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**Review** article

# Exploring the nutritional and therapeutic potentials of red seaweeds: a review

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# ABSTRACT -

Seaweeds stand out as a cost-effective, ecologically friendly, and productive source of bioactive compounds, Additionally, readily available in natural ecosystems. With growing interest, Seaweeds are finding widespread application in various sectors particularly in food, healthcare and cosmetics owing to their abundance in bioactive substances and minimal competition for freshwater and land resources. Seaweeds hold promise in preventing and treating chronic diseases and in producing functional food, attributed to their rich array of bioactive compounds. Among them, red seaweeds (Rhodophyta), the most prevalent class, boasts a diverse profile of seaweeds, that are potentially rich in bioactive compounds, including polysaccharides, soluble dietary fibers, proteins, peptides, polyunsaturated fatty acids, vitamins, minerals, pigments, phycobiliproteins and secondary metabolites (polyphenols, flavonoids, steroids, glycosides, alkaloids, tannins, saponins and triterpenoids). These compounds exhibit various biological activities, such as antibacterial, anti-inflammatory, anticancer, antidiabetic, anti-obesity, and anti-hypertensive properties. This review delves into the bioactive components, characteristics, and applications of red seaweeds, aiming to raise awareness among the public regarding seaweed consumption as a dietary source.

Keywords: Seaweed; Bioactive; Functional food; Red algae; Secondary metabolites.

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# 1. Introduction

In recent decades, there has been a surge in consumer interest in healthy food, with a focus on nutrition in product development. Algae are being intensively investigated for human nutritional purposes and so employed as a functional food. Their natural abundance, diversity, and global availability make them a valuable source of biologically functional substances (Domínguez, 2013).

The marine macroalgae known as seaweeds are recognized as one of the biological resources with the greatest economic significance. Seaweeds are a huge, diversified collection of eukaryotic, photosynthetic organisms without blossom and significant renewable marine resources. It is found in shallow open water up to 180 meters deep and grows best in brackish or salty environments (Khalid et al., 2018). Based on their pigmentation, seaweeds are classified into three main groups Rhodophyta (red), Chlorophyta (green algae), and Phaeophyta (brown algae) (Mohammadigheisar, 2020). Approximately 221 different seaweed species have been commercially exploited as of today and ten species, including red seaweed (*Glacilaria, Porphyra, Eucheuma Kappaphycus alverazii*), green seaweed ((*Ulva clathrata, Monostrom anitidum, Cauleurpa spp.*), and brown seaweed (*Undaria pinnatifida, Saccharina japonica, fusiforme, Sargassum*) are intensively cultivated (FAO, 2018). Seaweed agriculture's main advantage lies in its lack of competition with other terrestrial plants. An estimated 2,000,000 tons of dried seaweed are used annually for direct sources of consumption and derived products like hydrocolloids (Nakhate, & van der Meer, 2021). Seaweed production is a major industry in many Asian nations, including

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Japan, China, Vietnam, Korea, the Philippines, and Thailand. Additionally, Canada, New Zealand Chile, and certain European nations of Ireland, France, Norway, the UK, and Spain are engaged in seaweed production (Nakhate, & van der Meer, 2021) with over 48 percent of global seaweed production. China remains the world's leading producer, followed by Indonesia (39%) and the Philippines (5%) (FAO, 2018).

Seaweeds have high nutritional value due to their chemical composition, promoting human nutrition and well-being. According to Makkar et al. (2016), environmental factors such as light, and temperature, nutrient content in water, as well as species type, collection time, and habitat, all contribute to the variation in seaweed composition. Seaweeds have an excellent nutritional profile and are high in macro- and micronutrients (Subbiah et al., 2022). According to Sudhakar et al. (2018), macroalgae have a high content of water, carbohydrates, and proteins and a low amount of lipids in their chemical composition. Seaweeds and their extracts are novel sources of several bioactive substances rich in proteins, amino acids, vitamins, minerals, polysaccharides, fiber, fatty acids, terpenoids, alkaloids, polyphenols and pigments. These metabolites have antioxidant, antidiabetic, anti-inflammatory, antimicrobial, antiviral, anticancer, anti-aging and anti-obesity properties (Khalid et al., 2018). Due to the perception that the bioactive substances found in seaweeds are natural and harmless, they have found application in the culinary and medical Sectors (Lomartire, & Gonçalves, 2022).

Among marine algae, red algae (Rhodophyta) are the most prevalent and commercially vital ones and can grow in temperate, subtropical, or tropical climates (Lim et al., 2017). Among thirty thousand tons of algae grown worldwide, red algae make up more than sixty percent (FAO, 2018). According to the Food and Agriculture Organization of the United Nations (FAO, 2018), among red seaweed, four species: Porphyra spp., Eucheuma spp., Kappaphycus alvarezii, and Gracilaria are being intensively cultivated. Rhodophyta has the most bioactive substances with about 1600 distinct compounds comprising 53% out of discovered all bioactive (Leal et al., 2013). Red seaweed contains several biologically active compounds with a wide range of therapeutic uses (Carpena et al., 2022). Recent research emphasis on extraction and application of bioactive compounds from red seaweeds. This review aims to provide a detailed description of the nutritional and bioactive compounds found in red seaweeds and their functional and therapeutic potentials and their current applications in the food and pharmaceutical industries.

# 2. Nutritional and bioactive compounds

Red seaweeds have a lot of potential to improve human health, security of food, and access to affordable healthy nourishing food because nutrients are linked to a wide range of bioactivities and nutritional qualities. Well et al. (2017) reported that seaweeds are high in essential and nutrient-dense components such as polysaccharides, fatty acids, proteins, amino acids and phenolic compounds and show biologically active and health-enhancing properties. Nutrient content and bioactive compounds of seaweeds are highly varied with season, location, light intensity, water salinity and temperature (Lafeuille et al., 2023). Bioactives play an important role in nutrition (Shahnaz et al., 2009). Bioactive molecules such as polysaccharides, dietary fiber, pigments, protein, minerals, vitamins, lipids, polyunsaturated fatty acids (PUFA), steroids, phenolics, alkaloids, saponins, and terpenes can be used in numerous fields of study, including biomedical and food industries, (Ejaz et al., 2020).

# 2.1. Polysaccharides

Seaweeds are a rich source of carbohydrates used as an energy source for numerous living functions. The majority of the structural polysaccharides that make up the cellular matrix and other elements of seaweed's cell wall are heteropolysaccharide complexes. The seaweed species of interest had total polysaccharide contents ranging between 4% and 76% (dry weight basis) (Paniagua-Michel et al., 2014). A considerable amount of these polysaccharides is in sulfated form (Porse & Rudolph, 2017). The majority of the polysaccharides in red seaweed are sulphated galactans. Polysaccharide shows bioactivity (antioxidant, anticancer and anti-hypertension) can be altered by this degree of sulphation (Makkar et al., 2018). Polysaccharides are rich in bioactive compounds consisting of alginate, carrageenan, agar, ulvan, laminaran, fucan and cellulose (Stiger-Pouvreau et al., 2016). Red seaweeds are rich in agars and carrageenans, while alginates and ulvan are abundant in brown and seaweeds respectively (Agrawal et al., 2022). green Multidisciplinary study fields have focused on seaweed-derived polysaccharides because of their distinct physiochemical characteristics and range of bioactivities (Tanna et al., 2019). Sulfated polysaccharides exhibit a variety of bioactivities, including antioxidant, anti-inflammatory, anticarcinogenic, anticoagulant and antimicrobial effects (Palani et al., 2022). Agar, and carrageenan are the main hydrocolloids in red seaweed that have the greatest economic and commercial importance because they are high in molecular weight and viscosity, in addition to their superior ability to form gel and emulsifying and stabilizing qualities (Pereira, 2018). Edible seaweeds have 33-50% fiber which is higher than that found in higher plants (Baghel et al., 2023). Seaweed's undigested polysaccharides can be a substantial source of dietary fiber. Seaweed-derived dietary fibers demonstrate a range of therapeutic effects, including antioxidant, anticancer, anticoagulant, and antiviral effects (Tanna & Mishra, 2019).

