

Bioactive components of red seaweeds: a promising source for therapeutic uses in the future

Samira El Majnaoui,¹ Mounia Lekrati,² Ahmed Belmouden,³ Hind Dehbi,^{4,5} Joumana El Turk,⁶ Abdellah Houari,¹ Nadia El Kadmiri¹

¹Molecular Engineering, Biotechnology, and Innovation Team, Geo-Bio-Environment Engineering and Innovation Laboratory, Polydisciplinary Faculty of Taroudant, Ibn Zohr University, Taroudant City; ²Fisheries Technologies Department, Higher Institute of Marine Fisheries, Agadir City; ³Laboratory of Cell Biology and Molecular Genetics, Faculty of Sciences, Ibn Zohr University, Agadir City; ⁴Medical Genetics Laboratory, Ibn Rochd University Hospital of Casablanca, Casablanca City; ⁵Laboratory of Cellular and Molecular Pathologies, Faculty of Medicine and Pharmacy, Hassan II University of Casablanca, Casablanca City; ⁶Faculty of Health Sciences, International University of Casablanca, Casablanca City, Morocco

Abstract

Seaweeds grow and reproduce in intertidal and subtidal regions where photosynthesis is possible due to the available lighting. Marine macroalgae are classified into three main groups according to their pigment content: red algae (Rhodophyceae), green algae (Chlorophyceae), and brown algae (Phaeophyceae).

They are becoming a valuable resource and are distinguished by their rapid growth capacity with high nutritional value. Red algae contain a wide variety of biochemical substances, including: phenolics, polysaccharides, proteins, bromophenols, pigments, low amounts of fatty acids, and they are essentially the only species capable of producing long-chain Polyunsaturated Fatty Acids (PUFAs), vitamins specially B12, minerals. Those compounds have anti-tumor, antioxidant, anti-inflammatory, antibacterial, and antiviral properties. Additionally, seaweeds have an excellent nutritional profile highly supplying macro and micro nutrients; thus, they can be used as food in diets. They can also be an essential source of novel pharmaceutical and therapeutic compounds. This review summarizes the potential of the bioactive substances obtained from diverse red seaweeds around the world, which are expected to be promising components for application in the medical industry. The pharmaceutical industry could use red seaweeds to prevent or treat several illnesses, including: cancer, obesity, and other chronic diseases, as their medicinal benefits are considerably more intriguing than their purely nutritional advantages. Novel natural drugs developed from algae could act as alternatives for artificial substances in the future.

Correspondence: Nadia El Kadmiri, Molecular Engineering Biotechnology and Innovation Team, Geo-Bio-Environment Engineering and Innovation Laboratory, Polydisciplinary Faculty of Taroudant, Ibn Zohr University, Taroudant City, Morocco. Tel.: +212.641619835 - Fax: +212.528551020. E-mail: n.elkadmiri@uiz.ac.ma

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Introduction

Seaweeds represent economic and environmental advantages over terrestrial biomass.¹ They are regenerative, edible, and exhibit a high growth rate, growing up to ten times faster than land plants.² Red algae (Rhodophyceae) have the largest group containing 7,554 species, compared to the green algae (Chlorophyceae) 3,974, and brown algae (Phaeophyceae) 2,124.³ Globally, 221 species of seaweeds are cultured or wild-harvested for multiple industries, including 125 red seaweeds which is the highest commercially used group compared to green and brown seaweeds (32 green seaweeds, 64 brown seaweeds).⁴ They are able to develop several active compounds,⁵ and present the highest amount of bioactive compounds, accounting for more than 1,600, representing the 53% of those reported in algae.⁶

