Bioproducts From Seaweeds: A Review With Special Focus On The Iberian Peninsula

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Abstract: Seaweeds, *i.e.* macroalgae that occupy the littoral zone, are a great source of compounds with diverse applications; their types and content greatly determine the potential applications and commercial values. Algal polysaccharides, namely the hydrocolloids: agar, alginate and carrageenan, as well as other non-jellifying polysaccharides and oligosaccharides, are valuable bioproducts. Likewise, pigments, proteins, amino acids and phenolic compounds are also important, exploitable compounds. For the longest time the dominant market for macroalgae has been the food industry. More recently, several other industries have increased their interest in algal-derived products, *e.g.* cosmetics, pharmaceuticals and more recently, as a source of feedstock for biorefinery applications. This manuscript reviews the chemical composition of dominant macroalgae, as well as their potential added-value products and applications. Particular attention is devoted to the macroalgal species from the Iberian Peninsula. This is located in the Southwest of Europe and is influenced by the distinct climates of the Mediterranean Sea and the Atlantic Ocean, representing a rich spot of marine floral biodiversity.

Keywords: Seaweeds, macroalgae, hydrocolloids, phenolic compounds, proteins, bioactives, fucoidans, ulvans, laminarans.

1. INTRODUCTION

Seaweeds (or macroalgae) are aquatic, photosynthetic organisms belonging to the Eukaryota Domain and the Kingdoms Plantae (the green and red algae) and the Chromista (the brown algae). Although classification systems have changed over time, it is generally accepted that: a) the green algae are included in the phylum Chlorophyta and their pigmentation is identical to that of terrestrial plants (*i.e.* chlorophylls a, b and carotenoids); b) the red algae belong to the phylum Rhodophyta and their photosynthetic pigments are chlorophyll a and the phycobilins (*i.e.* R-phycocyanin and R-phycoerythrin) and carotenoids, mostly β-carotene, lutein and zeaxanthin and c) the brown algae are included in the Phylum Ochrophyta (or the Heterokontophyta), Class Phaeophyceae and their pigments include the chlorophylls a and c, as well as carotenoids, dominated by fucoxanthin [1, 2].

Seaweeds are fundamental to the food chain of all aquatic ecosystems. As primary producers they produce oxygen and organic compounds which serve as the basic trophic level or food for many other living beings. They have also found a role of great importance to mankind. Indeed, coastal communities have been using macroalgae in the preparation of home medicines for the treatment of distinct ailments for centuries. Green algae are useful as anthelmintics, astringents and to treat gout, while brown algae are commonly used in the treatment of rheumatic processes, arteriosclerosis, menstrual disorders, hypertension, gastric ulcers, goiter, skin diseases and syphilis. In turn, red algae can be used as anticoagulants, antihelmintics and for treating gastritis and diarrhea [3]. These applications are based on the empirical knowledge of many generations and, in most cases, the bioactive compounds and their respective mechanisms of action remain unknown. Still, the recent interest for drugs of marine origin and the concomitant, exponential investigation focusing that issue is perhaps delivering its first fruits. This is the case for the beneficial properties of various kelps (*Laminaria* spp. and *Saccharina* spp.) for the treatment of goiter, which are now known to be due to the relatively high iodine levels in these macroalgae [4].

Today, seaweeds are used in many countries for very different purposes, including their direct consumption as food or supplements (by animals and humans), as feedstock for the extraction of phycocolloids, or for their bioactive components and as biostimulants and biofertilizers. Notably, direct use as food has strong roots in the East Asia, whereas the West seems to be more committed to the extraction of the hydrocolloids, namely carrageenan, agar and alginate (European registration numbers -

E407, E406 and E400, respectively) [3, 5]. In addition, many seaweeds are receiving increasing attention as a potential, renewable sources for the food industry, as a feed for livestock and as food directly [6]. Industrialized countries are currently increasing efforts regarding the manufacturing of high-value products derived from algae, since these contain chemical components (*e.g.* polysaccharides, proteins, lipids and polyphenols) with a wide range of biological activities. This range of activities leads to promising applications in nutraceutical/functional food, cosmetic, and pharmaceutical industries [7-9]. (Table **1**) reviews the seaweed orders reported from the Iberian Peninsula with some known bioactivities.

Table 1. Sytematics of orders of Iberian Peninsula seaweeds with some documented bioactivity (after [2])

Phylum/Class	Order	Genera	Species
Chlorophyta	Bryopsidales	4	13
	Dasycladales	1	1
	Siphonocladales	1	1
	Cladophorales	2	9
	Ulvales	2	8
	Ulotrichales	1	1
Rhodophyta			
	Bangiales	2	4
	Ahnfeltiales	1	1
	Bonnemaisoniales	2	3
	Ceramiales	22	29
	Corallinales	7	14
	Gelidiales	3	7
	Gigartinales	18	22
	Gracilariales	2	5
	Halimeniales	1	2
	Nemaliales	5	6
	Neamatomales	1	1
	Palmariales	2	2
	Plocamiales	1	1
	Rhodymeniales	5	5
Heterokontophyta/Phaeophyceae			
	Cutleriales	2	2
	Desmarestiales	1	2
	Dictyotales	7	15
	Ectocarpales	9	10
	Fucales	8	30
	Laminariales	6	9
	Ralfsiales	1	1

Sphacelariales	3	3

Moreover, as world energy demands continue to rise and fossil fuel resources are increasingly reduced, macroalgae have attracted attention, as a possible renewable feedstock to biorefinery applications, for the production of multiple streams of commercial interest including biofuels such as bioethanol and biogas [10-12], particularly because they have considerable contents of carbohydrates. In this field, macroalgae have several advantages over terrestrial biomass, primarily because of their potentially high yields, no competition with food crops for the use of arable land and fresh water resources, and utilization of carbon dioxide as the only carbon input [13]. Despite their merits, most macroalgae-based biofuels are relatively unexplored resources. The main reason is that macroalgae have several carbohydrates which are distinct from those of terrestrial biomass sources. Hence, improvement of terrestrial-based technologies in macroalgae or the development of new more effective technologies are needed and these are still under evaluation [2, 13-15]. One technical solution that would speed the economic viability of this process would be the co-production of biofuels with other higher value products, e.g. the extraction of high-value components or the production of animal feed biomass [16].

The industry uses 7.5-8 million tonnes of wet seaweed annually [17]. This is harvested either from naturally grown (wild) seaweed, or from, open-water, cultivated (marine agronomy, farmed) crops [6]. The farming of seaweeds has expanded rapidly as demand has outstripped the supply available from natural resources. Commercial harvesting occurs in about 35 countries, spread between the Northern and Southern Hemispheres, in waters ranging from cold, through temperate, to tropical [17]. The consumption and utilization of seaweed worldwide are associated with a myriad of products that generate nearly US$ 8 billion per year [6]. Almost 90 percent are food products for human consumption; the remainder is for the hydrocolloid industry focused on agar, carrageenan and alginates. Macroalgae for direct or indirect consumption (i.e. coloring, flavoring agents and biologically active compounds sold as dietary supplements) have been gaining market share, mainly due to the recognition of Man´s seaweed traditional uses in their daily lives.

1.1. The macroalgal biodiversity of the Iberian Peninsula

The Iberian Peninsula is located in the warm temperate, Mediterranean-Atlantic region and the Iberian coasts are under unique circumstances, receiving climatic influences from the North Atlantic Ocean (western, north coasts, and adjacent islands) and the Mediterranean Sea (southern, eastern coasts, and adjacent islands), thus generating a sharp latitudinal gradient in the macroalgal flora. Along the coastline, rocky shores are separated by extended areas of sandy beaches. Most of the beaches from the western coasts are very exposed and the algae which do occur in the intertidal zone are mainly found closest to the low tide level. The intertidal algal flora of the northern zone is similar to that of the coast of Central Europe (i.e. Brittany, France and the southern parts of the British Isles), while the intertidal algal flora of southwestern and eastern coasts is very different, responding to a marked influence from the Mediterranean and the North West African Coast species. Temperate species gradually decline in number southwards along the Western Iberian coast, where some taxa have their southern limit [18, 19].

The intertidal flora of the northwestern zones are dominated by *Ascophyllum nodosum*, *Bifurcaria bifurcata, Himanthalia elongata, Saccorhiza polyschides* (Phaeophyceae, Fucales), *Gelidium corneum*, *Gelidium pulchellum* (Rhodophyta, Gelidiales), *Chondrus crispus*, *Mastocarpus stellatus*, *Calliblepharis jubata*, *Gigartina pistillata*, *Chondracanthus acicularis* (Rhodophyta, Gigartinales), *Osmundea pinnatifida*, *Pterosiphonia complanata* (Rhodophyta, Ceramiales) and *Corallina elongata* (Rhodophyta, Corallinales). The southwestern zones are dominated by *Corallina elongata* (Rhodophyta, Corallinales), *Caulacanthus ustulatus*, *Chondracanthus acicularis* (Rhodophyta, Gigartinales), *Gelidium pusillum*, *Osmundea pinnatifida* and *Chondria coerulescens* (Rhodophyta, Ceramiales). *Codium adherens* (Chlorophyta, Bryopsidales) may have a significant presence on the rocky shores in this location [18, 19]. In the southward direction of the Iberian coasts, the number of species of red algae increase due to the presence of warmer waters and in areas subject to less anthropogenic pressure, where they naturally dominate in numerically over the brown algae and green algae. With increasing disturbances, the number of red algal taxa decline, ultimately affecting diversity and species richness [20, 21].