#### 2.1.1. Agar

The cell wall of red algae contains these sulfated galactans, which are soluble in water. Agar is one of the sulphated polysaccharide entailing of residues of 9(1-3)-D-galactose and (1-4)-3, 6-anhydro-L-galactose (Otero et al., 2021). The most often utilized genera for agar extraction are *Gracilaria Spp, Pterocladiella capillacea, and Gelidium Spp* (Nishinari, 2017). It is used to stabilize the ice cream and enhance the texture of dairy products including cream, cheese, and yogurt, and clarify the wines (Tiwari and Troy, 2015). Agar from *Gelidiella acerosa* (red seaweed) showed antiplatelet (inhibit the platelet aggregation by 45%) and antithrombotic effect (Da Silva Chagas et al., 2020).

### 2.1.2. Carrageenan

The primary structural component of red algae and marine hydrocolloids is carrageenans (Martin-Del-Campo et al., 2021). Carrageenan is the most abundant sulfated form of polysaccharide in red seaweed (Pangestuti et al., 2018). The linear structure of carrageenans forms glycosidic linkages between units of D-galactose  $\alpha$ -(1,3) and 3,6-anhydrogalactose $\beta$ -(1,4 alternatively (McKim, 2016). Carrageenans are typically isolated from *Kappaphycus alvarezii* (*Eucheuma cotonii*) and *Eucheuma denticulatum* for commercial use (Shao et al., 2022). Carrageenan has three different forms: kappa ( $\kappa$ ), lambda ( $\lambda$ ) and iota ( $\iota$ ) based on the composition of structure and sulfate content (Otero et al., 2021). The European Food Safety Agency (EFSA) and Food and Drug Administration (FDA) grant permission to use commercially available  $\kappa$ ,  $\lambda$ , and  $\iota$  carrageenans in food products (Younes et al., 2018). Two prominent commercial carrageenans with unique gelatinization capabilities are  $\kappa$ -carrageenans and t-carrageenans, primarily derived from *Kappaphycus alvarezii* and *Eucheuma denticulatum* respectively (Bahari et al., 2022). Due to the physicochemical characteristics (gelling, thickening, stabilization and emulsification) of  $\kappa$ carrageenans, has a wide range of food applications (Torres et al., 2019). Carrageenans are soluble in water. Organic solvents like ketones and alcohols do not dissolve any kind of carrageenan (Marburger et al., 2003).  $\kappa$ -carrageenan exhibits significant bioactivities, including immunomodulation, antioxidant and anticancer properties (Yuan et al., 2006), anticoagulant properties (Farias et al., 2000), immobilize the enzyme (Popa et al., 2012) and antiviral, and wound healing activities (Santo et al., 2009).

# 2.2. Lipids and fatty acids

Seaweed species have a low amount of lipid that varies from 0.1% to 5% on a dry weight basis (Padam, & Chye, 2020). Seaweeds are low calorie with high non-digestible carbohydrate content due to their low-fat content. Neutral lipids such as triglycerides, fatty acids and compound lipids like phospholipids and glycolipids are abundant in seaweed (Lopes et al., 2012). Fatty acids, including monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), and saturated fatty acids are among the nutritionally significant components of seaweed lipids (Padam, & Chye, 2020). Essential fatty acids are high in seaweeds compared to terrestrial plants (Gosch et al., 2012). According to Schmid et al. (2018) seaweed lipids contain a considerable amount of PUFA, including  $\alpha$ linolic acid (ALA) (18:2n-6), α-linolenic acid (ALA) (18:3n-3), eicosapentaenoic acid (EPA, 20:5 ω -3), octadecatetraenoic acid, docosahexaenoic acid (DHA, 22:6n-3) and arachidonic acid (ARA,20:4n-6), among this omega-3 fatty acid and EPA help to improve the mental health, immune system and reduce the blood pressure. A balanced consumption of  $\omega$  -3 and  $\omega$  -6 fatty acids are essential for the prevention of chronic disorders, such as cardiovascular disease, inflammation arthritis and diabetes (Simopoulos, 2008). Fucosterol and isofucosterol are the principal nutrients present in seaweeds (Kendel et al., 2015). Red seaweed (Rhodophyta) has a wide variety of essential fatty acids (EFAs) (Cotas et al., 2020). Compared to brown algae, red algae often contain greater amounts of Eicosapentaenoic acid (EPA), arachidonic, oleic and palmitic acid (El-Beltagi et al., 2022). Sterols such as desmosterol, cholesterol, sitosterol, fucosterol, and chalinasterol are found in red seaweeds (Sánchez-Machado et al., 2004).

### 2.3. Protein, peptides and amino acids

One of the main components of seaweeds, seaweed proteins varies greatly among different groups. (Padam, & Chye, 2020). Seaweed protein has a good amino acid profile and good functional qualities (gel-forming ability, emulsification and foaming capacity, water and fat absorption capacity) compared to other plants (Chronakis, & Madsen, 2011). Seaweeds' protein content varies depending on the species; highly (up to 47% dw) found in red seaweeds, moderately (9- 26% dw) in green algae and low in brown seaweeds (3-15% dw) (Fleurence et al., 2018). The protein content of red algae can reach 49% of dry weight, a level comparable to that of terrestrial plants like mung, cereals, lentils, chickpeas and soybeans, eggs and fish (García-Vaquero et al., 2015). High-protein seaweeds might serve as excellent non-animal sources of protein,

making them suitable as nutritional supplements and culinary ingredients. Red algae are revealed to have a higher amount of protein compared to the other two varieties (Barral-Martnez et al., 2020). Seaweed contains different forms of proteins, including mycosporine-like amino acids, peptides, glycoproteins, phycobiliproteins, lectins and enzymes (Samarathunga et al., 2022).

Bioactive peptides generally consist of amino acids ranging from 2 to 20 and are ineffective, when they are encoded with their native structure of protein (Admassu et al., 2017). Therefore, it is important to find a suitable source of protein and extraction methods to produce bioactive hydrolysates protein and peptides (Cheung et al 2015). Macroalgae have been reported to contain peptides and hydrolysates of proteins that are bioactive which can be extracted using novel techniques (Ultrasonication, Microwave, Pulse electric field, supercritical CO<sub>2</sub>) or enzymatic hydrolysis or fermentation technology. It shows Angiotensin-converting-enzyme (ACE) inhibition, antihypertensive, antioxidant, anticancer, anticoagulant, antimutagenic, calcium precipitation inhibition, plasma and hepatic cholesterol reduction (Holdt, & Kraan, 2011). Generally, bioactive components and their properties are species-dependent.

