as Gracilaria (Gracilariaceae) and Pterocladia (Gelidiaceae).[5] In Japan these red algae are typically cultivated on bamboo structures located in the ocean and are harvested from May to October.

The compound agarose is composed of approximately 6% nitrogen-containing material and 3.5% nitrogen-containing substance.[4,5] One of its components agaropectin is a polysaccharide that has undergone sulphonation with some of its galactose and uronic acid units being esterified with sulphuric acid. This process contributes to the viscosity of agar solutions. Agar which is obtained through the process of cold water extraction has been found to possess anti-tumor properties.[4,5,6] It is believed that this effect is achieved by inhibiting mitosis at the metaphase stage in cancer cells. Agar is thought to achieve this by binding to various sites on tubulin a protein involved in the formation of microtubules and disrupting its function.[7,8] These microtubules are highly dynamic structures that continuously polymerize and depolymerize undergoing a process known as dynamic instability and treadmilling.[8] By altering the normal polymerization process of microtubules agar may effectively block cell division and lead to apoptosis or programmed cell death.[8]

Carageenan:

Carrageenan is a derived polysaccharide from the red algae *Chrondus crispus* which belongs to the family Rodophytaceae.[1] This phycocolloid also known as a water-soluble colloid is obtained in the form free flowing powder with a molecular weight that varies between 10,000 – 50,000 and a pH level of 9.0. It is found in both the intercellular matrix and cell wall of the algae.[9] To extract carrageenan, the dried seaweed is first rinsed with cold water to eliminate any salt or impurities. The seaweed is then heated and treated with either NaOH or CaOH to adjust its pH to a slightly alkaline state. Finally the extract is filtered to obtain the pure carrageenan.[10]

Chemically carrageenan has two forms known as kappa (k) and lambda depending on the presence or absence of anhydrogalactose. Kappa carageenan contains D-galactose 3 6anhydrous-D-galactose and an ester sulfate group while lambda carageenan contains D-galactose with its mono and bisulfate esters.[9,10] These compounds have been found to possess anti-coagulant and anti-thrombotic properties, with lambda being more effective than kappa carageenans. [10] Furthermore the potential of carrageenan extends to antiviral activity against herpes simplex virus types 1 and 2, particularly due to the abundance of alpha-D-galactose 2 6-disulfate residuals in natural carrageenan. [10,11]

Carrageenan possesses anticoagulant properties through the inhibition of thrombin. Thrombin plays a crucial role in converting soluble fibrinogen into insoluble fibrin and promoting platelet activation. Direct thrombin inhibitors (DTIs) work by binding directly to the active site of thrombin with three possible target sites: the active sites as well as exosites 1 and 2. [10,11]

As a vital component in cosmeceutical production this substance is highly valued for its powerful antioxidant effects. Not only does it possess impressive antioxidant, and anti-carcinogenic properties, but it also serves as a valuable gelling agent in the food industry. Its multifunctional nature makes it a popular choice for use as a stabilizer and viscosity enhancer.[10,11] Within the carrageenan market the food sector holds the largest share with its use in dietary products being particularly prominent. The purity of carrageenan is largely determined by the extraction process employed. While alcohol extraction yields anhydrous carrageenan at approximately 90% gel pressing techniques result in a slightly lower concentration of around 77%. These extractions are sourced from various species within the families of Gigartinaceae, Hypneaceae, Solireaceae, Phyllophoraceae, and Furcellariaceae.[11,12]

Porphyran:

Porphyran also known as sulphated galactan is a complex polysaccharide found in red algae of the genus porphyra. This unique molecule is composed of 1 4-linked alpha-l-galactopyranose-6-sulphate (L6S) and 1 3-linked beta-D-galactopyranose (G).[12] Its presence is widespread in the rocky coastlines of various regions around the world including Japan where it is commonly referred to as 'nori' 'laver' in the UK US and Canada 'purple laver' in Britain and Ireland 'kim' in Korea and 'zicai' in China. Apart from its culinary importance in traditional Japanese dish 'sushi' [1, 13] porphyran is also highly valued for its rich content of Vitamin B_{12}. Up to this date more than 130 species of red algae have been found to produce porphyran. The extraction process of this valuable compound can be achieved through water extraction or ultrasonic microwave assisted extraction methods. In the former the ground algae is soaked in water and stirred for 15 hours using a mechanical stirrer at room temperature.[13,14] The resulting mixture is then subjected to centrifugation and the supernatant fluid is treated with ethanol to precipitate the polysaccharide.[14] The technique of extraction utilized in this process is uncomplicated and straightforward however one of its notable drawbacks is its low productivity rendering it uneconomical. Porphyran with its diverse range of bioactive compounds possessing properties such as antioxidant, immunemodulation, anti-tumor, neuroprotection, anticancer, and anti-aging effects has made its way into various industries including pharmaceuticals, food, and cosmeceuticals.[14,15] It has been observed that Porphyran is highly effective in scavenging superoxide radicals due to its strong antioxidant characteristics. Recent research has indicated that Porphyran acts as a protective agent against the neurotoxicity caused by amyloid beta peptide (Abeta)