Seaweeds are responsible for a significant proportion of the primary production of the Iberian Peninsula. Its traditional collection and uses were described in the fourteenth century and, in particular, the harvesting of kelp, which is still done in the north of Portugal, was regulated in 1308 by King D. Dinis. This usage was constant until the twentieth century [18, 22]. By that time, the lack of Japanese Agar during World War II allowed for the emergence of an Portuguese agar industry, due to the abundance and quality of local red seaweeds (mainly *Gelidium corneum* and *Pterocladiella capillacea*) [23]. However, the unfavourable international economic conditions led to the marked reduction of this industry; today only one company persists (i.e. Iberagar - Luso-Spanish Society of Marine Colloids, SA) [3, 22]. Iberagar is actually Portugal's leading company engaged in the manufacture and distribution of hydrocolloids derived from seaweeds. Iberagar was created through the merger of two companies, Biomar and AGC, and was established shortly after World War II. In 1970, Iberagar acquired a Japanese company, Unialgas, and transferred its operations to a plant in Barreiro, 30 km from Lisbon.

The carrageenan production in Iberian Peninsula began in the 1960's, when a factory (CEAMSA, Marine Algae Company) was established in Galicia, Spain. At the beginning, supply was dominated by the local resources of *C. crispus* and *M. stellatus* combined with carrageenophytes imported from Canada and USA. Maximum level of exploitation was attained the 1970's [18, 24]. This activity declined in the 1980's, mainly due to the competition with developing tropical countries that produced *Euchema* and *Kappaphycus* [24, 25].

Recently some young companies (i.e. Algaplus, Wedotech, AlgaFuel, among others) are initiating activities in order to harness the biotechnological potential of the Iberian marine flora. In this context, the present manuscript describes the major groups of seaweed-derived compounds that have been successfully commercialized, and/or appear to be good candidates for future exploitation and commercialization.

2. POLYSACCHARIDES

Macroalgae are known to be rich in polysaccharides, with concentrations that can vary in the range of 4 to 76% of dry weight [26]. Globally, these are mainly structural cell wall polysaccharides, although considerable amounts of mucopolysaccharides and storage polysaccharides can occur in specific species [27, 28].

2.1. Macroalgal Hydrocolloids (Phycocolloids)

Of all the polysaccharides, macroalgal hydrocolloids, or phycocolloids, are by far the most relevant in terms of their industrial commercialization, with an estimated global value of approximately $US 1 billion in 2009 and representing more than half of the non-food macroalgal market products [29, 30].

Macroalgal hydrocolloids are high molecular weight, structural polysaccharides, found in the cell wall of freshwater and marine algae that typically form colloidal solutions, i.e. an intermediate state between a solution and a suspension. This property provides polysaccharides with the ability to be used as thickeners, gelling agents and stabilizers for suspensions and emulsions in diverse industries, including the food, biotechnological, paint, textile and biomedics (Table 2). To the present day, hydrocolloids of significant commercial value include the sulfated galactans, agar and carrageenans (obtained from red algae) and the alginates (obtained from brown algae). These are extracted in fairly high amounts from various algal raw materials, with maximum extraction yields obtained with hot water or alkaline solutions [31].

Specific European codes for different phycocolloids, as used in varied food industries as natural additives, are E400 (alginic acid), E401 (sodium alginate), E402 (potassium alginate), E403 (ammonium alginate), E404 (calcium alginate), E405 (propylene glycol alginate), E406 (agar), E407 (carrageenan) and E407A (semi-refined carrageenan or processed eucheuma seaweed). Note that presently hydrocolloids are gaining even more value in the food industry (and others) as a result of their potencial as robust functional food ingredients.

Table 2. Applications of Macroalgal Phycocolloids (after [32-35]).

Use	Phycocolloid	Function
Food additives		
Baked food	agar kappa, iota, lambda carrageenan	Improving quality and controlling moisture
Beer and wine	alginate kappa	Promotes flocculation and sedimentation of suspended solids
Canned and processed meat	alginate kappa	Hold the liquid inside the meat and texturing
Cheese	kappa	Texturing
Chocolate milk	kappa, lambda	Keep the cocoa in suspension
Cold preparation puddings	kappa, iota, lambda	Thicken and gelling

Condensed milk	iota, lambda	Emulsify
Dairy Creams	kappa, iota	Stabilize the emulsion
Fillings for pies and cakes	kappa	Give body and texture
Frozen fish	alginate	Adhesion and moisture retention
Gelled water-based desserts	kappa + iota kappa + iota + CF	Gelling
Gums and sweets	agar iota	Gelling, texturing
Hot preparation flans	kappa, kappa + iota	Gelling and improve the mouth-feel
Jelly tarts	kappa	Gelling
Juices	agar kappa, lambda	Viscosity, emulsifier
Low calorie gelatins	kappa + iota	Gelling
Milk ice-cream	kappa + GG, CF, X	Stabilize the emulsion and prevent ice crystals formation
Milkshakes	lambda	Stabilize the emulsion
Salad dressings	iota	Stabilize the suspension
Sauces and condiments	agar kappa	Thicken
Soymilk	kappa + iota	Stabilize the emulsion and improve the mouth-feel
Cosmetics		
Shampoos	alginate	Vitalization interface
Toothpaste	carrageenan	Increase viscosity
Lotions	alginate	Emulsification, elasticity and skin firmness
Lipsticks	alginate	Elasticity, viscosity
Medicinal and Pharmaceutical uses		
Dental mould	alginate	Form retention
Laxatives	alginate carrageenan	Indigestibility and lubrication
Tablets	alginate carrageenan	Encapsulation
Metal poisoning	carrageenan	Binds metal
HSV	alginate	Inhibit virus
Industrial and Lab Uses		

Paints	alginate	Viscosity and suspension, glazing
Textiles	agar, carrageenan	Sizing and glazing
Paper making	alginate, agar, carrageenan	Viscosity and thickening
Analytical separation	alginate, carrageenan	Gelling
Bacteriological media	agar	Gelling
Electrophoresis gel	agar, carrageenan	Gelling

Non-seaweed colloids: CF - Carob flour; GG - Guar gum; X - Xanthan

Sulfated Galactans

Sulfated galactans are abundant in red algae (but also found in brown and green algae), being the most common the agarans (agar) and the carrageenans. Typically, these polysaccharides have a linear backbone with repeating disaccharide units which are made of alternating 3-linked β-D-galactopyranose and 4-linked α-galactopyranose or 3,6-anhydro-α-galactopyranose residues [36]. This "masked repeating" unit of disaccharides was first reported for the agar-like porphyran stereochemistry [37, 38].

Agar

This hydrocolloid was the first to be discovered for applications and received its name from Malaysia, where it means "red alga". The structure was initially believed to be a simple, sulfated poly-galactose polymer, but later studies demonstrated that agar consisted of a mixture of at least two polysaccharides, i.e. agarose and agaropectin [39]. Typically, agarose is the predominant fraction of agar (50-90% [40, 41]) and also the responsible for its gelling properties [41]. It consists of high molecular weight polysaccharides composed of repeating units of (1→3)-β-D-galactopyranosyl-(1→4)-3,6-anhydro-α-L-galactopyranose (Fig. 1), although some variations can occur, depending on factors such as the species of seaweed, as well as environmental and seasonal conditions [39]. In turn, agaropectin is a less clearly defined, it is a more complex polysaccharide of lower molecular weight than agarose and it has thickening properties [5, 39]. Its structure is essentially made up of alternating (1→3)-β-D-galactopyranose and of (1→4)-3,6-anhydro-α-L-galacto-pyranose residues, where the former can be modified by acidic side-groups which are primarily sulfate (up to 32%), plus uronate or pyruvate groups, as well by non-ionic methoxyl groups [39, 42].

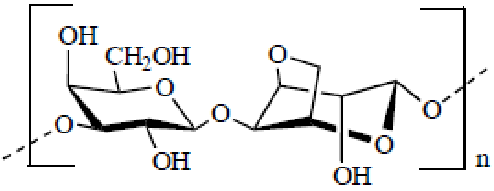

Fig. (1). Idealized structure of the chemical units of agarose.

The gelation mechanism of agar is based on the ability of agarose to form double-helix networks, in which each chain forms a left-handed, three-fold helix [43]. The latter becomes stable in the presence of water molecules, bound inside of the double helical cavity [44], together with exterior, hydroxyl groups which permit the aggregation of up to 10000 helices, with concomitant formation of microdomains of spherical microgels [45].

Remarkably, the reversible gels of agar are formed by simply cooling hot aqueous extraction solutions. In general, the agar gels are strong, but their rheological strength is greatly affected by sulfate substitution levels (i.e. stronger gels are obtained for those agars with lower sulfate levels) [39]. Other physicochemical factors affecting the gelling properties of agar include the molecular weight and substitution [46]. Indeed, agar may be modified by substitution of sulfate, pyruvate, uronate or methoxyl groups. Modern alkali treatment methods tend to increase the level of anhydrous bridging in the molecule, resulting in an enhancement of gel strength [39, 47].

Agar was, and still is prepared and sold as an extract in solution (hot) or in gel form (cold), to be used promptly in areas near the factories [6]. The product was known as “tokoroten”. Its industrialization as a dry and stable product began in the early 18th century and since then, has been called "Kanten". Presently, "agar-agar" and “agar” are the most accepted worldwide terms. However, it is also called “gelosa” in French- and Portuguese-speaking countries [6, 31, 48].

Agar production by modern techniques of industrial freezing (the gel is slowly frozen in order to eliminate water), started in California by Matsuoka, who registered his patents in the United States in 1921 and 1922 [39, 48, 49]. During the Second World War, the lack of available agar was a stimulus for countries with coastal resources of

Gelidium corneum (formerly *Gelidium sesquipedale*), which is very similar to the *Gelidium pacificum* used by the Japanese industry. In Portugal, the agar industry was started in Oporto, by Loureiro, while in parallel, J. Mejias and F. Cabrero (Spain) started the establishment of the Iberian agar industry [48]. Other European countries which did not have access to agarophytes tried to prepare agar substitutes from other seaweeds [31, 48].