Proteins have all essential amino acids, which are rich in bioactives and have functional properties. Since the human body is unable to produce essential amino acids such as methionine leucine, tyrosine, cysteine, lysine, valine, isoleucine, alanine and phenylalanine, they are vital for nourishment. Nearly all algae have amino acid sequences that are similar to those of other dietary proteins, which makes them suitable for use in food as well as in feed (Spolaore et al., 2006). Amino acids found in seaweeds, such as taurine, isoleucine, valine, and leucine, have biological functions as antioxidants (Kadam et al., 2013). Red seaweeds have higher levels of essential amino acids than what is recommended by the FAO and WHO (Raja et al., 2022). Red algae have an Essential amino acid (EAA) to Non-essential amino acid (NEAA) ratio ranging from 0.98 to 10.2 (Abirami et al., 2012). Tabarsa et al. (2012) reported that leucine (76.6 mg/g), valine (41.4 mg/g) and lysine (77.1 mg/g) are present in Gracilaria salicornia. Seaweed has substantially more sulfur-containing amino acids than the majority of terrestrial plants. Red seaweed has significantly more cysteine and methionine (sulfurcontaining amino acids) than protein isolate from soy, implying that red seaweed may be a rich source of sulfur-containing amino acids, which play a key role in growth of humans and synthesis of protein (Rawiwan et al., 2022) while red seaweed species contains low percentage of leucine and isoleucine (Marinho et al., 2015). Up to 30% of the total amino acid content of red seaweed are aspartic and glutamic acids (non-essential acidic amino acids), which contribute to the unique umami taste of seaweed (Harrysson et al., 2018). Most red species are excellent sources of protein and possess significant amounts of essential amino acids, for example, Grateloupia turuturu (31.1%) and Porphyraa canthophora (42.1%) (Rawiwan et al., 2022).

# 2.4. Minerals

The mineral content of seaweed may vary from 7% to 38% of the dw (Vijay et al., 2017). Compared to terrestrial plants, seaweeds have 10-20 times more mineral content with greater bioavailability (Lozano-Muñoz et al., 2020). Seaweed contains large amounts of potassium (K), sodium (Na), calcium (Ca), phosphorous (P), and magnesium (Mg). Furthermore, there are significant amounts of trace elements such as iron (Fe), zinc (Zn), copper (Cu), chlorine (Cl), manganese (Mn), and iodine (I) (Beltagi et al., 2022). Seaweeds contain greater quantities of Fe or Cu compared to meat and spinach (Cherry et al., 2019). *Palmaria palmata* (Red seaweed) contains 6.4 mg of iron per 8g of serving (Shannon, & Abu-Ghannam, 2019).

Lozano-Muñoz et al. (2020) found that red seaweed contains potassium (K) (27.2-81.0 mg/g d.w), calcium (Ca) (3.39-4.02mg/g d.w.) phosphorous (P) (2.0 to 18.2mg/g d.w) and sodium (Na) (5.87-54.65mg/g d.w). (Kappaphycus alvarezii (Rhodophyta) extracts contain high levels of calcium (460.11 mg/L and magnesium 581.20 mg/L (Rathore et al., 2009). According to Mohamed, Hashim, & Rahman (2012), the Na/K ratio of seaweed is low with a range of 0.14 to 0.16. The Na/K ratio is important due to the association of high Na/K diets with hypertension (Lozano-Muñoz et al., 2020). Marine seaweeds have a large amount of iodine content when compared to terrestrial plants is favorable for congenital iodine deficiency syndrome and goiter (Padam, & Chye, 2020). Compared to brown seaweed, red seaweeds have more iodine content. For instance, Palmara palmita collected from North Atlantic areas has iodine of nearly 293 µg/g dw (Cotas et al., 2020). Porphyra tenera contains 60-102 µg/g dry wt of Iodine (Van Netten et al., 2000). The global recommended iodine consumption is 150 µg/day. Red seaweed's iodine shows antiproliferative and antioxidant properties, which help prevent cancer and cardiovascular disease and are also necessary for the generation of thyroid hormone (Zava et al., 2011).

### 2.5. Vitamins

Certain vital vitamins must be obtained from dietary sources because the human body cannot produce several essential vitamins. Red algae have a wide range of vitamins, including water-soluble vitamins like B complex (B1, B2, B12) and C and also lipid-soluble vitamins such as  $\beta$  carotene and vitamin E (Carpena et al., 2022). Seaweeds possess higher levels of vitamins compared to fruits and vegetables (Kumar et al., 2021). The majority of plants on Earth are not able to synthesize B12 vitamins. Red algae: Gracilaria changii and Porphyra umbilicalis comprise all essential and non-essential vitamins, as well as large amounts of vitamins C and A (carotenoids) (Cotas et al., 2020). Consuming seaweeds (100g per day) provides more than the daily needs of vitamins A, B2, and B12 and provides the two-thirds requirement of vitamin C (Ortiz et al., 2006). Vitamins found in seaweeds have antioxidant activity as well as multiple health advantages like reducing cardiovascular diseases, cancer risk, and high blood pressure (Gupta et al., 2020).

#### 2.6. Pigments

Similar to other land plants, marine seaweeds are considered the main sources of health-promoting pigments which include chlorophylls, carotenoids, and phycobiliproteins (Rodriguez-Amaya, 2016). Green seaweed contains the highest amount of chlorophyll, while brown macrophytes have fucoxanthin and red ones have phycobilins (Cikos et al., 2022). The main photosynthetic water-soluble pigment found in red seaweed is Phycobiliproteins (Dumay et al., 2014) which make up about 50% of the seaweed's total protein content. Seaweeds have different pigment concentrations depending on factors including light incident, composition, species, and depth of cultivation (Pangestuti et al., 2018). All of the pigments are utilized as food colorings and nutraceutical additives since they are biologically active compounds that act as antioxidants, antidiabetic, antiangiogenic, and antiinflammatory (Aryee et al., 2018).

#### 2.6.1. Phycobiliproteins

Water-soluble proteins called phycobiliproteins are naturally

fluorescent and crucial for photosynthesis in Red macroalgae (Beltagi et al., 2022). Rhodophyta possess significant quantities of phycobiliproteins (PBPs) that contribute to the red to blackish-red color in red algae and obscure the color of carotenes and chlorophylls (Dumay et al., 2014). Phycobiliproteins are non-toxic, non-carcinogenic natural protein dyes used commercially in the food and cosmetic industry (Freitas et al., 2022). By inhibiting the angiotensin I converting enzyme, phycobiliproteins act as an antihypertensive effect (Furuta et al., 2016). Phycobiliproteins have bioactivities that include anti-tumor, antioxidant, antiviral, antiinflammatory, hepatoprotective, hypocholesterolemic, and neuroprotective effects (Sekar, & Chandramohan, 2007; Gomes et al., 2022). By using the water extraction technique, phycobiliproteins can be quickly isolated from macroalgae (Lee et al., 2017).

According to the colour phycobiliproteins can be divided into two primary categories, phycoerythrin (PE), and phycocyanin (PC). A large amount of the pigment PE contributes to the red color in Rhodophyta. Red seaweeds thrive in the deep ocean, because of its high quantity of phycoerythrin, which effectively absorbs light between 450 and 570 nm wavelength (Wang et al., 2015). Phycoerythrin is the most prevalent phycobiliprotein identified in red algae (Sathuvan et al., 2016). Holdt, & Kraan (2011) reported that P. palmata and Gracilaria tikvahiae contain 1.2% and 0.5% (dw) of phycoerythrin. The phycoerythrin levels in Rhodophyta ranged from 10.20 to 24.64 mg/g FW, Whereas in Chlorophyta (1.4 to 3.9 mg /g FW) and in Ochrophyta (2.5 to 5.3 mg/g FW) (Kumar et al., 2010). Phycocyanin is a blue, light-harvesting pigment ( $\lambda$  max = 610-625 nm) found in seaweeds, which is made up of a conjugate polypeptide chain that also carries the substance phycobilin (Yu et al., 2017). Phycocyanin is a natural blue food colorant and is used in candies, chewing gum, dairy products, soft drinks, and also in cosmetic products such as lipsticks, sun-protecting cream, and eyeliner (Sonani et al., 2016). Beyond its nutritional benefits for usage as food and feed, phycocyanin has the potential to be exploited in pharmaceutical and bioactive applications as an anti-irradiative, anti-inflammatory, anti-cancer, antioxidative, neuroprotective agent, immunomodulatory function, and the cell growth promotion (Yu et al., 2017; Cotas et al., 2020; Thiviya et al., 2022) and also has light and heat stable property is advantageous in food application.