The vast majority of red algae are multicellular and marine. Red seaweeds are known for their striking and distinctive red colour due to the high amount of red pigment phycobillin over-riding the green pigment chlorophyll. Phycobilisomes are highly efficient light-harvesting antennae allowing them to photosyn-

thesise.⁷ They have the ability to thrive at depths of up to 200 meters.⁸

The main contribution of red seaweed biomass in the world is provided by cultivation. Approximately about 55.8% of the total global seaweed production of the world comes from red algae.⁹ The global industry targets the production of sulfated polysaccharides, mainly agar and carrageenans being the most relevant and exploited compounds of red algae,⁶ where *Gelidium* sp., *Pterocladis* sp., and *Gracilaria* sp. are the main species used in the production of agar while *Gigartina* spp., *Chondrus crispus*, *Euchoema* spp., and *Hypnea* spp. are used in the production of carrageenan.^{3,10} Other potential molecules are essential fatty acids, phycobiliproteins, vitamins, minerals, and other secondary metabolites; all these compounds have been demonstrated to exert several biological activities, among which antioxidant, anti-inflammatory, antitumor, and antimicrobial properties can be highlighted.⁶ Thus, we can conclude that red seaweeds are emerging as one of the greatest and promising natural resources.

This review aims to provide an overview of the nutritional profile of diverse red macroalgae (Rhodophyta) and summarize several decades of research (*in vivo* and *in vitro*) around the world about the therapeutic potential of their bioactive compounds on human health.

Materials and Methods

Extensive searches were carried out in the PubMed, EBSCOhost, and Scopus databases, and 772 published papers were examined. A set of keywords was evaluated to select relevant articles: [red algae (Rhodophyta)] [seaweeds] [bioactive compounds of seaweeds] [therapeutic effect of algae]. Records not meeting the eligibility criteria were excluded, and 55 of them meeting the following were considered (Figure 1): i) written in the English language; ii) published in peer-reviewed journals from 2002 to 2024; iii) studies related to red seaweeds (Rhodophyta), bioactive compounds, therapeutic effect.

Main components of red seaweeds

The quantity and quality of the bioactive compounds from red seaweed depend on the species and the extraction methods. Geographical distribution, habitat, season, nutrient content of the growth medium, life cycle, the harvesting season, and changes to the environment, such as radiation, water pressure, salinity, and water movement are other parameters influencing the compound's variation in the species.¹¹ Red seaweeds have a wide range of bioactive substances. Among them there are: polysaccharides, proteins, minerals, phenolics, vitamins, carotenoids, and lipids. Their biological activities have huge utility in the food industry. Recently, many researches, focused on benefits proving their potential in the biotechnological as well as biomedical field.^{4,12}

Polysaccharides

Seaweeds' polysaccharides have specific characteristics and physicochemical properties that are totally absent in terrestrial plant polysaccharides due the high portion of mucilage on the skeleton; they ensure mechanical resistance to deformation of the thalli.¹³

Red seaweeds contain large amounts of polysaccharides ranging between 8.3–68.2% of the Dry Weight (DW).⁴ They contain particular poly-uronides, including pyruvylated, methylated, sulfated, or acetylated. Agar and carrageenan are known as phycocolloids, the most relevant and exploited compounds in red seaweeds.¹⁴ Agar is mostly composed of agarpectin and agarose that represents up to 70% of the mixture; it is responsible for gelling, whereas thickening properties are due to agarpectin.¹⁵ Carrageenans, polysaccharides found in red algae,¹⁴ are classified into three categories based on their sulfation level: Iota (ι -), kappa (κ -), and lambda (λ -). Recent research has demonstrated that sulfated polysaccharides possess a range of beneficial activities, including antioxidant, anticancer, anti-inflammatory, anti-diabetic, anticoagulant, immunomodulatory, and anti-HIV properties. These findings highlight their potential uses as thickening, stabilizing, and gelling agents in food, as well as in biotechnology, cosmetics,