Currently, the freeze-thawing technology remains in use, although most processors have adopted the press/syneresis technology (i.e. a method through which the absorbed water can be eliminated by means of an applied force), or alternatively, a mixture of the two technologies [5, 48]. While the basic processes may not have changed, improvements in presses and freezing equipment must be noted. High-pressure membrane presses have greatly improved the dewatering of agar and thereby reduced energy requirements for final drying, prior to milling to powder [29].

About 90% of the agar produced globally is for food applications [16]. The origin of agar as a food ingredient was in Asia, where it has been consumed for several centuries [5]. Agar has excellent qualities as a thickening, stabilizing and gelling agent, making it a crucial ingredient in the preparation of processed foods including fruit jellies, dairy products, fruit pastilles, chewing gum, canned meats, soups, confectionery and baked goods, icings, frozen and salted fish (Table 2) [39, 41]. Moreover, agar has satiating and gut-regulating characteristics contributing to its characteristics as an ideal fiber ingredient in the preparation of low-calorie food products. Furthermore, agar is tasteless and hence it does not interfere with the flavors of foodstuffs, in contrast to some of its competitive gums, where the addition of calcium or potassium salts is required to form gels. It is also important that agar has been classified as GRAS (Generally Recognized as Safe) by the United States of America, Food and Drug Administration (FAD), which has established maximum usage levels, depending on particular applications [6].

In addition to food applications, about 10% of all agar is currently being used for biotechnological applications (e.g. preparation of inert, solidified culture media for bacteria, microalgae, fungi, tissue culture as well as for separation of macromolecules by electrophoresis) [5, 16]. Although, agar applications are expected to increase in the near future, mainly because of the health-associated properties claimed for the gel. Indeed, agars are not digested by humans and therefore can be regarded as dietary fibers [50-52]. These are water-soluble and were found to be effective in the reduction of obesity, hypercholesterolemia, diabetes [53] and intestinal cancer [28]. It has been reported that agar consumption leads to a decrease in the concentration of blood glucose and causes an anti-aggregation effect on red blood cells [28]. Antitumor activity was associated with a highly sulfated, agar-type polysaccharides derived from a cold water extraction of *Gracilaria dominguensis,* which inhibited the transplantation of Ehrlich ascites carcinoma in mice [54]. Agaro-oligosaccharides (AGO), obtained by hydrolysis of agar, have been shown to suppress the production of a pro-inflammatory cytokine and an enzyme associated with the production of nitric oxide (patented by Enoki et al. [55]). This anti-inflammatory activity of AGOs was recently reported in rats with chemically-induced colitis (by 2,4,6-trinitrobenzene sulfonic acid (TNBS)) and the results suggested that the oral administration of AGOs could be a possible therapeutic strategy for the treatment of the inflammatory bowel disease [56]. AGOs' activity against α-glucosidase as well as its antioxidant ability has also been demonstrated [57].

Currently, agar is extracted from species of *Gelidium* and *Gracilaria*. Species of *Pterocladiella*, are closely related to *Gelidium* and small quantities of these are collected, mainly in the Azores (Portugal) and New Zealand. *Gelidiella acerosa* is the main source of agar in India. *Ahnfeltia* species have been used in both Russia (in particular the island of Sakhalin) and Japan. *Gelidium* spp. and *Gracilaria* spp. are collected in Portugal, Morocco, Tunisia and Chile for agar production [58, 59]. Along the Iberian Peninsula, the main agarophytes present are *Gelidium corneum, G. spinosum, G. pulchellum, Pterocladiella capillacea, Gracilaria gracilis, G. multipartita, G. vermiculophylla, Gelidiella acerosa,* and *Ahnfeltia plicata* (see Table 3) [3, 4, 19].

Carrageenans

The first formal recognition of the gelling properties of boiled *Fucus crispus* were discovered by Turner in 1809, and this mucilaginous matter was named "carrageen*in*", by Pereira (1840). The gelatinous, hot water-soluble mucilage of *Chondrus crispus* was first isolated by Schmidt (1844). Coincidentally, in the same year, Forchhammer reported on the high sulphur content of the ash from *C. crispus* [60]. The term "carrageen*in*" was later changed to "carrageenan" so as to comply with the "-an" suffix of terminology as applied to polysaccharides [1, 5].

Chemically, carrageenans are high molecular weight, sulfated D-galactans composed of repeating disaccharide units with alternating (1→3)-β-D and (1→4)-α-D-galactose or (1→4)-3,6-anhydro-α-D-galactose residues. There are at least 15 different carrageenan structures that are normally classified on the basis of distinct features, including the number and position of sulfate groups, the presence of 3,6-anhydro-D-galactose and the conformation of the pyranose ring [61, 62].

The three most relevant commercial carrageenans are kappa (κ), iota (ι) and lambda (λ) carrageenans. The idealized, disaccharide repeating units of these carrageenans are given in Fig. 2. κ-carrageenans have alternating (1→3)-β-D-galactose-4-sulfate and(1→4)-3,6-anhydro-α-D-galactose units [37], while the ι-carrageenans have an additional sulfate group on C-2(O) of the (1→4)-3,6-anhydro-α-D-galactose sugars, resulting in two sulfates per disaccharide repeating unit [37]. Moreover, the λ-carrageenans have an additional sulfate group linked to the C-6 position of the 4-linked residue, but in turn this is a (1→4)-α- D-galactopyranose [63].

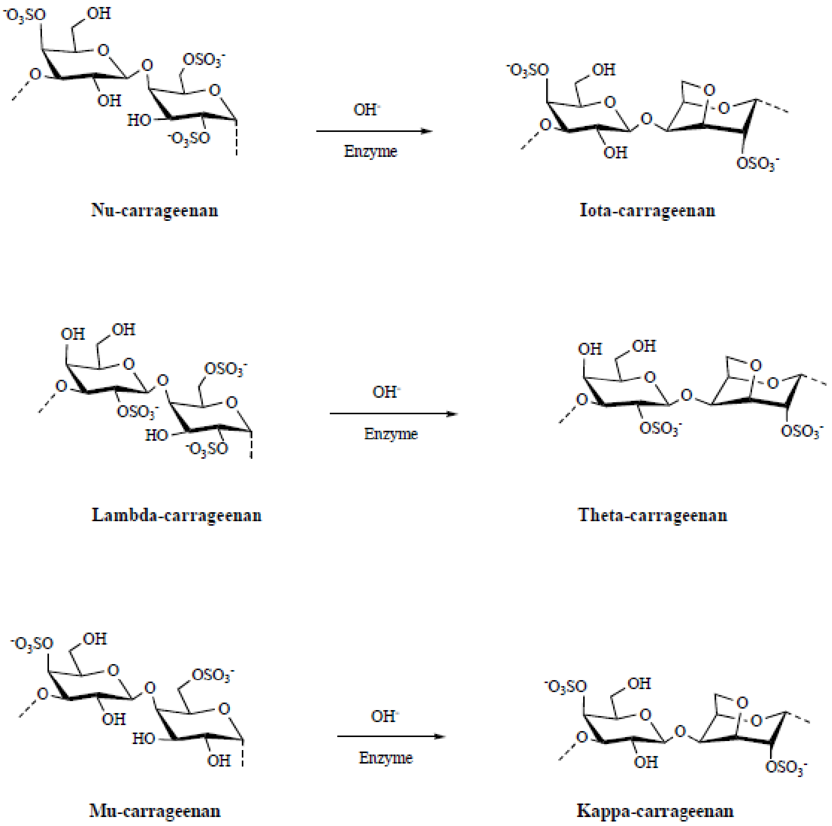

Fig. (2). Idealized structure of the chemical units of nu (ν), iota (ι), lambda (λ), theta (θ), mu (μ), kappa (κ), xi (ξ) and beta (β) carrageenans.

It should noted that in general seaweeds do not produce these idealized and pure carrageenans, but more likely a range of hybrid structures and/or precursors (Fig. 2).

When exposed to alkali conditions, the precursors (particularly mu and nu forms) are modified into kappa and iota, respectively, through formation of the 3,6-anhydrogalactose bridge [64-66]. Other existing carrageenans include the xi (ξ), theta (θ) and beta (β) (Fig. 2).

The main structural characteristics affecting the chemical and functional properties of carrageenans are the number and position of the ester sulfate groups on the repeating galactose units [67]. In general, the higher the sulfate levels, the lower the temperature of solubility and the gel strength of the carrageenan [47].

Indeed, although all carrageenans are highly flexible molecules, able to wind around each other to form double-helical zones, the ι and κ-carrageenans form gels, whereas λ-carrageenan does not. Gel formation in κ-carrageenan requires a gel-inducing agent and involves a coil-to-double helix conformational change, followed by the formation of an infinite network through aggregation of ordered molecules [68, 69]. The strongest gels of κ-carrageenan are formed with K^+ rather than Na^+, Li^+, Mg^{2+}, Ca^{2+}, or Sr^{2+} [70, 71]. In contrast, ι-carrageenan gels are formed in the presence of Ca^{2+}. In this particular case, the 2-sulfate group on the outside of the ι-carrageenan molecule does not allow the helices to aggregate as well as those of κ-carrageenan, although additional bonds occur through calcium interactions [47]. As a result, ι-carrageenan gels are more elastic than those of κ-carrageenan. At the industrial level, carrageenan gels can be recovered by alcohol precipitation, drum drying or freezing.

The modern carrageenan industry dates from the 1940´s, receiving its impetus from numerous dairy applications. Carrageenans were found to be the ideal stabilizer for the suspension of cocoa in milk chocolate [1, 72]. These polysaccharides are “generally regarded as safe” (GRAS) and are presently the third most utilized stabilizer/emulsifier agents in the food industry (after gelatin of animal origin and starch of plant origin) [32]. The most common food applications of carrageenans include dairy creams, dessert mousses, salad dressings, bakery fillings, ice cream and instant desserts (Table 2). Carrageenan gels/emulsifiers also have several applications in other diverse industries, including the cosmetic, pharmaceutical, textile and paints [16, 26].