which is associated with Alzheimer's disease. Additionally studies have demonstrated that Porphyran can increase the content of cerebral acetylene improve memory impairment and learning abilities by enhancing choline acetyltransferase (ChAT) activity and reducing acetylcholine transferase (AChE) activity.[15,16] Furthermore Porphyran has been found to reverse cell morphological changes decrease the activity of SA-beta-galactose, inhibit the p53-p21 pathways, regulate the cell cycle and promote apoptosis thus producing anti-aging effects [16]. It has also been shown to have hypolipidemic effects by decreasing the concentration of serum levels and increasing excretion through feces.[16]

Fatty Acids:

Fatty acids are crucial for human health and preventing diseases. Traditionally people relied on fish, fish oils, and vegetable oils as sources of these essential compounds in their diets. Chemically fatty acids are carboxylic acids with aliphatic chains that can be either saturated or unsaturated.[17] Saturated fatty acids with short or medium-length chains are commonly found in milk fat, palm oil, and other sources while longer-chain saturated fatty acids are present in meat, butter fats and certain vegetable oils.[17] Various types of algae specifically from the Gigartinales, Corallinales, and Gracilariales orders are known to have high levels of lipids and fatty acids. These include arachidonic acid (20:4 w-6), linoleic acid (18:2 w-6), alpha-linolenic acid (18:3 w-3), stearidonic acid (18:4 w-3), and eicosapentaenoic acid (20:5 w-6). Studies on animals and non-human primates have shown that alpha-linolenic acid and its longer-chain derivatives eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are essential components of a healthy diet.[1,2] These fatty acids are critical for the structure and function of the central nervous system and the retina.[1]

Polyunsaturated fatty acids also known as PUFA are essential fatty acids that contain more than one double bond in their molecular structure. These vital components are found in phospholipids and cell membranes particularly those responsible for immune response.[18] Omega-3 and Omega-6 are the primary types of PUFA that are crucial for human nutrition and well-being. Traditional sources of PUFA are predominantly derived from marine sources.[18,19] Seaweeds on the other hand are recognized as a low-calorie food option with significantly lower lipid content. In industries fatty acids are typically extracted through mechanical press or hexane leaching methods.[19] However there are now several alternative techniques available such as ultrasound-assisted extraction, microwave-assisted extraction, and supercritical fluid extraction.[19]

Phenolic Compounds:

Phenolic substances are plant-based compounds that contain benzene rings with one or more hydroxyl groups attached. These organic substances are found abundantly in nature and are known for their diverse chemical structures. They are characterized by the presence of one or more aromatic rings made of six carbon atoms connected to a hydroxyl (OH) group. The main attribute of phenolic compounds is their powerful antioxidant properties which serve as a defense mechanism against oxidative stress caused by free radicals. By scavenging these harmful chemicals phenolic compounds may reduce the risk of chronic conditions such as cancer, heart disease, and neurological disorders.[20,21] The process of neutralizing free radicals involves different methods such as chelation of metal ions, sequential proton loss electron transfer, hydrogen atom transfer or single electron transfer. In addition to their antioxidant role phenolic compounds have also been studied for their anti-inflammatory, antimicrobial, anticancer, and anti-diabetic effects. [21,22] Furthermore they have shown potential in regulating the immune system and promoting cardiovascular health. The presence of bromophenols a type of phenolic compound with a single benzene ring has been identified in algae of the Gracilaria genus.[22] Other compounds found in this genus include benzoic acid, vanillic acid, gallic acid, salicylic acid, protocatechuic acid, syringic acid, and p-hydroxy benzoic acid.[1,22] Overall the diverse and beneficial properties of phenolic compounds make them a valuable subject of study in the field of natural medicines.