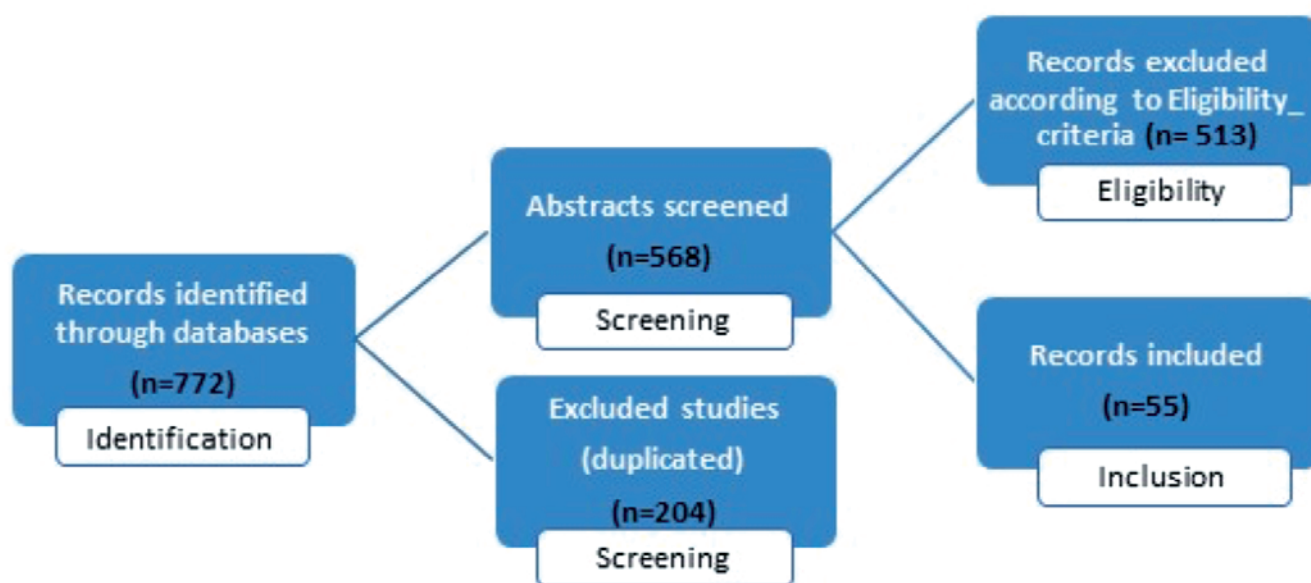


Figure 1. Diagram flow.

and biomedical industries.^{6,16} Red seaweeds also contain sulfated polysaccharide porphyran and xylan, providing high-quality dietary fiber.¹⁷

Proteins

Red seaweeds have the greatest protein content among seaweeds, followed by green, while brown have the least,^{18,19} making them superior than vegetables.²⁰ The amount of protein in red algae generally ranges from 3.5–47% DW.⁴ However, *Palmaria palmata* has the highest protein concentrations (47% DW).¹³ They contain many Essential Amino Acids (EAAs), whose content depends on the season and species. The EAAs in red algae account between 25 to 50% of the total Amino Acids.¹⁵ The ratio between EAAs and Non-Essential Amino Acids (EAA/NEAA) ranged between 0.98 to 10.2.²⁰ The proportion of lysine is generally lower in seaweeds as a whole, but it is more important in red species than in other phyla.²¹ Digestibility is the key factor that defines the nutritional value of a protein and is influenced by the proportion of soluble fibre in the seaweed. Compared to animal proteins, red algae proteins are relatively important. They seem to be an excellent potential source of dietary proteins. Phycobiliproteins responsible for the bright pink colour of the red seaweed are the principal proteins representing up to 50% of the overall protein content.⁸ Through cysteine amino acids, coloured phycobilins are covalently attached to phytobiliproteins. In red seaweeds, they serve as the primary photoreceptor for photosynthesis. They have not only antioxidant but also anti-inflammatory, antiviral, and neuroprotective properties.¹⁵ A class of proteins or glycoproteins known as lectin, can reversibly bind to carbohydrates or substances containing them. Algal lectins typically have a lower molecular weight than higher terrestrial lectins.²²