In addition, the biological properties of carrageens also provide them several (potential) applications. Carrageenans are traditionally used in the treatment of bowel problems such as diarrhea, dysentery and to make internal poultices to control stomach ulcers [73]. Also, carrageenan-bearing seaweeds, namely Irish Moss (*Chondrus crispus* and *Mastocarpus stellatus*) are traditionally consumed in the form of teas and other kind of medicines to combat colds, bronchitis and cronic coughs [26]. Moreover, the anticoagulant activity of carrageenans and inhibition of human blood platelet aggregation has been reported [74]. Among the carrageenans, λ-carrageenan from *C. crispus* has approximately twice the activity of unfractionated carrageenan and four times the activity of κ-carrageenan (*Kappaphycus alvarezii* – formerly *Eucheuma cottonii*). The most active carrageenan has approximately 1/15 of the activity of heparin [74], an animal-derived highly sulfated, glycosaminoglycan, widely used as an injectable anticoagulant. It seems that this biological activity is based on the antithrombotic properties of carrageean [26]. Additionally, applications of carrageenan gels from *C. crispus* may block the transmission of the human papillomavirus types (that can cause cervical cancer), of HIV, as well as other sexually transmitted diseases (STD), viruses such as gonorrhoea, genital warts and the herpes simplex virus (HSV) [26].

The first source of carrageenans was the red seaweed *Chondrus crispus,* which continues to be used in restricted quantities. *Betaphycus gelatinum* is used for the extraction of β-carrageenan. Presently, wild-harvested genera such as *Chondrus*, *Furcellaria*, *Gigartina*, *Chondracanthus*, *Sarcothalia*, *Mazzaella*, *Iridaea*, *Mastocarpus*, and *Tichocarpus* are, some of them, also cultivated as carrageenan raw materials [64]. Producing countries include Argentina, Canada, Chile, Denmark, France, Japan, Mexico, Morocco, Portugal, North Korea, South Korea, Spain, Russia, and the USA [1, 29].

Some South American red algae, which were only used traditionally in minor quantities, have more recently attracted attention from carrageenan producers, as they seek to increase diversification of raw material supplies of carrageenophytes with different physical functionalities of their extracted gels [16, 61]. In this context, *Gigartina skottsbergii*, *Sarcothalia crispata* and *Mazzaella laminaroides* are being harvested from natural populations in Chile and Peru, though the recent earthquake in Chile (February 27th, 2010) caused the elevation of intertidal areas and the consequent large losses of harvestable biomass [5]. Small quantities of *Gigartina canaliculata* are harvested in Mexico while *Hypnea musciformis* has been used in Brazil [1, 16].

Large carrageenan processors have fuelled increased farming activities of *Kappaphycus alvarezii* (commercial name “cottonii”) and *Eucheuma denticulatum* (commercial name “spinosum”) in several countries including Indonesia, Malaysia, Philippines, Tanzania, Kiribati, Fiji, Kenya and Madagascar [16]. Indonesia has recently overtaken the Philippines as the world‘s largest producer of dried carrageenophyte biomass.

Shortages of carrageenan-producing seaweeds suddenly appeared in mid-2007, consequently doubling the price of carrageenans [61]. Probably, this reduced access to carrageenophytes biomass resulted from a combination of environmental factors. Monocultures of some carrageenophytes, such as *Kappaphycus alvarezii*, have encountered several problems when submitted to environmental changes as well as an increased susceptibility to diseases. The problems with ice-ice and epiphytes have resulted in large scale crop losses [75-77].

The main carrageenophytes from the Iberian Peninsula are *Chondrus crispus, Gigartina pistillata, Calliblepharis jubata, C. ciliata*, *Chondracanthus teedei* var. *lusitanicus, C. acicularis, Mastocarpus stellatus, Gymnogongrus crenulatus, Ahnfeltiopsis devoniensis,* and *Caulacanthus ustulatus* (Table 3) [1, 64, 23]. It should be noted that, in addition to the traditionally harvested carrageenophytes in the northwest of the Iberian Peninsula (i.e. northern coast of Portugal and Galicia) [18, 78, 79], *C. teedei* var. *lusitanicus* is clearly a potential source of industrial co-polymers of carrageenan from the Iberian Peninsula. This algae has a high content of kappa/iota and xi/theta carrageenans and it is widespread on the north coast of Iberian Peninsula [80, 81].

Table 3. Documented and potential Iberian sources of seaweeds products with current or future commercial significance

Compound	Uses	Documented sources	Potential sources
Agar	Thickener, emulsifier, and gelling agent.	*Gelidium corneum* (formerly *G. sesquipedale*), *Gelidium microdon, Pterocladiella capillacea* (Rhodophyta)	*Gracilaria* spp., *Gelidium spinosum, G. pulchellum, Gelidiella* acerosa, and *Ahnfeltia plicata* (Rhodophyta)
Alginate	Thickener and emulsifier. Drug delivery systems. Relevant to meat processing and pet food production.	*Laminaria* spp. (Phaeophyceae)	*Ascophyllum nodosum, Bifurcaria bifurcata, Laminaria* spp., and *Saccorhiza polyschides* (Phaeophyceae)
Carrageenan	Thickener, emulsifier, and gelling agent. Pet food production. Antiviral.	*Chondrus crispus, Mastocarpus stellatus* (Rhodophyta)	*Chondracanthus* spp., *Calliblepharis* spp., *Gigartina pistillata* (Rhodophyta)
Fucoidan	Anti-aging, antimicrobial, antitumor, anticoagulant, anti-inflammatory, contraceptive.		Fucales and Laminariales (Phaeophyceae)
Fucoxanthin	Anti-obesity, antidiabetic, anti-inflammatory, antimalaria, anti-aging, antitumor and		*Ascophyllum nodosum, Himanthalia elongata, Fucus* spp., *Laminaria* spp., *and Undaria pinnatifida*

	neuroprotective.		(Phaeophyceae)
Phycoerythrin	Used in the cosmetic industry for production of lipsticks, eyeliners and other cosmetics. Potential use on nutritional supplements.		*Corallina elongata, Gracilaria gracilis, Grateloupia turuturu,* and *Palmaria palmata* (Rhodophyta)
Phlorotannins	Antioxidant, anti-inflammatory, algicidal and bactericidal.		Brown alga
Terpenoids	Antitumor, antiviral, and antifouling agent.		Dictyotaceae (Phaeophycaeae) and *Laurencia/Osmundea* spp. (Rhodophyta)
Ulvan	Antiviral, antitumor, anticoagulant, anti-hyperlipidemic, and immuno-stimulating.		*Ulva* spp. and other Ulvales (Chlorophyta)
Dietary fibers, proteins, and vitamins	Gastronomic use.	*Chondrus crispus, Mastocarpus stellatus, Palmaria palmata, Porphyra* spp. (Rhodophyta), *Laminaria* spp., *Saccharina latissima* (Phaeophyceae)	*Chondracanthus* spp., *Gracilaria* spp., *Grateloupia turuturu, Osmundea pinnatifida* (Rhodophyta), *Codium tomentosum, Ulva* spp. (Chlorophyta), *Undaria pinnatifida* (Phaeophyceae)

Uronates (Alginates)

"Alginate" is the term usually used for the salts of alginic acid, although this is also commonly used to refer to all the derivatives of alginic acid and to alginic acid itself. Some authors use the term "algin" (i.e. the name given by E.C.C. Stanford to alginic acid by the time of its discovery, in the 1880´s [82]. Alginic acid is present in the cell walls of brown seaweeds, where it is partially responsible for their flexibility. In this context, brown seaweeds that grow in more turbulent conditions usually have higher alginate content than those in calmer waters [16].

Chemically, alginates are linear copolymers of β-D-mannuronic acid (M) and α-L-guluronic acid (G) (1→4)-linked residues, arranged either in heteropolymeric (MG) and/or homopolymeric (M or G) blocks (see Fig. 3) [61, 79, 83]. Alginates extracted from different sources differ in their M and G ratios, as well as on the length of each block. It is noted that more than 200 distinct alginates are presently produced [84]. Importantly, mannuronic acid residues establish β-(1→4) linkages, while guluronic acid forms α-(1→4) linkages. As a consequence, M-block segments have a linear and flexible conformation whereas the G-block segments cause a folded and rigid structural conformation, which is responsible for a pronounced stiffness of the polymer [47]. It is accepted that only G-blocks participate in the gel formation and hence, their length is a main factor affecting the functional properties of the gels [85].

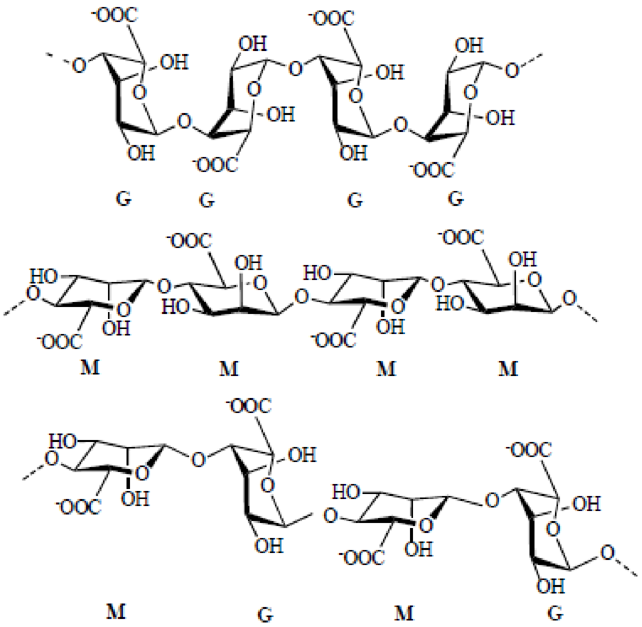

Fig. (3). Idealized structure of the chemical units of poly L-guluronic acid (G blocks), poly D-mannuronic acid (M blocks) and alternate L-guluronic and D-mannuronic acid (GM blocks) in alginates.