Pigments:

Pigments are the coloured substances responsible for the diverse range of colours present in the nature, including those found in flora, fauna, and microorganisms.[1] These polar compounds possess a regulatory protein complex known as phycobilisomes and play a crucial role in photosynthesis by harvesting light.[1,2] In addition to their role in biological function pigments have also been utilized for their medicinal properties such as their antioxidant, anti-inflammatory, and cancer-fighting effects.[3] The presence of carotenoids and phycobiliproteins is a distinguishing feature of red seaweeds. Acting as photoprotective agents these pigments use their antioxidative properties to deter the harmful effects of reactive oxygen species (ROS).[23]

Phycobiliproteins:

Phycobiliproteins are the group of highly fluorescent pigments found in specific varieties of Crimson Algae. These components play a critical function in capturing and utilizing light energy contributing to their characteristic colors.[23] They consist of two parts: the protein element known as phycobiliprotein or apoprotein and the attached chromophore which is responsible for the pigmentation.[1,23] The chromophores include phycocyanobilin (blue), phycoerythrobilin (red), and phycourobilin (orange).[23] Phycobiliproteins are organized into large complexes called phycobilisomes acting as light collectors that channel energy to the chlorophyll molecules.[23] These remarkable compounds are mostly derived from Cyanobacteria which are classified under the phylum Rodophyta. They have gained considerable attention for their powerful antioxidant properties and

have been utilized in nutraceutical and cosmetic industries as a natural colorant.[2,23]

Phycoerythrin:

Phycoerythrin a type of phycobiliprotein found in algae is responsible for the red colour observed in alga.[2] Phycoerythrin consists of an apoprotein and attached chromophores typically phycoerythrobilin, this pigment exists in various forms such as phycoerythrin I (PEI) and phycoerythrin II (PEII). Phycoerythrin is mainly extracted from species like *Galphimia gracilis* and *Grateloupia turuturu*. [2,3] Phycoerythrin's distinct absorption spectrum enables it to absorb light in the blue region of the spectrum.[3,23] Beyond its striking colors this protein stands out for its remarkable fluorescence quantum yield and unique photophysical characteristics which are ideal for fluorescence resonance energy transfer (FRET) investigations. Notably *C. crispus* and *Gelidium amansii* are also valuable sources of phycoerythrin for industrial purposes.[23]

Phycocyanin:

Phycocyanin a blue hue pigment present in seaweeds known as blue green algae is composed of a polypeptide chain bound to the chromophore phycobillin. The extraction of this compound is predominantly derived from *G. gracilis*, *C. crispus,* and *G. amansii* utilizing methods such as ultrasonification bead milling or chemical osmosis.[1,3,23] This compound has been a subject of interest in recent years due to its potential health benefits. It boasts high levels of antioxidants that safeguard cells against the harmful effects of free radicals.[2,23] Additionally studies have shown its potential in fighting cancer improving chemotherapy outcomes, reducing inflammation and enhancing immune function.[1,2,3]

Carotenoids:

Carotenoids are a collection of natural pigments that can be found in red algae and are present in high amounts as alpha and beta carotenoids.[3] Other types of carotenoids include antheraxanthin, lutein, violaxanthin, cryptoxanthin, and zeaxanthin. One of the main functions of carotenoids is to act as accessory pigments during photosynthesis.[2,3] These pigments can be categorized into two main groups: xanthophylls and carotenes. Examples of carotenes include beta-carotene and lycopene which have a hydrocarbon structure and appear orange or red. In contrast xanthophylls contain oxygen atoms and exhibit yellow color.