Vitamins

Seaweeds are exposed to sunlight; as a result, they are rich in antioxidants in many forms, including vitamins.²³ Red algae are rich in fat and water-soluble vitamins such as: A, tocopherol (vitamin E), C, B12, B1, niacin (B3), folic acid (B9), pantothenic acid (B5), and riboflavin (B2).^{20,24} Previous studies mentioned that in some red seaweeds vitamin E content ranged from 10 to 26 mg/kg.¹⁹ The majority of terrestrial plants are incapable to produce vitamin B12.¹³ In general, red macroalgae have the highest vitamin B12 concentrations; ranging between 96.1–1338 mg/100 g DW.²⁵ As an example, *Porphyra* spp. and *P. palmata* have respectively 760.1 and 733.6 µg/kg.²⁶ Red seaweeds also contain vitamin B3 with values ranging between 95.1 to 100 mg/100 g DW, and vitamin C with values ranging from 35.3 to 1,601.6, mg/100 g DW.²⁵ Along with other vitamins, red seaweeds have 1.34 mg vitamin E/g DW, 4.61 g-tocopherol/g DW, 0.05 to 1.54 mg vitamin B2/g DW, 3.8 to 4.8 mg vitamin B6/g DW, 0.4 to 1.0 mg vitamin B9/g DW, and 2.1 to 2.7 mg pro-vitamin A/g DW.¹ Also, *Grateloupia turuturu* contains Phytonadione (vitamin K1) and α -tocopherol (vitamin E), proving the capacity to exhibit significant nutritional properties.²⁰

Lipids

Seaweeds typically contain low levels of lipids or fatty acids, ranging from 0.60% to 4.14% DW. They are capable of synthesizing long-chain Polyunsaturated Fatty Acids (PUFAs), typically ranging from 14 to 24 carbon atoms.²⁰ Red algae are particularly rich in fatty acids with chains of 20 carbon atoms often with four

or five double bonds such as eicosapentaenoic acid (20:5-3) and arachidonic acid (20:4-6). PUFAs represent 65.6% of all fatty acids in red algae.¹ In *Solieria chordalis*, for example, Saturated Fatty Acids (SFAs) have chain lengths between C14 and C18.^{27,28} The two primary lipid groups found in seaweed are phospholipids and glycolipids, with PUFAs making up a substantial portion, around 65.6%, of all fatty acids in algae; the ω -3 and ω -6 PUFA families are key components of seaweed lipid compositions making them valuable dietary sources which play vital roles in human health.¹

Minerals

Minerals, particularly macro- and micronutrients, are abundant in seaweeds, due to their ability to be adsorptive and bio-accumulative in marine habitats. The average mineral composition ranges from 8 to 40%.²⁹ Seaweeds contain vital minerals and trace elements necessary for personal dietary intake, namely iron (Fe), Zinc (Zn), Copper (Cu), Selenium (Se) and Iodine (I), as well as Potassium (K), Calcium (Ca), Magnesium (Mg), Manganese (Mn), and Sodium (Na).³⁰ Edible land plants and animal products do not contain this large range of minerals.^{1,30} Red seaweeds include 1.8 to 8.1 g/100 g DW of Sodium, 6.1 to 21.9 g/100 g DW of Potassium, 0.2 to 0.9 g/100 g DW of Calcium, and 0.2 to 0.5 g/100 g DW of Magnesium, which are all essential macro-minerals. Among the trace minerals, in red algae Fe is the most abundant element; as an example, *Palmaria palmata* (Rhodophyta) contains 800 mg/kg DW, followed by Zn which is relatively abundant.^{1,20} In *Chondrus crispus*, the concentration of Zn is 74 mg/kg DW,¹ and for *Porphyra* spp. it is 82 mg/kg DW. Na/K ratio for red algae ranges between 0.1 and 1.8. These seaweeds' low Na/K ratio is advantageous for managing hypertension.²⁰ However, algae can also accumulate significant amounts of heavy metals such as Arsenic (As), Cadmium (Cd), Copper (Cu), Mercury (Hg), and Lead (Pb) which can limit their consumption.²⁹ In general, seaweed content is below the toxic limits allowed in several countries.²⁹

Phenolic compounds

Seaweeds synthesize phenolic compounds, sometimes called polyphenolics produced by secondary metabolites, exhibiting free-radical scavenging properties. They are known for their structure where there is at least one hydroxyl group (-OH) bound directly to an aromatic ring. They are classified into numerous categories and possess a variety of characteristics including resistance to predators and pests, strong flavours, colours, aromas; many other (tannin) phenolic compounds play a role of protection.^{31,32} The majority of phenolic elements in red seaweeds are flavonoids (mostly flavonols and flavan-3-ols),⁶ bromophenols, phenolic acids, phenolic terpenoids, and Mycosporine-like Amino Acids (MAAs) that play a major role in photo-protection against UV radiation.³³ Twenty (20) MAAs have already been identified in various red macroalgae.³³ Secondary metabolites called Bromophenols (BPs) play ecological roles, such as chemical defence and deterrence. They share one or several benzene rings with bromine substituents of indistinct degrees.³² In seawater and marine algae, bromide concentrations are approximately 0.65 mg/kg.³¹