Ionic cross-linking with divalent ions (e.g. calcium) is the most common method of obtaining hydrogels from an aqueous alginate solution, in a model that is termed “egg-box” [86, 87]. In this model, the divalent cations are trapped in a stable, continuous and thermo-irreversible, three dimensional network, allowing interaction with COO^- groups of guluronate residues, of two adjacent G-block polymers chains (junctions). This results in a gel structure [87].

Algins/alginates are commercially available in both acid and salt forms. These are typically extracted by treating the seaweeds with aqueous alkali solutions (NaOH) [88] that converts all the alginate to the sodium salt. Later the salt is dissolved in water and separated from the seaweed residue by filtration [16, 89, 90]. The alginate salt can be transformed into alginic acid by treatment with dilute HCl [84].

About 30 years ago, almost all extraction of alginates took place in Europe, USA and Japan. This picture is now changing since the emergence of producers in China in the 1980´s [29]. Initially, this production was limited to low cost (low quality) alginate for the internal, industrial markets produced from locally cultivated *Saccharina japonica*. In the 1990´s, Chinese producers were competing in western, industrial markets to sell alginates, primarily based on low cost [5].

Alginates have several commercial applications based on their thickening, gelling, emulsifier and stabilizing abilities. They are used in the food industry for improving the textural quality of numerous products such as salad dressing, ice-cream, beer, jelly and lactic drinks, but also in cosmetics, pharmaceuticals, textiles and painting industries (Table 2) [28, 91].

Moreover, due to its outstanding properties in terms of biocompatibility, biodegradability, non-antigenicity and chelating abilities, the use of alginates in a variety of biomedical applications (e.g. tissue engineering, drug delivery and in some formulations of preventing gastric reflux) is growing [84]. The use of alginates and/or alginate derivatives as remedies for the treatment of gastritis and gastroduodenal ulcers is protected by patents in several countries [72]. Also, numerous products of alginate-containing drugs, like “Gaviscon”, have been shown to effectively suppress postprandial (after eating) acidic refluxes, binding of bile acids and duodenal ulcers in humans [92].

The binding capacity of alginates also includes cholesterol/lipids that are then eliminated from the digestive system and result in hypocholesterolemic and hypolipidemic responses, as well as an antihypertension effects [72]. This is often coupled with an increase in the faecal cholesterol content and a hypoglycaemic response. Furthermore, and since alginates bind to divalent metallic ions, heavy metals taken into the human body are gelated or rendered insoluble in the intestines and cannot be absorbed into the body tissue [93].

Additional biological properties of alginates that might potentiate their applications in the future include their antibacterial activity [26], anticancer [28], antitoxic effects on hepatitis [93] and prevention of obesity and diabetes [94].

A good raw material for alginate extraction should also give a high polysaccharide yield. Brown seaweeds that fulfill the above criterion include species of *Ascophyllum*, *Durvillaea*, *Ecklonia*, *Fucus*, *Laminaria*, *Saccharina*, *Lessonia*, *Macrocystis* and *Sargassum.* However, *Sargassum* is only used as a “last resource” because its alginate is usually of borderline quality and the yield is also low [16, 95].

Ascophyllum nodosum, Fucus spp.*, Laminaria hyperborea, L. ochroleuca, Sargassum vulgare, S. flavifolium, S. muticum, Saccorhiza polyschides, Saccharina latissima, Bifurcaria bifurcata* and *Padina pavonica* represent the main alginophytes which occur along the Iberian Peninsula (Table 3) [3, 4, 19].

Ulvans

The name "ulvan", as first proposed by Lahaye and Axelos in 1993, refers to acidic water-soluble single sulfated heteropolysaccharides which are present in the cell walls of green seaweeds (*Ulva* and as previously know *Enteromorpha*), where it contributes to the maintenance of the osmolar stability and the protection of the cell [96]. The yield of ulvans ranges from 8 to 29% of the algal dry weight [97].

The sugar composition of ulvans is extremely variable but uronic acids (i.e. glucuronic acid and iduronic acid), sulfated rhamnose, xylose and glucose have been identified as the main constituents of the polymer [96, 98]. The presence of iduronic acid in the ulvan polysaccharide chain is a striking characteristic of these polysaccharides and is unique amongst algae [99]. This feature also renders ulvans a close similarity to mammalian glycosaminoglycans.

In general, the structure of ulvans is influenced by taxonomy (i.e. species used) and ecophysiology (i.e. geographical distribution of species, age/maturity, environmental conditions, seasonality, etc.) factors [97]. In addition, methods of extraction also have impacts. This obviously has an enormous impact on variability and hampers the establishment of an accurate structure for the ulvans. Nevertheless, it is now generally accepted that the backbone of ulvans is mainly composed of repeating sequences of aldobiuronic acid disaccharides, in particular of β-D-glucuronosyluronic acid-(1→4)-α-L-rhamnosyl-3-sulfate [(β-D-Glc*p*A-(1→4)-α-L-Rha-3-SO_3^-), named as ulvanobiuronic acid A or A3s] or of α-L-iduronosyluronic acid-(1→4)-α-L-rhamnosyl-3-sulfate [(α-L-Ido*p*A-(1→4)-α-L-Rha*p*-3-SO_3^-), named as ulvanobiuronic acid B or B3s] (see Fig. 4). Additionally, other repeating units in ulvans have been reported, namely the ulvanobiose 3-sulfate [U3s, →4)-β-D-Xyl-(1→4)-α-L-Rha-3-SO_3^--(1→]] and ulvanobiose 2',3-disulfate [U2´s3s, →4)-β-D-Xyl-2-SO_3^--(1→4)-α-L-Rha-3-SO_3^--(1→] [97-100].

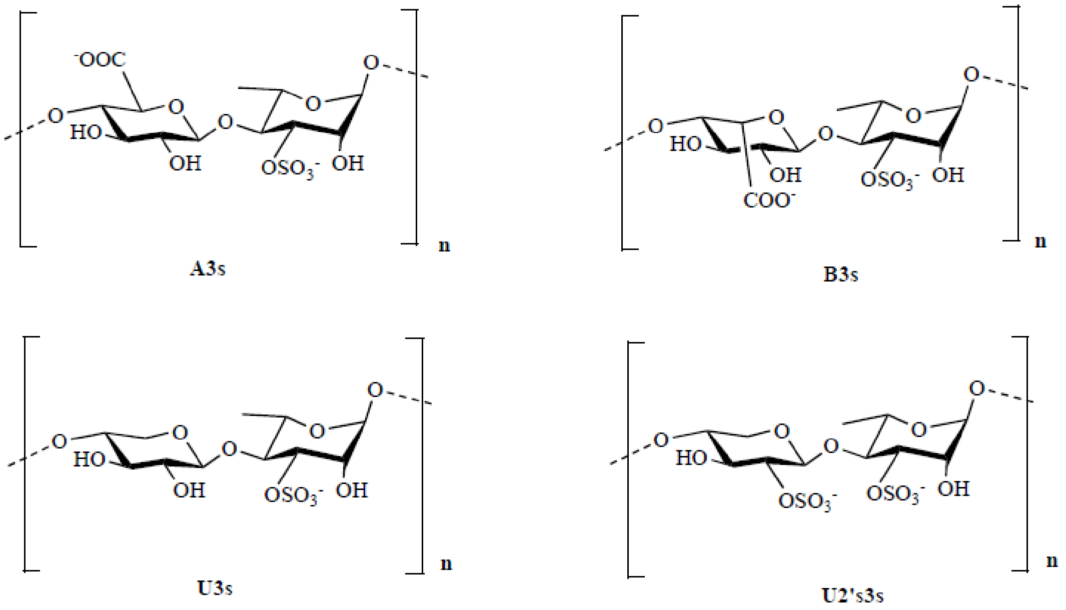

Fig. (4). Structure of the main repeating disaccharides found in ulvan, ulvanobiuronic acids A3s and B3s, and ulvanobioses U3S and U2′s 3s

Ulvans form thermoreversible gels, without thermal hysteresis, by a unique and complex mechanism which is believed to occur through the formation of borate esters with ulvan 1,2-diols, followed by cross-linking via Ca^{2+} ions [101]. Optimal gelling conditions thus require the presence of boric acid and calcium ions, at slightly basic conditions (pH 7.5). Since the gel is thermoreversible, the “junction-zones” that crosslink the polymer are thought to include weak linkages, probably based on labile borate ester groups and ionic interactions that are easily disrupted by thermal treatments [97].

Overall, the gelling properties of ulvans offer them a potential application where texture needs to be precisely controlled (by pH or temperature), such as those designed for the release of entrapped molecules or particles under specific physicochemical conditions [26, 102]. Commercial applications of these gels are undoubtedly fewer than those of other hydrocolloids, although other properties of these polysaccharides provide them with potential industrial applications in several areas, including the chemical, pharmaceutical, biomedical and agricultural, amongst others [103-105]. Indeed, fine chemicals may be produced from rare, sugar precursors obtained from ulvan biomass. Ulvan is enriched in rhamnose (a rare sugar) which is used in the synthesis of aromas [97]. The production of this sugar from *Monostroma* has been patented. L-rhamnose is also an essential component of the surface antigens of many microorganisms, and is specifically recognized by a number of mammalians lectins. Hence, ulvan applications in pharmaceutical domains are expected to increase [97]. Apart from the rhamnosyl units, ulvan is also a source of iduronic acid, which is another rare sugar required in the synthesis of heparin analogues with antithrombotic activities [100].

Besides monomers, it has been demonstrated that ulvan (polymer) and its oligosaccharides have applications related to their biological properties, including antitumor and immune modulation, anticoagulant, antioxidant, strain-specific anti-influenza, hepatoprotection, protection of the colonic mucosa, modulation of lipid metabolism and a decrease of the atherogenic index [96, 97, 106].