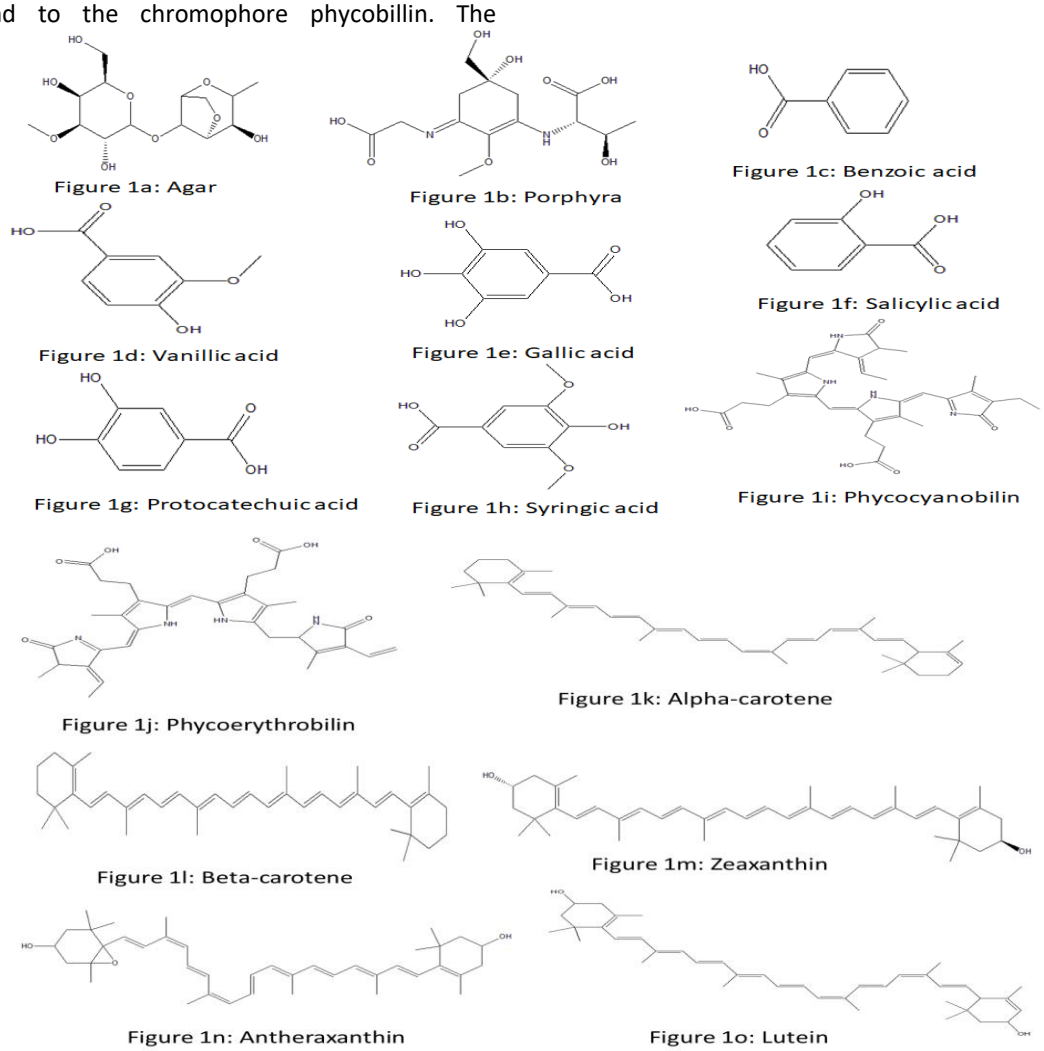

Figure 1: Different phytoconstituents are present in algae

Table 1: Name of the different algae and their uses

Sl. No	Name of algae	Family	Uses	Region available	References
1	*Porphyra umbilicalis*	Bagiaceae	Antioxidant, antitumour, anti-inflammatory, antiviral	Japan, Hawai, Scotland, Wales Ireland, Vietnam, Korea	[24]
2	*Gelidium corneum*	Gelidiaceae	Antioxidant, Antibacterial, Anti tumoral	France, Northern Spain, Portugal and Morroco	[25]
3	*Ascophyllum nodosum*	Fucaceae	Anti-ageing, Anti-inflammatory, immunomodulatory and antioxidant	North west coast of Europe and northeastern coast of North America	[26]
4	*Hypnea valentiae*	Cystocloniaceae	Antiviral, Antibacterial, Antioxidant, Antifungal	China, South Africa, Australia, Japan, Indonesia, Mauritius, Phillipines, India, and Brazil	[27]
5	*Grateloupia lanceolata*	Halymeniaceae	Antioxidant, Hypolipidemic	East Asia	[28]
6	*Hypnea spinella*	Cystocloniaceae	Immunomodulators	North, Central and South America, Atlantic islands, Africa,Indian ocean ,Asia (China, Korea, Japan, Vietnam, Mynmar, Thailand, Singapore), Australia, New Zealand	[29]
7	*Gelidium spinosum*	Gelidiaceae	Gelling Agent, Anti-diabetic.	European North Atlantic (England) to Japan and tropical Indo-Asian waters.	[30]
8	*Gracilaria gracilis*	Gracilariaceae	Antioxidant	Asia, South America Africa and Ocenia	[31]
9	*Sphaerococcus coronopifolius*	Sphaerococcaceae	Antibacterial, Antitumor.	Meditteranean Sea	[32]
10	*Gracillaria changii*	Gracillariaceae	Vitamin C supplement, gastro protective, anti-ulcerogenic	Malaysia, Thailand.	[33]
11	*Saccharina latissima*	Laminariaceae	Production of Mannitol	Atlantic ocean, Artic Ocean and North Pacific ocean.	[34]
12	*Hypnea musciformis*	Cystocloniaceae	Antiviral, antibacterial, Antioxidant and antifungal	Philippines, Brazil, Bangladesh, India and Vietnam.	[35]
13	*Gelidiella acerosa*	Gelidiellaceae	Anti-Alzheimer	Indian Ocean (France)	[36]
14	*Palmaria palmata*	Palmariaceae	Food Supplement	Northern coast of the Atlantic and Pacific Oceans.	[37]
15	*Chrondus crispus*	Gigartinaceae	Thickening and stabilizing agent.	Parts of Atlantic coast of Europe and North America	[38]
16	*Crassiphycus corneus*	Gracilariaceae	Food supplement, Antioxidant, Antiageing	West coast of Atlantic Ocean	[39]
17	*Porphyridium cruentum*	Porphyridiaceae	Antioxidant, Anticancer, Antitumora	Europe, North America, South America, Asia, Australia, Africa.	[40]
18	*Grateloupia turuturu*	Halymeniaceae	Food supplement, Colouring Agent	China, Japan, Korea and parts of Eastern Russia	[41]
19	*Pyropia yezoensis*	Bangiaceae	Anti-mutagenic, antioxidant, hepatoprotective	China, Korea and japan	[42]
20	*Kappahycus alvarezii*	Solieriaceae	Anti-cancer	Philippines, Indonesia, Malaysia	[43]