Carotenoids

Carotenoids are natural pigments that serve photosynthetic organisms in capturing light and protecting themselves from it.³⁴ They are the major terpenoids found in red seaweed and also con-

tribute to their special pigmentation.² They can be classified into two groups according to their carotene content; carotenes (α -carotene, β -carotene) and xanthophylls.³³ Red macroalgae contain 0.2 to 1.8 mg/g DW of carotenoids.¹

Therapeutic benefits of red algae

Traditionally, red algae have been valued as a source of hydrocolloids such as agar and carrageenan used as gelling and thickening agents in foods. However, red seaweeds also contain a wide array of bioactive compounds with therapeutic potential (Table 1). Many Rhodophyceae species worldwide offer health benefits that can help prevent and treat various diseases.

The primary polysaccharides in red seaweeds are sulfated galactans, notably porphyran and carrageenan, which have shown anti-cancer benefits when used with conventional drugs by enhancing compromised immune function; red algae polysaccharides have been reported to inhibit Hepatitis C Virus (HCV),³⁵ exhibit anti-tumor, anti-thrombotic, and anticoagulant activities.²⁰ *Ethanoeloupia elliptica* and *Plocamium telfairiae* have been deemed safe and effective as anti-obesity agents.³⁶ Furthermore, red seaweeds phenolic compounds, including polyphenols, are potent free-radical scavengers. These compounds, known for their antioxidant properties, help lower the risk of several diseases and offer significant pharmacological benefits.³¹ New pigments found in red algae, suciliproteins, carotenoids, and chlorophyll-a, have demonstrated anti-diabetic, anti-mutagenic, and anti-hypertensive properties.³⁷ Certain pigments, like lutein and zeaxanthin, may prevent and treat eye conditions like age-related macular degeneration, cataracts, and retinitis pigmentosa.³⁷ The red macroalgae *Gracilaria corticata* showed therapeutic effects, including antibacterial, anti-inflammatory, antioxidant, anti-cholesterolemic, and hepatoprotective properties, as well as antipyretic activity comparable to paracetamol.^{38,39}

Although the lipid content in red algae is low, it is valuable. PUFAs, specifically ω -3 and ω -6, constitute a significant portion of red algae lipids and are recognized for their antioxidant abilities, cholesterol-lowering effects, cell and tissue repair functions, and contributions to heart health and cancer prevention.²⁰ The ratio of ω -6/ ω -3 fatty acids in seaweeds is always below the ratio recom-

mended by the World Health Organization, which recommends 10.⁴⁰ They can contribute to the prevention of inflammatory, cardiovascular, and nervous system disorders in addition to the reduction of low-density lipoproteins and cholesterol. Also, they can reduce the risk of breast, prostate, colon and renal cancers.^{20,41} Phospholipids found in red seaweeds are also utilized pharmaceutically for their beneficial effects on the central nervous system and anti-tumour properties.⁴²

Due to exposure to nutrient-rich seawater, red algae contain high concentrations of essential minerals. They are particularly high in iron, which is vital for oxygen transport, electron transfer, and oxidase activity, and manganese, which acts as a cofactor for several enzymes. Red algae also have higher sodium (Na) and potassium (K) levels than many vegetables, but a lower Na/K ratio, an important factor in cardiovascular health, as low Na/K ratios are linked to blood pressure reduction.³⁰ *Palmaria palmata*, for instance, has an Na/K ratio as low as 0.1. compared to the World Health Organization's recommendation of a ratio close to one.³⁰ The chemical composition of seaweed is notably similar to human plasma, contributing to its ability to regulate blood pressure.⁴³ Consequently, Rhodophyta species are regarded as a rich ecological source of bioactive compounds, offering potential for pharmaceutical research and posing no known health risks due to their diverse compound profile.