Notably, the strategy of chemical cross-linking ulvans overcomes previous limitations for their application in tissue engineering (due to mechanical instability and uncontrolled dissolution in physiological conditions) [107]. Alves and co-workers combined ulvan with poly-D,L-lactic acid (PDLLA) in order to produce a novel scaffold for bone-tissue engineering applications. This matrix was then characterized (by micro-computed tomography, mechanical compression testing, water uptake and degradation testing and cytotoxicity assays); the results demonstrated appropriate physicochemical and cytocompatible features for the envisaged applications [104]. In addition, ulvan particles loaded with dexamethasone dispersed within the PDLLA matrix showed an adequate release profile of the steroid drug, suggesting that this system can be potentially suitable for localized drug delivery [104]. Cross-linked ulvan membranes also confirmed their potential as drug delivery devices and suggest a great potential of these natural sulfated polysaccharides in wound dressings [105]. These results further contribute to the establishment of ulvan as a potential novel biomaterial.

Applications of ulvans in animal feed detoxification were also patented, based on the capacity of ulvan to intercalate into clay opening the way for the synthesis of new nanocomposites of interest with use in different areas. Moreover, besides the traditional use as a fertilizer, the elicitation of plant defenses has been added to ulvan bioactivities, including nitrogen uptake improvement and disease resistance [97].

The mechanisms by which ulvans interfere with the different biological systems are yet to be identified. They may do it in diferent ways, such as targeting specific cell receptors where ulvan competes amongst other molecules and/or physicochemical properties related to particular ion-exchange. The latter mentioned interactions are at the basis of choice of these seaweeds as bioindicators for monitoring coastal water heavy metal pollutions [73, 106, 108] and could be further exploited to develop ion exchangers from ulvalean cell walls, with particular ion selectivity for industrial effluents de-pollution or the enrichment of food, feed, or soils with specific trace mineral elements [109].

In general, ulvans can be solubilized by hot water [99], with higher molecular weight polysaccharides, being obtained in the range 80-90 °C, when compared to those extracted with temperatures above 100°C [97]. Ulvans can also be extracted with sodium carbonate solution, with calcium chelating agents (e.g. ammonium oxalate or ethylenediaminetetraacetic) or with acidic solutions [98, 100]. Calcium chelating agents sequester calcium ions and disrupt the ulvan chemical bonds, within the cell wall and hence facilitate their solubilization [99]. An increased yield of ulvans is likewise obtained for low pH extraction solutions, due to the de-stabilisation of ulvan aggregates [98]. In general, the most employed method for extracting ulvans employs the use of high temperature water (80-90°C), containing ammonium oxalate as a divalent cation chelator, followed by the recovery of the polysaccharides by ethanol precipitation [102]. Additional purification processes are fundamental to clean-up the contaminating matter, such as lipids and pigments (as removed by Soxhlet extraction, or by organic solvents - acetone or ethanol), proteins (proteinase k) and starch (α-amylase) [99].

Regarding the macroalgae of the Iberian Peninsula, ulvans could be produced from *Ulva clathrata*, *U. compressa*, *U. intestinalis*, *U. lactuca*, *U. linza*, *U. prolifera, U. rigida* (Chlorophyta, Ulvales) and *Monostroma latissimum* (Chlorophyta, Ulotrichales). These species are distributed on an almost worldwide basis, growing in the intertidal and subtidal zones, attached to hard substrata or as free-living forms. In addition, they are also considered opportunistic seaweeds and proliferate in eutrophic coastal waters. Despite this, and taking into account its biotechnological potential, green algae remain largely unexploited in the commercial arena, providing an opening window of opportunity for future research [99].

2.2. Fucoidans

Fucoidans are a complex series of sulfated polysaccharides found widely in the cell walls of brown seaweeds, where they are thought to play a protective role against the effects of desiccation [26]. These polysaccharides were first isolated by Kylin in 1913 and named as “fucoidin”. Presently, they are mainly named according to the IUPAC terminology (fucoidans), although other terms such as fucans, fucosans, fucose containing polymers or sulfated fucans have also been adopted [110].

For the majority of algal sources, the chemical composition of fucoidans is mainly composed of fucose and sulfate, together with minor amounts of distinct molecules (Table 4), that can vary from monosaccharides (i.e. mannose, glucose, galactose, xylose, etc.), acidic monosaccharides, acetyl groups to proteins [110]. Fucoidans with a low fucose content are also found in nature.

Table 4. Composition of some fucoidans and/or water extracts from brown seaweed (based on [110-112]).

Seaweed specie	**Order**	**Chemical composition***
Adenocystis utricularis	Ectocarpales	fucose, galactose, mannose, xylose, GlcA, sulfate
*Ascophyllum nodosum***	Fucales	fucose (49%), xylose (10%), GlcA (11%), sulfate
*Bifurcaria bifurcata***	Fucales	fucose, xylose, mannose, glucose, galactose, sulfate
*Chorda filum***	Laminariales	fucose, xylose, mannose, glucose, galactose, uronic acid, sulfate
Cladosiphon okamuranus	Ectocarpales	fucose, glucose, uronic acid, sulfate
*Dictyota menstrualis***	Dictyotales	fucose/xylose/galactose/sulfate (1/0.5/2/2)
Ecklonia kurome	Laminariales	fucose, galactose, mannose, GlcA, glucose, xylose, sulfate
Fucus distichus	Fucales	fucose/sulfate/acetate (1/1.21/0.08)
Fucus evanescens	Fucales	fucose/sulfate/acetate (1/1.23/0.36)
*Fucus serratus***	Fucales	fucose/sulfate/acetate (1/1/0.1)
*Fucus spiralis***	Fucales	fucose, xylose, mannose, glucose, galactose, uronic acid, sulfate
*Fucus vesiculosus***	Fucales	fucose,sulfate
*Himanthalia elongata***	Fucales	fucose, xylose, GlcA, sulfate
*Laminaria hyperborea*** (formerly *Laminaria cloustonii*)	Laminariales	fucose, galactose, xylose, uronic acid, sulfate
*Laminaria digitata***	Laminariales	fucose, xylose, mannose, glucose, galactose, uronic acid, sulfate
Lessonia flavicans (formerly *Lessonia vadosa*)	Laminariales	fucose/sulfate (1/1.12)
Macrocystis pyrifera	Laminariales	fucose/galactose (18/1), sulfate
*Padina pavonica***	Dictyotales	fucose/galactose, sulfate (9/1/9)
Saccharina angustata (formerly *Laminaria angustata*)	Laminariales	fucose, galactose, mannose, xylose, GlcA, sulfate
Saccharina religiosa (formerly *Laminaria religiosa*)	Laminariales	fucose, xylose, mannose, glucose, rahmnose, uronic acid, sulfate
Sargassum acinarium (formerly *Sargassum linifolium*)	Fucales	fucose, mannose, galactose, xylose, uronic acid
Sargassum fusiforme (formerly *Hizikia fusiformis)*	Fucales	fucose/xylose/uronic acid/galactose/sulfate (1/0.8/0.7/0.8/0.4) and (1/0.3/0.4/1.5/1.3)
Sargassum stenophyllum	Fucales	fucose, galactose, mannose, sulfate
Silvetia babingtonii (formerly *Pelvetia wrightii*)	Fucales	fucose/galactose (10/1), sulfate
*Undaria pinnatifida***	Laminariales	fucose, mannose, xylose, rhamnose, galactose, glucose, sulfate
Undaria pinnatifida (Mekabu)	Laminariales	fucose/galactose (1/1.1), sulfate

*Fucoidans were obtained by acidified or alkali/water solutions, followed by precipitation, mostly with ethanol.
**Present in the Iberian flora.

Notably, the structure of fucoidans has been described to vary significantly between macroalgal species and even within species, even though the latter can be mainly attributed to the distinct extraction conditions applied [9, 110].

Regardless of the enormous variability of fucoidans, two general groups are assumed for their backbones: The type I polymers, which contain a large proportion of repeating (1→3)-linked α-L-fucopyranose residues and the type II polymers which typically have alternating (1→3)- and (1→4)-linked α-L-fucopyranose residues. In such polymers, sulfation may occur at positions 2, 3 and 4 and the monosaccharides are associated via α-1→2, α-1→3, or α-1→4 glycosidic bonds [113]. In general, Type I fucoidans are found in *Saccharina latissima*, *Analipus japonicas, Chorda filum*, *Cladosiphon okamuranus* and *Laminaria digitata*, while Type II fucoidans include those isolated from the order of Fucales (i.e. *Ascophyllum nodosum* and *Fucus* species) [37, 114]. Individual representative structures of Type I and II fucoidans are depicted in Fig. 5.

Fucoidans with a high content of uronic acid (UA) and hexose may have a backbone built of alternating UA-hexose, due to the high stability of this structure. Other monosaccharide residues are normally observed in the fucoidans branches [110].

Fucus vesiculosus is the seaweed most enriched in fucoidans (up to 20% on a dry weight basis). This polysaccharide was first believed to comprise a linear structure mainly composed of (1→2)-linked 4-*O*-sulfated fucopyranose residues [115], but later Patankar et al. [116] rebuilt its structure model and established that the backbone of this fucoidan was a fucose polymer, bonded through α-(1→3) with a sulfate group, substituted at C-4, in several fucose residues and with branched fucose (linked to fucose) moieties appearing in every 2-3 residues. More recently, Chevolot et al. [117] reported that the fucoidan from *F. vesiculosus* (and of *Ascophyllum nodosum*) have a core disaccharide motif of Type II containing sulfate at the 2-position of the 3-linked fucose and sulfate groups on the 2- and 3-positions of the 4-linked fucose (see structure in Fig. 5B) [37, 118].