#### 2.6.2. Carotenoids

Carotenoids are pigments that range in color from yellow to orange-red. They are made up of eight tetraterpene units, each containing five carbons, 40 atoms altogether 15 conjugated double bonds (Bohn et al., 2021). Carotenoids contain carotenes and xanthophylls, which help chlorophylls in photosynthesis. Red seaweed contains lutein,  $\alpha$  and  $\beta$  carotene and zeaxanthin (Kraan, 2013). All algae groups contain  $\beta$ -carotene (Gomes et al., 2022). Rhodophyta mainly contains  $\alpha$ -carotene, (Othman et al., 2018).  $\alpha$ and  $\beta$ -carotene show anti-inflammatory, anti-aging, anti-cancer, and antioxidant activity (Stahl et al., 2000; Manivasagan et al., 2017) and have the potential to be used in food, cosmetic and pharmaceuticals sectors.  $\beta$ -carotene's natural colorant and antioxidant have received more attention from food sectors (Holdt, & Kraan, 2011).

#### 2.6.3. Chlorophyll

Green, fat-soluble pigments called chlorophylls are present in cyanobacteria, algae and higher plants that perform photosynthesis ((Manivasagan et al., 2017). Chlorophylls play a vital role in absorbing light, transfer of energy, and the movement of electrons in photosynthetic organisms (Gomes et al., 2022). Wavelength (430

and 680 nm) is an active range for chlorophyll a and the 450 and 660 nm range is important for chlorophyll b activity (Freitas et al., 2022). chlorophyll a and d are found in Rhodophytea (Cikos et al., 2022). The amounts of total chlorophylls in *Gracilaria tikvahiae* and *Eucheuma denticulatum* (Rhodophyta) are lower, ranging from 2.8 to 4.5  $\mu$ g/ g DW (Othman et al., 2018).

# 2.7. Secondary metabolites

# 2.7.1. Phenolic Compounds

Phenolic compounds are generated when one or more hydroxyl groups are directly linked to one or more aromatic hydrocarbon rings. Polyphenols are one of the important groups of secondary metabolites which are interesting because of their significance in biomedicine (Besednova et al., 2020). The primary phytochemicals produced by algae are polyphenols that have pharmacological effects and other beneficial effects on health including, antioxidant, antibacterial, antiviral, antidiabetic, antihypercholesterolemic, anticancer, hepatoprotective, anti-inflammatory, neuroprotective, anti-obesity and antiproliferative properties (Cotas et al., 2020; Kanatt et al., 2023). Algal polyphenols are receiving attention extensively for their possible applications in nutraceuticals, cosmetics, and pharmaceuticals because of their nutritional and health benefits (Fernando et al., 2016). Flavonoids, phenolic acids, phlorotannins, Catechins, tannins, and other phenolic compounds are found in seaweed. The main phenolic compounds present in green and red algae are phenolic acids, flavonoids, and bromophenols (Besednova et al., 2020). Phlorotannins are predominantly found in brown algae and lower levels in red algae (1.8-3.2%) (Machu et al., 2015). Different seaweed types have a big impact on the volume and kind of phenol extraction. Polyphenols from seaweed are traditionally extracted using organic solvents (solid-liquid extraction). Polar solvents, like methanol, ethanol, and acetone, and their various ratios with water are used to extract the phenolic compounds (Machu et al., 2015; Mojzer et al., 2016). One of the primary obstacles to the extraction of polyphenols from the cell walls of algae is the existence of polysaccharide complexes (Lee et al., 2023). Supercritical fluid extraction, enzymatic method, pressurized liquid extraction, microwave, and ultrasonication are more effective extraction techniques for separating polyphenols from plant sources (Besednova et al., 2020). Extraction is often done at a temperature of no more than 52 °C since polyphenolic compounds degrade at temperatures higher than 92 °C (Machu et al., 2015).

Phenolic acids found in red algae are vanillic, syringic, salicylic, p-Coumaric, chlorogenic, benzoic, p-hydroxybenzoic, 2,3-Dihydroxybenzoic, caffeic, and hypogallic acids (Onofrejová et al., 2010; Kazłowska et al., 2010). Phlorotannins were formerly thought to be only found in brown algae, however, they have also recently been identified in red algae (Ejaz et al., 2020). Bromophenols are phenolic compounds with different amounts of bromination found in red algae as secondary metabolites (Kanatt et al., 2023).

Algal species that belong to the Phaeophyceae, Chlorophyta, and Rhodophyta families have been reported to contain flavonoids, including rutin, hesperidin, quercetin, kaempferol, and catechins (Gomes et al., 2022). Various flavonoids, mostly flavan-3-ols and flavonols have been identified in red seaweed, further, catechin and rutin in *Porphyra dentata* and catechin, quercetin and rutin in *Euchema cottonii* were found (Kazłowska et al., 2010; Namvar et al., 2012). Flavonoid content in *kappaphycus alvarezii* was reported to be high by Ling et al., 2015.

Red and brown seaweeds contain secondary metabolites phenolic terpenoids (ranging from sesquiterpenoids to tetraterpenoids). Red seaweeds produce phenolic terpenoids such as sesquiterpenes and diterpenes (Beltagi et al., 2022). Numerous seaweeds produced terpenoids that exhibited a broad range of cytotoxic, nematicidal, and anticancer properties (Culioli et al., 2001). Carotenoids which mostly consist of  $\alpha$ - and  $\beta$ -carotene, zeaxanthin, and lutein are principal terpenoids present in Rhodophyta and responsible for their unique colouring (Carpena et al., 2021).

#### 2.7.2. Alkaloids

Indoles and halogenated alkaloids are unique to algae, distinguishing them from terrestrial plants (Güven et al., 2013). Marine alkaloids are found in abundance in red algae and the major compound identified in the *Gracilaria* genus is azocinyl morpholinone, which shows antimicrobial and anti-inflammatory activity (de Almeida et al., 2011).

# 2.7.3. Mycosporine like Amino Acids

Low molecular weight (400 Da) secondary metabolites with UV protection ( $\lambda$  max = 309–360 nm) are mycosporine-like amino acids (MAAs) (Cian et al., 2015). There are more than twenty MAAs identified in macroalgae. The most prevalent ones in seaweeds palaythine, include asterina, shinorine, porphyra-334, mycosporineglycine, and palythene (Charoensiddhi et al., 2017). These are naturally produced by a variety of marine species but are particularly rich in seaweed and microalgae. This type of amino acid is present highly in red seaweeds and low in green and brown algae. (Sun et al., 2020). These mycosporine-like amino acids show antiaging, anti-inflammatory, antioxidant and immunomodulatory properties (Lawrence et al., 2019).

# 3. Biological properties / Therapeutic activity

# 3.1. Antioxidant activity

Various chronic disorders are linked to damage to living cells generated by free radicals, particularly reactive oxygen species (Engwa, 2018). Antioxidants scavenge reactive oxygen species (ROS) such as superoxide anion (O<sub>2</sub><sup>-</sup>), hydroxyl radical (OH), and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and also reactive nitrogen species (RNS), all of which induce oxidative stress in humans (Chew et al., 2008). Reactive oxygen species (ROS) can lead to serious tissue injuries, diabetes mellitus, cancer, cardiovascular diseases, and inflammatory or neurological illnesses (Alzheimer's, Parkinson's) by attacking or damaging essential macromolecules including proteins, DNA, and lipid membranes (Sellimi et al.,2014).