Conclusions

Red seaweeds (Rhodophyta) have a profound nutritional and therapeutic potential, positioning them as one of Nature's most promising and versatile resources. The bioactive compounds found in red seaweeds, including polysaccharides, proteins, low lipids, vitamins, minerals, phenolic compounds, and pigments are distinguished by their unique structural and functional properties, which contribute to their wide range of applications across multiple industries. Red seaweeds not only serve as a sustainable food source, but also play a critical role in the fields of biotechnology, pharmaceuticals, and biomedicine. Unlike terrestrial plants, red seaweeds offer distinct compounds such as sulfated polysaccharides and specialized fatty acids that exhibit notable biological

Table 1. Compounds extracted from Rhodophyta species and their therapeutic properties.

Rhodophyta species/region	Bioactive compound	Therapeutic properties/case study
<i>Palmaria palmata</i> (Japan)	Phycobiliproteins	Prevention of hypertension/ <i>in vivo</i> ³⁷
<i>Bangia atropurpurea</i> (Malaysia)		Antioxidant/ <i>in vitro</i> ⁴⁴
<i>Pterocladiaella capillace</i> (Brazil)	Lectins	Antinociceptive and anti-inflammatory/ <i>in vivo</i> ^{45,46}
<i>Solieria filiformis</i> (Brazil)		Anti-inflammatory/ <i>in vivo</i> ²²
<i>Bryothamnion triquetrum</i> (Brazil)		
<i>Sarcodia ceylanica</i> (Taiwan)	Ethyl acetate	Anti-inflammatory and antinociceptive/ <i>in vivo</i> ⁵
<i>Gracilaria cornea</i> (Brazil)	Sulfated polysaccharide	Anti-inflammatory/ <i>in vivo</i> ⁴⁷
<i>Ania rubens</i> (Egypt)	Polysaccharide	Anticancer/ <i>in vitro</i> ⁴⁸
<i>A. devoniensis</i> (Estonia)		Anti-coagulant/ <i>in vitro</i> ⁴⁹
<i>Kappaphycus alvarezii</i> and <i>Gracilaria opuntia</i> (India)	Sulphated polygalactans	Anti-diabetic and anti-inflammatory/ <i>in vitro</i> ⁵⁰
<i>Grateloupia elliptica</i>	Ehanol extract of <i>G. elliptica</i> and	Anti-obesity/ <i>in vivo</i> ^{51,52,36}
<i>Plocamium telfairiae</i> (Korea)	<i>Plocamium telfairiae</i>	
<i>Sphaerococcus coronopifolius</i> (Corfu Island, Greece)	Brominated diterpenes	Antitumor activity/ <i>in vitro</i> ⁵³
<i>Gigartina pistillata</i> (Portugal)	Carrageenans	Antitumour potential against colorectal cancer/ <i>in vivo</i> ⁵⁴
<i>Laurencia obtusa</i> (Egypt)	Polysaccharide	Anti Hepatitis C virus/ <i>in vitro</i> ³⁵
<i>Gracilaria verrucosa</i> (Korea)	Seaweed water extract	Anti-diabetic/ <i>in vivo</i> ⁵⁵

activities. They serve as effective agents in combating various health issues, including antioxidant, anti-inflammatory, anticancer, antiviral, and neuroprotective properties. Furthermore, the bioactive compounds derived from red seaweeds, such as carrageenan and agar, exhibit a variety of therapeutic benefits, including anti-diabetic, antimicrobial effects as well as anti-clotting, anti-tumour, anti-Hepatitis C virus, antioxidant, anti-allergic, anti-inflammatory, hypoglycemic, anti-obesity, antiviral, and antifungal effects. Studies have shown that compounds like phycobiliproteins and PUFAs are particularly beneficial for cellular health, cardiovascular function, and immune support. In addition, the mineral content in red seaweeds provides vital nutrients that are often limited in other food sources. Their favourable Na/K ratio, beneficial for cardiovascular health, further distinguishes them as an ideal dietary component. Through decades of research, it has become evident that red seaweeds are emerging not only as a dietary supplement but as a powerful natural resource for advancing human health and supporting sustainable practices. Several studies on seaweed compounds and extracts have been completed; however, future research must be conducted to identify and extract bioactive molecules from red seaweeds in order to create new biomedical applications and medicinal treatments.

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