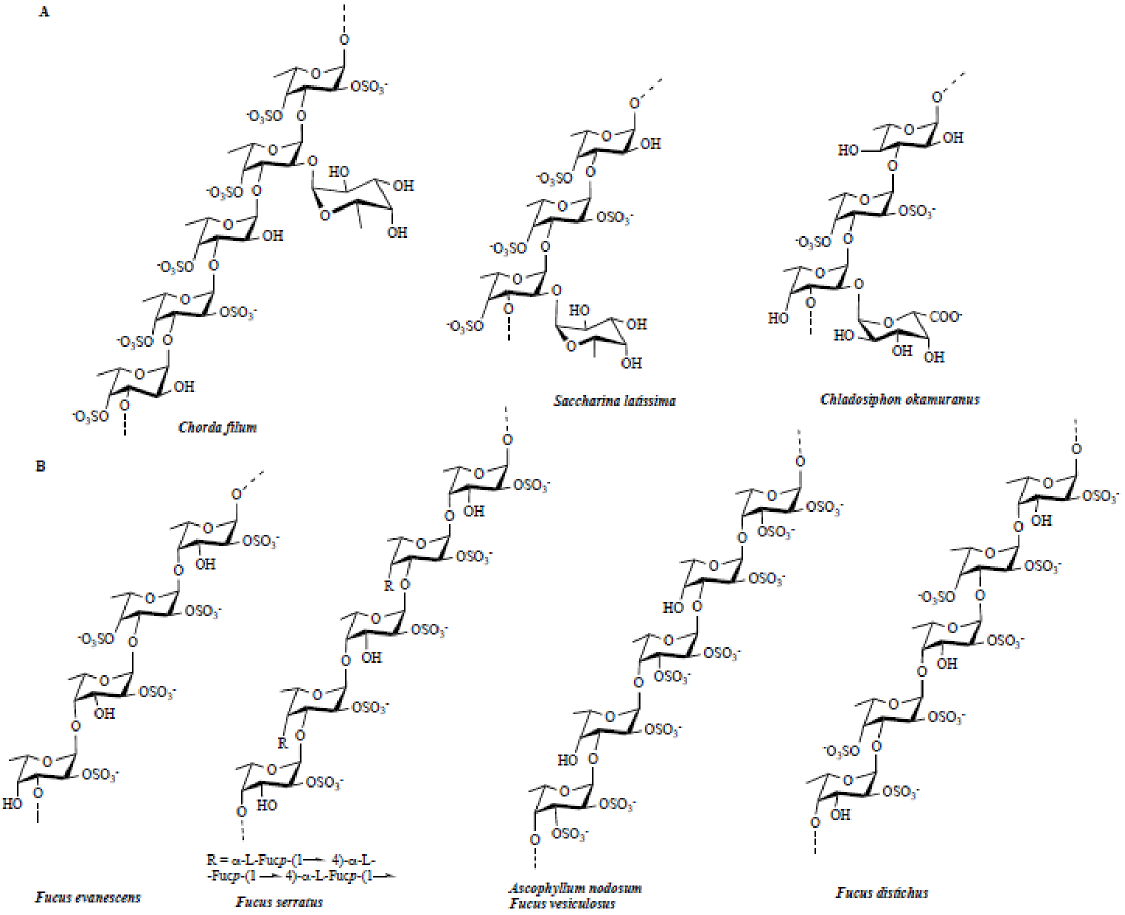

Fig. (5). Representative chemical structures of Type I (A) and Type II (B) fucose-containing sulfate polysaccharides described in several seaweed species.

Structural features of fucoidans from other *Fucus* species have also been described. As reported by Bilan et al. [119-121], the fucoidans from *F. evanescens* C. Ag, *F. distichus* and *F. serratus* L. are also composed of fucose, sulfate and acetate, with structural variations. In particular, the fucoidan from *F. evanescens* has a linear backbone of alternating →3)-α-L-Fuc*p*-(2-SO_3^-)-(1→4)-α-L-Fuc*p*(2-SO_3^-)-(1→ disaccharides, with the 3-linked fucose residues being randomly sulfated or acetylated in the position 4 (see structure in Fig. 5B) [110, 120]. Instead, *F. distichus* is mainly composed of disaccharide repeating units →3)-α-L-Fuc*p*-(2,4-di-SO_3^-)-(1→4)-α-L-

Fuc*p*-(2-SO_3^-)-(1→, where only slight variations might exist by random acetylation and sulfation of several disaccharide repeating units (see structure in Fig. 5B) [37, 121].

The fucoidan from *F. serratus* L. has a branched structure. Its core backbone, as depicted in Fig. 5B, is mainly composed of →3)-α-L-Fuc*p*-(1→4)-α-L-Fuc*p*-(1→ repeating units, in which half of the 3-linked residues are substituted by α-L-Fuc*p*-(1→4)-α-L-Fuc*p*-(1→3)-α-L-Fuc*p*-(1→ trifucoside units at C-4 [119]. Sulfate groups occupy mainly C-2 and sometimes C-4, although 3,4-diglycosylated and some terminal fucose residues may be nonsulfated. Acetate groups occupy C-4 of 3-linked Fuc and C-3 of 4-linked Fuc in a ratio of about 7:3 [119].

Atypical fucoidans were described for several seaweeds, e.g. *Himanthalia elongata* and *Bifurcaria bifurcata*, for which the fucoidan structure has a main backbone of (1→2)- and (1→3)-alternating fucose residues with sulfation at C-4 and (1→4)-GlcA and (1→4)-Xyl linked non-sulfated residues, appear at the periphery of highly branched molecules [110, 122].

The extraction method for fucoidans can be quite simple. A native extraction with hot water can result in a good method, but an acid extraction or a combined hot acidic extraction with ethanol precipitation is the most commonly applied method [110, 113]. The variation of extraction methods is known to result in the extraction of structurally distinct fucoidans [110, 113].

The commercial importance of fucoidans is presently much lower than that of seaweed hydrocolloids however, these polysaccharides are attracting considerable attention because of the growing market for them as bioactive polysaccharides in wide areas of applications [30]. More recently, anticoagulant and antithrombotic activities are the most studied effects of fucoidans. Commonly, the anticoagulant activity of fucoidans is mediated through the activation of thrombin inhibitors, although direct thrombin inhibition and competitive binding of fibrinogen to block thrombin's actions are also possible [30, 123].

Previous studies reported that the anticoagulant functionalties of fucoidans extracted from *F. vesiculosus* and *Eklonia cava* were due to thrombin-inhibition-mediated via plasma antithrombin-III, and their anticoagulant activity was similar to that of heparin [37, 110, 114]. Moreover, fucoidans from *Saccharina longissima*, *S. latissima*, *L. digitata*, *F. serratus*, *F. distichus*, and *F. evanescens*, *A. nodosum* were also described to reveal strong anticoagulant activity *in vitro* and *in vivo* models [110, 113].

In general, structural-bioactive studies suggested that the anticoagulant /antithrombin activities of fucoidans are mainly dependent on the content and/or positioning of sulfate groups, as well as the molecular weight of the polymer [110]. Moreover, monomeric composition, types of linkages and branching might exert moderate modulation on biological properties of fucoidans [30, 37, 114]. In this context, it is possible that the greater anticoagulant/antithrombin activities exhibited by longer fucoidans are due to the higher content of fucose and sulfate groups [37, 110, 114], though this is still under debate.

Fucoidans are also reported to inhibit the replication of several enveloped viruses such as human immunodeficiency and human cytomegalovirus, among others [37, 110]. The mechanisms for such activity are thought to occur via inhibition of cell infection by viral sorption or due to hampering of viral-induced syncytium formation [110, 114]. Fucoidans from *Saccharina japonica, Cladosiphon okamuranus, Adenocystis utricularis, Stoechospermum marginatum, Cystoseira indica, Dictyota mertensii*, *Lobophora variegata*, *Fucus vesiculosus*, *Spatoglossum schroederi* and *Undaria pinnatifida* (cultivated plus wild types) showed impressive positive results *in vitro* and *in vivo* models of infection by poliovirus III, adenovirus III, ECHO6 virus, coxsackie B3 virus, coxsackie A16, Newcastle Disease Virus (NDV), HSV-1, HSV-2 , HIV and avian reverse transcriptase [110, 114].

Antitumor activities of fucoidans include the inhibition of tumor proliferation, the stimulation of tumor cells apoptosis, blocking of tumor cell metastasis and enhancement of various immune responses [124]. In this context, fucoidans from several macroalgal species (e.g. *Saccharina japonica, S. latissima, Laminaria digitata, Fucus serratus, F. distichus* and *F. vesiculosus*) proved to be useful and are regarded as good candidates for future cancer therapy [110, 114]. Besides those, the commercial fucoidans branded Tokida (from cultured *Cladosiphon okamuranus*) and that from the Korean cultured sporophyll (Miyeokgui) of *Undaria pinnatifida* also revealed promising antitumoral activities, as tested in *in vitro* models [114].

Other important biological activities of fucoidans include antioxidant, anti-inflammatory and anti-allergic, although others cannot be overlooked (e.g. hepatoprotection, cardioprotection, stomach protection and anti-obesity) [37, 110, 114]. Examples of fucoidans showing promising antioxidant in *in vitro* models include those obtained from *S. japonica, Canistrocarpus cervicornis, F. vesiculosus, Dictyota cervicornis, Sargassum filipendula, Dictyopteris delicatula* and *S. japonica* [37, 110, 114], while the anti-inflammatory activity of several fucoidans (*Laminaria saccharina, L. digitata, Fucus evanescens, F. serratus, F. distichus, F. spiralis, Ascophyllum nodosum, Cladosiphon okamuranus* and *Padina gymnospora*) has been described to occur through the inhibition of leucocyte recruitment in an inflammation model in rats [108]. Moreover, inhibition of the expression of inducible nitric oxide synthase (iNOS) has also been demonstrated for fucoidans, such as that from the Sigma-Aldrich Chemical Co. (from *F. vesiculosus*). Furthermore, commercial fucoidans (from Mekabu and Sigma-Aldrich Chemical Co) together with those isolated from *A. nodosum*, *F. evanescens*, *C. okamuranus* and from other several brown algae of Laminariales order were described to exhibit anticomplementary activities, rendering them potential as anti-allergic agents [37, 110, 114].