Compared to other marine sources, macroalgae are highly rich in natural antioxidants (Cornish et al., 2010). Antioxidant metabolites are produced as a result of environmental stress that seaweed experiences in their marine habitat, such as exposure to oxygen and UV radiation (Shannon et al., 2019). Bioactive compounds with antioxidant potential have numerous applications. Red algae contain antioxidant components such as phenolic compounds (phenolic acid, bromophenols, flavonoids, Phlorotannins) pigments: ( $\beta$ -carotene, Bromophenol, Phycophilliprotein, Chlorophyll), sulfated Galatians: (carrageenan, agar), vitamins: (B1, B3, C, and E), terpenoids, tannin, and peptides (Kumar et al., 2021; Wells et al., 2017). Table 1 illustrates the antioxidant activity of different red seaweeds. The free-radical scavenging activity (RSA) of phenolic compoundenriched extracts from various Rodophyta species was evaluated by

| Species                                      | Antioxidant<br>Compound    | Activity   | References                       |
|--|----------------------------|--|----------------------------------|
| Porphyra tenera                              | Phenolic acid              | Trolox equivalent antioxidant activity: 20-25 µmol/g   | Onofrejová et al. (2010)         |
| Porphyra yezoensis                           | Polysaccharide<br>fraction | Superoxide radical scavenging activity: 0.182 mg/mL and hydroxyl radical Scavenging activity:0.065 mg/mL   | Zhou et al. (2012)               |
| Palmaria palmata                             | Phenolic compounds         | Oxygen radical scavenging capacity: 35.8 mmol TE/g extract and DPPH: EC50 value-: 0.6–1.9 mg/mL  | Wang et al. (2010)               |
| Kappaphycus alvarezii<br>(Eucheuma Cottonii) | Terpenoids                 | Antioxidative activities (IC50 < 0.35 mg/mL)   | Makkar and Chakraborty<br>(2018) |
|  | Phenolic compounds         | IC50 values of radical scavenging activity of methanolic, ethanolic and water extract are 3.08 mg ml <sup>-1</sup> , 3.03 mg ml <sup>-1</sup> and 4.76 mg ml <sup>-1</sup> respectively. | Kumar et al. (2008)              |
|  | Crude extract              | DPPH free radical scavenging (34.27%)  | Prasasty et al. (2019)           |
| Gracilaria corticate                         | Extract                    | Antioxidant activity: 36.78% nitric oxide (NO*) radical scavenging<br>activity, 32.65% ABTS radical scavenging activity and 20.32%<br>DPPH radical scavenging activity.                  | Arulkumar et al. (2018)          |
| Gracilaria edulis                            | Extract                    | Antioxidant activity: shows 40.24% ABTS scavenging activity and 23.95% DPPH radical scavenging activity.   | Arulkumar et al. (2018)          |
| Hypnea valentiae                             | Carrageenan                | DPPH scavenging $65.74 \pm 0.58\%$ inhibition at $160 \mu g/mL$ and $65.72 \pm 0.60\%$ hydroxyl scavenging at $125 \mu g/mL$ concentration.  | Palani et al. (2022)             |
| Polysiphonia urceolata                       | Bromophenols               | At IC50 :9.67 $\mu$ M showed radical scavenging activity   | Li et al. (2007)                 |

Table 1. Antioxidant compounds in different red seaweeds and their activities.

measuring the 2,2-azinobis- (3-ethylbenzothiazoline-6-sulfonate) (ABTS<sup>++)</sup> and 2,2-diphenylpycril-hydrazyl (DPPH) radical scavenging capacity (Onofrejova et al., 2010). Hence, metal chelating ability and ferric-reducing antioxidant power (FRAP) assays were used to measure the antioxidant potentials of red algal extracts in Gracilaria birdiae and P. palmata (Fidelis et al., 2014; Hardouin et al., 2014). Phlorotannins are potent antioxidants that can prevent oxidative stress and cell damage (Shannon et al., 2019). Red algae contain sulfated galactan, or carrageenan, which has antioxidant components (Costa et al., 2009). Kumar et al. (2008) reported that phenolic compounds derived from Kappaphycus alvarezii (Rhodophytae) can chelate metal ions and scavenge free radicals. Bromophenols with an IC50 of 9.67 µM, showed radical scavenging activity in Red algae Polysiphonia urceolata (Li et al., 2007). Red algae contain antioxidant properties, which may be able to prevent or reduce the effects of skin aging, used in anti-aging products. Ngo et al. (2011) reported that high antioxidant properties have been linked to pigments found in seaweed such as chlorophylls, phycobiliproteins and carotenoids. Phycoerythrobilin from Porphyra sp. shows antioxidant activity (Yabuta et al., 2010). Porphyra umbilicalis, a red algal species, has Mycosporine-like amino acids (MAAs) that effectively protect skin from damage and premature aging caused by UV-A radiation (Daniel et al., 2004). The potential antioxidant impact of peptide chains is facilitated by hydrophobic amino acids (Cornish et al., 2010).

# 3.2. Antidiabetic activity

Diabetes mellitus arises when the pancreas is unable to secrete sufficient insulin. The primary source of blood glucose is the small intestine's subsequent absorption of dietary carbohydrates after they have been hydrolyzed by enzymes. Type II diabetes can be treated by retarding the activity of  $\alpha$ -amylase and glucosidase enzymes (Shan et al., 2016; Kim et al., 2008). Bioactive compounds such as polyphenolics, polysaccharides, phlorotannins and fucoxanthin present in seaweeds have been linked to the anti-diabetic action by reducing lipase,  $\alpha$ -amylase,  $\alpha$ -glucosidase enzyme activity and inhibiting hepatic gluconeogenesis (Kellogg et al. 2014; Murray et al. 2018). High fiber content, particularly soluble sulfated galactan (carrageenan and agar) helps to improve diabetes control in red seaweeds (Plaza et al., 2008). Shu-hong. (2011) reported that in diabetic rats, the Gelidium amansii polysaccharide produces a hypoglycemic impact. An 80% ethanolic extract of Gracilaria verrucosa can boost glucose absorption in 3T3-L1 adipocytes without causing cytotoxicity (Woo et al., 2012). According to Garcimartin et al. (2015) studies, Seaweeds such as Porphyra umbilicalis, Himanthalia elongata and Undaria pinnatifida incorporated structure-modified pork showed reduced blood glucose absorption due to α-glucosidase inhibitory action. Ethanolic extract of Eucheuma denticulatum (10 mg/ml) α-amylase was activity significantly inhibited by 67% (Al-Araby et al., 2020).

Bromophenols with  $\alpha$ -glucosidase inhibitory action are found in red algae.  $\alpha$ -glucosidases activity in rats is significantly inhibited by Bromophenols, 2,4-dibromophenol and 2,4,6-tribromophenol found in *Grateloupia elliptica* (Red algae) and makes bromophenols a promising natural nutraceutical for diabetes mellitus prevention (Kim et al., 2008). Antidiabetic activities of different red seaweeds are shown in Table 2. Animals with diabetes showed anti-hyperglycemic, antioxidant, and elevated plasma insulin properties from *hypnea musciformis* extract (Anandakumar et al., 2008).