21	*Eucheuma denticulatum*	Solieriaceae	Gelling, Thickening and Stabilizing agent, Anti-oxidant	Philippines, Topical Asia and western Pacific	[44]
22	*Erythrolobus australicus*	Porphyridiophyceae	Antihypertensive, antioxidant, antitumor	Australia, Queensland and New south wales	[45]

It has been observed that red algae have a limited variety of carotenoids with the Gigartinaceae family containing high levels of lutein Graciliarasis containing zeaxanthin and Corallinales containing antheraxanthin.[2,3,23] Aside from their important role in plant physiology carotenoids have also gained recognition for their potential health benefits. They are known to possess antioxidant properties which help protect cells from oxidative stress that is associated with chronic diseases such as cancer and cardiovascular disease.[23] Some carotenoids, such as beta-carotenoids have the ability to transform into vitamin A within the body. This nutrient is crucial for maintaining healthy vision, a strong immune system and promoting proper growth and cell development. While carotenoids can be acquired from a regular diet algae-derived carotenoids are now being added to various everyday items like daily products, cosmeceutical and pharmaceuticals.[2,3] The different phytoconstituents are present in algae in Figure 1. The name of the different algae and their uses are presented in Table 1.

DISCUSSION

Seaweeds are rising in popularity as a highly popular and commercially marketed source of nutrition due to their potent medicinal value, cost-effectiveness, high extract yield, and abundant availability in the ecosystem.[1,2] Some of the most widely consumed red algae include Nori (Porphyra spp) a renowned and edible seaweed commonly cultivated and consumed in East Asia. Its abundance in protein, dietary fiber, vitamins, and minerals make it a valuable addition to any diet. Another notable species is Dulse (*Palmaria palmata*) which can be found along the Atlantic and Pacific coastlines. Often consumed in a dehydrated form it boasts a rich supply of vitamins, minerals, antioxidants, and omega-3 fatty acids.[3] Carrageen moss (*Chrondus crispus*) also known as Irish moss is highly valued for its gelling properties in the food industry.[1] The use of red algae in food applications is garnering significant attention and research as these seaweeds possess high concentrations of phytochemicals that enhance the quality of various food products.[2,3] Overall these nutrient-rich seaweeds hold great potential for widespread use in the food industry

CONCLUSION

This review shows that use of red algae in pharmaceutical and neutraceutical industries holds a significant potential. However, the extent of use depends upon the continuous research, development and commercialization activities.

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