| Species                                      | <b>Bioactive Compound</b>                  | Activity  | References                        |
|--|--|---|-----------------------------------|
| Palmaria palmata                             | Protein<br>Hydrolysate                     | Antidiabetic activity: Inhibit the dipeptidyl peptidase (DPP) IV: $(IC_{50} \text{ range } 1.65 - 4.60 \text{ mg mL}^{-1})$   | Harnedy and FitzGerald.<br>(2013) |
| Kappaphycus alvarezii<br>(Eucheuma Cottonii) | Crude extract                              | Antidiabetic activity:<br>α-amylase inhibitory activity (59.33%)<br>in vivo: decreasing blood glucose level in diabetic mice below 100<br>mg/dL.  | Prasasty et al. (2019)            |
| Eucheuma denticulatum                        | Ethanolic extract                          | Antidiabetic activity: Inhibited $\alpha$ -amylase activity by 67% at 10 mg mL <sup>-1</sup>  | Al-Araby et al. (2020).           |
| Grateloupia elliptica                        | Bromophenols                               | Antidiabetic activity: Inhibit $\alpha$ -glucosidases in rats   | Kim et al. (2008)                 |
| Gracilaria opuntia                           | Sulfated polysaccharides                   | Antidiabetic activity: Inhibit the $\alpha$ - Glucosidase (IC <sub>50</sub> : 0.09 mg/mL), $\alpha$ -amylase (IC <sub>50</sub> : 0.04 mg/mL) and DPP-4 (IC <sub>50</sub> : 0.09 mg/mL).   | Makkar and<br>Chakraborty (2016)  |
| Kappaphycus alvarezii<br>(Eucheuma Cottonii) | Whole algae (5% supplementation)           | anti-hyperlipidemic effect<br>Reduction of plasma total cholesterol (TC) level from-11.4% to -<br>18.5%, triglycerides (TG) from -33.7% to -36.1%,<br>low-density lipoprotein cholesterol (LDL-C) from -22% to -49.3%<br>and High-density lipoprotein (HDL) level increased to 55% from<br>16.3%. | Matanjun et al.<br>(2010)         |
| Porphyra yezoensis                           | Sulfated polysaccharides                   | Lipid metabolism:<br>Increase the cholesterol excretion through fecal   | Tsuge et al. (2004)               |
| Gracilaria changii                           | 10% G.changii powder-<br>supplemented diet | Hypolipidemic effect: The amount of Triglycerides was<br>significantly reduced by 28.30 % in rats   | Chan et al. (2013)                |

Table 2. Antidiabetic and anti-hyperlipidemic activities of different red seaweeds.

# 3.3. Antimicrobial activity

Foodborne microorganisms pose a significant concern for the health of the public. Multiple antibiotic-resistant bacterial strains have emerged due to novel tactics that microorganisms have devised to dodge the effects of antibiotics. Public health priorities include researching and creating less expensive and efficient natural antimicrobial drugs that have improved potential, less adverse effects than antibiotics, low toxicity, and good bioavailability, (Thanigaivel et al., 2015). Antimicrobial agents primarily target the phospholipid bilayer of the microbial cell membrane by weakening the enzyme system and disturbing the genome of the microbes (Abu et al.,2013). The antimicrobial activity of seaweed is due to polyphenols such as tannins, chlorotannins, flavonoids, and quinones (Rajauria et al., 2013). Algal polysaccharides are believed to have antimicrobial action because they recognize glycoprotein receptors found on bacterial surfaces and attach to them, potentially leading to bacterial cell disruption (Abu et al., 2013). Table 3 illustrates the antimicrobial compounds found in red seaweeds and their functions. Seaweed extracts effectively inhibit pathogens such as Salmonella and E. coli (Charway et al., 2018). Seaweed contains fatty acids, peptides, polysaccharides, pigments, polyphenols, terpenes, alkaloids, and lectin that have been shown to have antibacterial action similar to that of pharmaceutical drugs against gram-positive and gram-negative bacterial pathogens (Shannon, & Abu-Ghannam, 2016). Osman et al. (2010) reported that crude extracts from the red, green, and brown species were found to have

antibacterial properties against Candida albicans, Klebsiella pneumoniae, Bacillus subtilis, Staphylococcus aureus and E. coli. Kappapycus alvarezii showed antibacterial efficacy against Pseudomonas aeruginosa, Proteus mirabilis, B. subtilis, Staphylococcus aureus, Escherichia coli, and Lactobacillus acidophilus was documented by Pusparaj et al. (2014). Methanolic extract of K. alvarezii showed the maximum inhibition against B. subtilis (12±1.02 mm (Jaswir et al., 2014). Protein extracts from red algae have been shown to exhibit natural antibacterial action. Boonsri et al. (2017) mentioned that the protein extract of red algae Gracilaria fishery showed antibacterial activity against Vibrio parahaemolyticus. Lectin and algal peptides showed antimicrobial activity (Carpena et al., 2022). According to Jiao et al. (2019) studies, Peptides from Porphyra yezoensis showed antimicrobial against Staphylococcus aureus. Lectin extracted from Solieria filiformis showed bacteriostatic effect at 1000 µg/mL on gramnegative bacteria such as Salmonella typhi, Proteus sp, Klebsiella pneumoniae Pseudomonas aeruginosa, Serratia marcescens, and Enterobacter aerogenes (Araújo et al., 2005).

The natural extract of algae is now commonly utilized to manage plant fungal diseases instead of synthetic fungicides (Bhakuni et al., 2005). Solieria robusta extract's antifungal ability was shown against several species of fungus such as *Phytophthora infestans*, *Aspergillus niger*, *Penicillium funiculosum*, *Rhizoctonia solani*, *Aspergillus flavus*, *Fusarium solani*, *Macrophomina phaseolina* and *Aspergillus ochraceus* (Khanzada et al., 2007).

| Species                                      | Antimicrobial Compound                               | Activity   | References  |
|--|--|--|---|
| Porphyra yezoensis                           | Peptide:<br>Thr-Pro-Asp-Ser-Glu-Ala-Leu<br>(TPDSEAL) | Antimicrobial against S. aureus  | Jiao et al. (2019)                                    |
| Hypnea muscifformis                          | Kappa-carrageenan                                    | Antimicrobial against S. aureus, E. coli, K. pneumoniae, C. albicans and E. faecalis   | Bouhlal et al.<br>(2010) & Souza et al.<br>(2018)     |
| Kappaphycus alvarezii<br>(Eucheuma Cottonii) | Ethanolic and hot water<br>extracts                  | Antibacterial activity against G+ Bacillus subtilis and<br>G- Klebsiella pneumoniae, Vibrio parahaemolyticus, V.<br>harveyi and V. alginolyticus                     | Das et al. (2023)                                     |
| Gracilaria corticata                         | Extract  | Antibacterial activity against Bacillus subtilis   | Arulkumar et al.<br>(2018)                            |
| Gracilaria edulis                            | Extract  | Antimicrobial activity against A.hydrophylla, B. subtili,<br>V. fluvialis, V. compbeli   | Arulkumar et al.<br>(2018) & Kasanah et al.<br>(2019) |
| Gracilaria fisheri                           | Proteins   | Antimicrobial effect against Vibrio parahaemolyticus<br>(MIC <sub>50</sub> = 30–38 µg mL-1)  | Boonsri et al. (2017)                                 |
|  | Ethanolic extract                                    | Antibacterial against V. harveyi   | Karnjana et al.<br>(2019)                             |
| Gracilaria cornea                            | Dichloromethane extract                              | Antibacterial effect against <i>Pseudomonas</i> anguilliseptica, and Vibrio anguillarum  | Bansemir et al. (2006)                                |
| Hypnea indica                                | kappa- carrageenan                                   | Antifungal activity against <i>A. niger</i> and <i>V. cholera</i> .  | Appu et al. (2023)                                    |
| Solieria robusta                             | Ethanolic extract                                    | Antifungal ability against F. solani, Aspergillus flavus,<br>A.niger, M. phaseolina Penicillium funiculosum,<br>Phytophthora infestans A. ochraceus, , and R. solani | Khanzada et al.(2007).                                |
| Porphyra umbilicalis                         | Fatty acids  | Antifungal activity against <i>Penicillium digitatum,</i><br><i>Botrytis cinerea</i> , and <i>Monilinia laxa</i>   | De Corato et al.<br>(2017)                            |

Table 3. Antimicrobial compounds in different red seaweeds and their activities.

Aspergillus niger, Penicillium funiculosum, Rhizoctonia solani, Aspergillus flavus, Fusarium solani, Macrophomina phaseolina and Aspergillus ochraceus (Khanzada et al., 2007).

Seaweed sulfated polysaccharides such as agar, carrageenans, fucans, alginates, and laminarans had antiviral activity against a variety of viruses that cause herpes, HIV, influenza A, dengue, vesicular stomatitis, and papilloma (Jiao et al., 2012). Carrageenan extracted from red algae such as *Eucheuma cottonii, Hypnea musciformis, Chondrus crispus,* and *Gigartina pistillata* reveals antiviral activity against many viral agents (Ejaz et al., 2020). Pereira & Critchley (2020) reported that seaweed-based substances including lectin griffithsin and carrageenan have the potential as antiviral agents against SARS-CoV-2.

# 3.4. Anti-inflammatory activity

Inflammation contributes to several diseases, including cancer, allergies, asthma, arthritis, myocardial ischemia and atherosclerosis. The body employs inflammation as a general defensive response to different types of harmful stimuli, including infections, cellular damage, specific disorders, and potentially hazardous materials. Platelet-activating factor, cytokines, vasoactive amines, bradykinin, eicosanoids, reactive oxygen species, nitric oxide, and fibrin are chemical mediators that regulate inflammation (Khalid et al., 2018). Red algae's anti-inflammatory properties are related to sulfated polysaccharides, particularly carrageenans, as well as proteins including lectins and phycobiliproteins (Carpena et al., 2022). Cian et al. (2012) found that phycobiliprotein-enriched extracts of *Porphyra columbina* increased anti-inflammatory cytokines, including IL-10. Glycoprotein found in *Porphyra yezoensis* inhibited NO generation in Lipopolysaccharide (LPS) stimulated cells and showed anti-inflammatory properties (Shin et al., 2011). Red seaweeds (*Crassiphycus corneus*, formerly known as *Gracilaria cornea*) contain sulphated polysaccharides with anti-inflammatory properties (Coura et al., 2012).

Alkaloids from marine algae exhibit anti-inflammatory effects (Güven et al., 2010). Several studies have shown that *Gracilaria edulis* aqueous extracts had the greatest level of anti-inflammatory activity (95.55%) and aqueous extracts of *Gracilaria salicornia* inhibited paw edema by 77.53%. The primary anti-inflammatory properties of Omega-3 polyunsaturated fatty acids (PUFAs) result from their competition with lipoxygenase and cyclooxygenase as substrates, reducing the synthesis of prostaglandins and leukotrienes (James et al., 2000). Fatty acids like (E)-9-Oxooctadec-10-enoic acid

Table 4. Anti-inflammatory compounds and their functions in different red seaweeds.

| Species               | Anti-inflammatory<br>Compound | Function   | References                          |
|-----------------------|-------------------------------|--|-------------------------------------|
| Porphyra yezoensis    | Glycoprotein                  | Anti-inflammatory: inhibit NO generation in LPS-stimulated cells   | (Shin et al. (2011)                 |
| Porphyra columbina    | Phycophilliprotein            | Anti-inflammatory: cytokines, including IL-10  | Cian et al. (2012)                  |
| Palmaria palmata      | Phospholipids                 | Inhibit the production of Nitric oxide (NO) by lipopolysaccharide (LPS)  | Banskota et al.<br>(2014)           |
| Chondrus verrucosus   | Sulfated polysaccharides      | Suppression of RBL-2H3 cell line   | He et al. (2019)                    |
| Gracilaria Salicornia | Chromenyl<br>Compounds        | Anti-inflammatory activity: Inhibit inflammatory enzymes 5<br>lipoxygenase (5-LOX) and: cyclooxygenase-2 (COX-2)<br>$(IC_{50} < 2.50 \text{ mM})$  | Antony and<br>Chakraborty (2019)    |
| Gracilaria verrucose  | Fatty acids (PUFA)            | Inhibit NO generation and Interleukin (IL) -6 in LPS-induced cells   | Lee et al., 2009                    |
| Gracilaria opuntia    | Sulphated galactan            | Inhibition of inflammatory enzymes: IC50 values of 5-<br>lipoxygenase (5-LOX), cyclooxygenase-1 (COX-1): and<br>cyclooxygenase-2 (COX-2) inhibitory activities are 0.24<br>mg/mL, 0.01 mg/mL, and 0.03 mg/mL respectively. | Makkar and<br>Chakraborty<br>(2016) |

Table 5. Anti-hypertensive and anti-proliferative activities of different red seaweeds.

| Species                                      | Bioactive compound           | Activity  | References                        |
|--|------------------------------|---|-----------------------------------|
| Pyropia pseudolinearis                       | Peptide<br>ARY, YLR, and LRM | ACE inhibitory: Inhibitory activity on angiotensin-<br>converting enzyme LRM, ARY and YLR $IC_{50}$ :0.15 $\mu$ mol, 1.3 $\mu$ mol and 5.8 $\mu$ mol respectively | Kumagai et al. (2021)             |
| Palmaria palmata                             | Protein<br>Hydrolysate       | Angiotensin converting enzyme (ACE)<br>inhibitory/Antihypertensive activity:<br>$IC_{50}$ : 0.19–0.78 mg mL <sup>-1</sup>   | Harnedy and<br>FitzGerald. (2013) |
| Gracilaria. Tenuistipitata                   | Peptide MQDAITSVINAADVQGK    | ACE inhibition rate of Neutrase hydrolysed peptide: 82.7%   | Su et al. (2022)                  |
| Palmaria palmata                             | Polyphenol                   | Anti-proliferative activity: Inhibit HeLa cell proliferation  | Yuan et al. (2005)                |
| Kappaphycus alvarezii<br>(Eucheuma Cottonii) | Polyphenols                  | Antitumor activity in MCF-7 // MB-MDA-231 cell<br>lines; IC50 = 20 and 42 μg/ml   | Namvar et al. (2012)              |
| <u>Solieria</u> filiformis                   | Lectin protein               | Antitumor activities against breast cancer  | De Arruda et al. (2023)           |
|  |                              | Cytotoxic effect: At 125 µg.mL-1, viability of MCF-7 cells inhibited by 50%.  | Chaves et al. (2018)              |
| Hypnea muscifformis                          | Kappa-carrageenan            | Anticancer activity: Decrease the proliferative potential in MCF-7 and SH-SY5Y cell lines   | Souza et al. (2018)               |

and (E)-10-Oxooctadec-8-enoic acid found in *Gracilaria verrucosa* exhibit the anti-inflammatory activity by inhibiting NO generation, Interleukin (IL) -6 and tumor necrosis factor - $\alpha$  (TNF- $\alpha$ ) in LPSinduced cells (Lee et al., 2009). Khan et al. (2018) reported that the anti-inflammatory activity of red seaweeds *Gracilaria verrucosa* and *Pachymeniopsis elliptica* extract showed more than 70% inhibition against edema. Furthermore, *Carpopeltis cornea, P. elliptica* and *Porphyra yezoensis* showed 55% inhibition against erythema. The most inhibitory action against erythema and edema is due to the significant PUFA concentrations. The anti-inflammatory activities of bioactive compounds from red seaweeds are shown in Table 4.

# 3.5. Antihypertensive activity

Stroke and numerous other cardiovascular conditions, such as myocardial infarction, are caused by concurrently rising blood pressure (Unger, 2002). The endocrine enzymes that control peripheral blood pressure, are angiotensin-converting enzyme (ACE) and renin which are found in the renin-angiotensin system (RAS) (Harnedy, & FitzGerald, 2013; Cheung et al., 2015). ACE inhibitors relax blood vessels and reduce blood pressure by preventing the transition of angiotensin I to angiotensin II (Cheung et al., 2015). Fucoxanthin, peptides and Phlorotannins show antihypertensive activity (Choudhary et al., 2021). Table 5 shows the antihypertensive activities of red seaweeds.

# 3.6. Antiproliferative/ Anticancer activity

Various mechanisms have been suggested for reducing or slowing cancer growth. These include lowering plasma cholesterol levels, binding biliary steroids, exhibiting antioxidant properties, capturing toxic substances, promoting apoptosis, inhibiting cell adhesion, and incorporating essential trace minerals into the diet (Pati et al., 2016). According to Ahmed et al. (2011), there is evidence of anticancer action in seaweed secondary metabolites, indicating the possibility of a new natural medicinal source. The antiproliferative activity of different red seaweeds is shown in Table 5. Halogenated metabolites and sulphated polysaccharides carrageenan are effective antitumor agents in red seaweeds. Lectins from Euchema serra and S. filiformis showed antitumor activity (Chaves et al., 2018; Hayashi et al., 2012). Moussavou et al. (2014) documented that several seaweeds showed anticancer effects against breast carcinoma and intestinal carcinoma. An extract from Kappaphycus alvarezii (Eucheuma cottonii), rich in polyphenols, demonstrated an antiproliferative effect in breast cancer cell line MB-MDA-231 (oestrogen-independent) and IC50 for this activity determined to be 42 µg/ml (Namvar et al., 2012).

#### 3.7. Anti-hyperlipidemic activity

Consuming a high-fat diet steadily increased the incidence of hyperlipidemia and obesity. the hypercholesterolemic effect is due to the high level of serum triglycerides, total cholesterol, low-density lipoprotein and low level of high-density lipoprotein (Ryu et al., 2021). Otero et al., (2021) reported that sulphated polysaccharides showed anti-hyperlipidemic activities. Porphyrin and carrageenan have a hypocholesterolemic effect. The dietary fiber present in seaweeds has a crucial function in lowering cholesterol levels (Chan et al., 2013). Anti-hyperlipidemic activities of different red seaweeds are shown in Table 2. Pophyran from *P. yezoensis* shows a hypolipidemic effect (Tsuge et al., 2004). Red seaweed, *G. amansii*, reduces adipose tissue accumulation by lipolysis in diabetic rats (Yang et al., 2015).

### 4. Commercial applications of seaweeds

Seaweeds may help to ensure forthcoming world food security in their natural state or as extracts (Wells et al., 2017). Seaweeds are highly rich in nutrients and offer great options for usage as functional foods. Additionally, their physical capacity to hold water and emulsification improves the techno-functional properties of food (Shannon et al., 2019). Hydrocolloids generated from seaweed have gelling emulsifying and thickening properties, which are essential for the development of functional food products (Qin, 2018).

The European Union, the United States, and South Asian nations produce novel snacks and ready-to-eat foods like flavored bits, noodles, cookies, health drinks, crackers, sauces, candies and salad (FAO, 2018). Seaweeds are well known for their "umami," taste. The umami flavor of seaweeds is mostly due to the occurrence of salts of amino acids such as aspartic and glutamic acids, organic acids, and short peptides (Bleakley, & Hayes, 2017). Because of their distinctive flavors, seaweed-based food products are increasingly popular on a global scale (Milinovic et al., 2021).

Incorporation of seaweed powder/extract into food products would help to meet the nutritional needs of consumers and sensory satisfaction. At the laboratory level, seaweed can be effectively included in various food products as a functional component. Due to their high protein and amino acid content, red seaweeds appear to be a viable source of dietary proteins. Currently, there is an increasing trend for alternative plant-based protein to suit the daily demands of vegans. Athletes who follow a vegetarian diet can ingest seaweed as an important source of all vital amino acids and protein (Bleakley, & Hayes, 2017).

Seaweed enhances the antioxidant abilities of farinaceous foods due to its bioactive components including carotenoids and polyphenols (Prabhasankar et al., 2009). Seaweed powder is added to bread to improve its nutritional qualities without detracting from its general acceptability or sensory qualities. Additionally, the textural qualities of noodles, such as water absorption, resistance to cooking loss, cooking yield, elasticity and hardness are improved by utilizing seaweeds (Raja et al., 2022). Keyimu. (2013) reported that noodles prepared from 3% Gracilaria seaweed were found to be both organoleptically and nutritionally acceptable, with 1.7% fiber and 1.05% ash content. The calcium level increases with the incorporation of seaweed. Dried, ground Eucheuma cottonii was added to wheat flour noodles to increase the fiber, lipid, protein, and mineral content (Kumoro et al., 2016). Quitral et al. (2022) reported that products containing seaweed should have a maximum seaweed content of 10% in noodles and for extruded maize, cakes, cookies, bread and biscuits are 3.55%, less than 10%, 5%,4%, and 5% respectively.

The inclusion of various seaweeds has made it possible to create several meat products with high consumer acceptance. Whole seaweed or seaweed extract can enhance the functional, nutritional, and sensory qualities of meat. For instance, seaweeds are known to improve the fat and water-holding characteristics of meat, improving its chewiness and hardness (Raja et al., 2022). These products often have reduced levels of salt and saturated fat, contain no chemical additives, and have an enhanced amount of fiber and polyunsaturated fat (Cofrades et al., 2017).

O'Sullivan et al. (2014) mentioned that seaweed-fortified fresh milk has high overall acceptance for a short period and degrades over storage. Seaweed incorporation in various cheeses improves nutritional and sensory properties (Raja et al., 2022). Seaweed powder considerably enhances the amount of protein in ice cream while maintaining the same level of fat content, allowing for low-fat ice cream. The seaweed used enhances the creamy nature and flavor of the ice cream by increasing the volume of froth during overrun (Winarni Agustini et al., 2016). The properties like viscosity, texture, and melting point of the ice cream are increased by the infusion of seaweed.

Spice adjunct was developed using red seaweed *Kappaphycus alvarezii* as an ingredient up to 20% increasing the protein crude fiber and the ash content by 10%, 9.4%, and 22.2% respectively without affecting sensory properties and the presence of vitamin E and trace quantities of vitamin B2 and B3 helps to lower the oxidative stress in human (Senthil et al., 2010).

Phloroglucinol-based phlorotannin compounds are accumulated by brown and red algae in different amounts. Their anti-HIV, antiproliferative, antidiabetic, anti-inflammatory, anti-Alzheimer, radioprotective, antibacterial and antihypertensive, make them useful as functional food additives with positive health effects (Qin, 2018).

However, the detrimental effect on the sensory qualities of flavour, colour, appearance and taste limit the incorporation of seaweeds as they impart strong flavor and colour to the products (Raja et al., 2022). The implementation of effective and affordable analytical technologies is essential to ensure the quality of seaweeds because they are important sources of raw materials and bioactive compounds for different industries.

# 5. Conclusion

As the world population grows, people seek alternate food, medicinal, and agricultural sources. Red seaweeds being the most abundant seaweeds offer a plethora of nutritional and beneficial bioactive compounds, that can help to meet the needs of a rapidly growing population. Red seaweeds are rich in sulfated polysaccharides including carrageenans and agar and also phycobiliproteins, vitamins, fatty acids, minerals and secondary metabolites and can be used to make food and supplements in the food sector. With bioactive compounds possessing various medicinal properties, including antioxidants, antidiabetic, antiinflammatory, anticancer, anti-hyperlipidemic, anticoagulant, antihypertensive and antimicrobial activities, red seaweed emerges as an essential natural source for commercial food products. Incorporating red seaweeds into the diet may help address health issues related to protein, mineral, and carbohydrate deficiencies. Furthermore, these are utilized commercially as stabilizers, emulsifiers, thickening agents, texture modifiers, phytochemicals, and dietary fiber sources. This study delved into the nutritional, bioactive compounds found in red edible seaweeds and their therapeutic potential. Therefore, this review is instrumental in advocating for the consumption and application of seaweed as functional components in food.

# **Conflict of interest**

The authors declare that there is no conflict of interest.

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