Overall, fucoidans have a number of potential applications, mainly associated to their claimed health benefits. Although there are only a few studies focusing on fucoidans isolated from Iberian brown seaweeds (mainly *Ascophyllum nodosum*, see Table 3) the previously reported data obtained from macroalgae of the same species (with an origin outside Iberian Peninsula), genera or order might indicate promising perspectives for Iberian specimens. Studies with Iberian fucoidan-bearing macroalgae should be undertaken, in order to prove their potential for commercial exploitation (e.g. nutraceuticals, supplements or even incorporated into processed foods). Moreover, the claims for health benefits of seaweeds are probably the best way to stimulate their consumption as food in occidental countries, including the Iberian Peninsula. Candidates of edible brown macroalgae, occurring on the Iberian Peninsula comprise: *Fucus vesiculosus*, *Undaria pinnatifida*, *Saccharina latissima*, *Laminaria* sp. and *Himanthalia elongata*. Note that these such utilization would not only contribute to a healthier diet but also to positive development for the local economy.

2.3. Laminarans

Laminarans are the main storage polysaccharide of brown algae (e.g. *Laminaria* spp., *Saccharina* spp.) [26, 125]. Their content can represent up to 32-35% of dry weight, with variations occurring between growth seasons of the seaweed [26, 103]. Laminarans are small glucans, with a degree of polymerization varying between 20 to 50 units. The structure of these polysaccharides includes β-(1→3)-linked glucose, containing randomly β-(1→6) intra-chain branching [126].

Laminarans can occur in soluble or insoluble forms, being the first totally soluble in cold water while the second can be solubilized with hot water [127]. The solubility is influenced by branching, with better solubility being observed for higher branched polymers [127]. Laminarans contain polymeric chains of two types, i.e, the G-chains which are built only of Glc*p* residues and the M-chains, with 1-*O*-substituted, D-mannitol residue at the terminal reducing end (Fig. 6) [128]. Laminarans from different seaweeds may vary with regard to their structural features, such as the M:G ratio, degree of branching and molecular weight [103, 127].

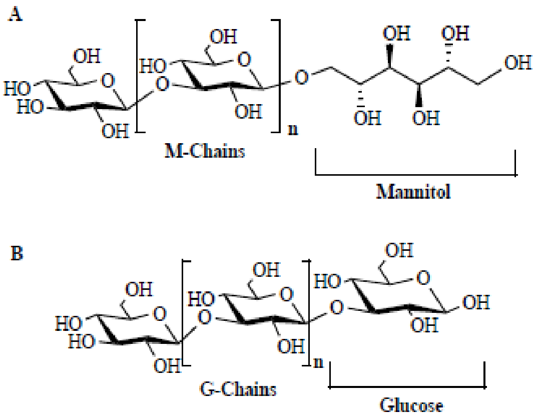

Fig. (6). Chemical structures of laminarans of two types of chains: mannitol (A) or (B) glucose is attached to the reducing end of the M-chains or G-chains, respectively.

Laminarans are presently attracting commercial interest because of some of their (or their derivatives) potential biological activities. These include antioxidant, antitumor, antimicrobial, immune modulation, drug delivery and anticoagulant properties [26, 129, 130]. In particular, *in vitro* studies revealed the interaction of laminarins in tumor cell metabolism, which suggest active functions in metabolic pathways leading to apoptotic cell death of the tumor cells [130, 131]. Lee et al. [132] also reported that laminaran stimulated and strengthed the immune system through metabolic expression and pathway interactions. Moreover, as for other seaweed polysaccharides, laminarans are not digested by the human digestive system, i.e. it is a natural fiber [125] and hence improves the gastro-intestinal health by decreasing the production of putrefactive compounds, known to induce cancer. Furthermore, they stimulate the growth of favorable intestinal microbiota such as *Bifidobacterium* strains [125, 133-135]. Note that antioxidant fibers are not only important for human digestive health, but also for animals, including livestock and fish. The fact that laminarans have antioxidant properties might even attract the meat industry to feed their animals with supplements containing laminarans since, besides the healthy improvement of the animals' intestines, it acts on the conservation of the meat after the animal is slaughtered [133-135]. In this instance, application of the polysaccharides could be an alternative to other synthetic antioxidants and antibiotics with known toxicity in the meat industry.

There are even feasible applications of laminarans in the agricultural field. These polysaccharides have been shown to provide protection against pathogens due to the stimulation of specific metabolic pathways of plants which result in the expression of specific compounds known to trigger the defense responses of plants to pathogens [103].

The main Iberian members of the Laminariales order include: *Saccharina latissima*, *Laminaria hyperborea*, *L. ochroleuca* and *L. digitata*; and the major member of the Tilopteridales order is *Saccorhiza polyschides*. The industrial application of these seaweeds locally are mostly focused on bioethanol and biogas production [136]. There are also applications for the cultivation of these brown seaweeds with salmon, where the macrolagae can enrich the waters of the aquaculture site with oxygen while also providing bioremediation services and reducing local pollution (eutrophication) from the salmon. This system has been called the integrated, multi-trophic aquaculture (IMTA) system. The seaweed biomass produced in this system can be sold as a direct food resource [137]. Moreover, harvested *L. hyperborea* is commonly used for supplementation of pig food [133, 138] and in cosmetics [61].

3. PIGMENTS

As previously mentioned, seaweeds are generally classified according to their pigment composition, which include chlorophylls, carotenoids and phycobilins. The majority of these compounds have been commercialized for many years for coloring purposes, but importantly, the interest in their commercial applications has significantly increased in recent decades as promising applications in human health are being established. In this context, fucoxanthin is probably the main macroalgal pigment under the spotlight of several industries.

3.1. Fucoxanthin

Fucoxanthin is an orange-colored accessory pigment, belonging to the xanthophylls (carotenoids) and one of the most abundant, representing about 10% of their total natural production [139-143]. It is the major carotenoid of edible brown seaweeds, where it binds to several proteins, together with chlorophyll a in the thylakoid of chloroplasts. Fucoxanthin was first isolated from the marine brown seaweeds: *Fucus*, *Dictyota*, and *Laminaria* by Willstätter and Page in 1914 [144] and its complete structure was elucidated by Englert *et al.* [145]. From the structural point of view, this compound is unique, with an unusual allenic bond and some oxygenic functional groups such as epoxide, hydroxyl, carbonyl and carboxyl moieties (Fig.7) [146].

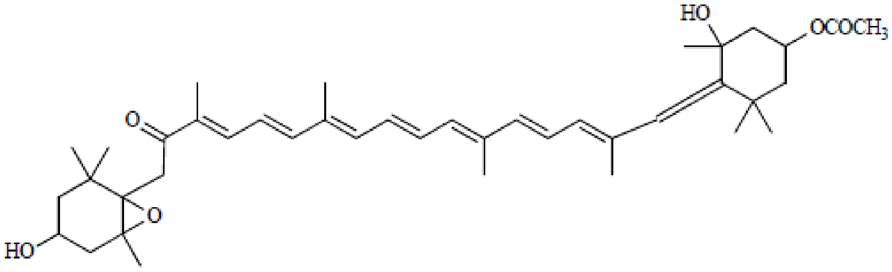

Fig. (7). Chemical structure of fucoxanthin [147]

Due to the presence of double bonds in the polyene chain of the carotenoid, fucoxanthin might exist in *trans* and/or *cis* configurations. As for carotenes in general, the *trans* forms of fucoxanthin are thermodynamically more stable than the *cis* counterparts due to reduced steric hindrance [148]. Accordingly, all-*trans* fucoxanthin has been isolated from several seaweed sources and in particular, it has been shown to account for 88% of the total fucoxanthin in fresh *U. pinnatifida* [26].

Fucoxanthin is extremely vulnerable to degradation which mainly occurs by oxidative cleavage and/or epoxidation of the backbone. Degradation might be triggered by diverse external agents such as high temperature, high pressure, light and the presence of acid or oxygen. In this sense, storage and processing conditions can compromise the stability of fucoxanthin resulting in oxidative degradation and isomerization [26]. Indeed, the levels of fucoxanthin were reported to significantly decrease after drying [149]. Moreover, light and pH decreases were reported to degrade the pigment, possibly related to *trans-cis* isomerization reactions [150]. These modifications currently limit the use of pure fucoxanthin as an ingredient of functional food preparations [151]. It is noteworthy that the stability of fucoxanthin might be improved in the presence of other organic ingredients such as polyphenols [151].

The content of fucoxanthin in seaweeds greatly differs between species, with reported contents between 0.022 and 3.7 mg g^{-1} of dry weight [26, 152-154]. Also, the fucoxanthin content can be highly variable during the season and life cycle of the macroalga. In general, the levels of fucoxanthin increase from winter to spring (mature phase of the sporophyte) and decrease during summer (during the senescence phase) [154, 155].

Several *in vitro* and *in vivo* experiments suggested that fucoxanthin exerts important health-promoting activities, mainly due to its antioxidant properties [156]. The pigment has been shown to possess a strong ability to scavenge or quench DPPH• radicals, nitrobenzene with linoleic acids radical adduct (NB-L) and 12-doxyl-steric acid (12-DS). It is generally accepted that its antioxidant capacities are closely associated to the presence of the unique double allenic carbon in its structure that combined with two hydroxyl groups, confer additional stability and resonance stabilization [157].

Besides being a good antioxidant, bioactivities reported for fucoxanthin also include anti-obesity, antidiabetic, anti-inflammatory, antimalarial, anti-aging, antitumural and protective effects on liver, brain, bones, skin and eyes [26, 30, 151, 157, 158]. As a result of its claimed health-associated properties, the pigment is being evaluated for further use as a food supplement, as a therapeutic agent in the treatment of obesity, metabolic syndrome, diabetes and wrinkle formation [30].

Fucoxanthin, as other algal carotenoids, is commonly extracted with hexane and other non-polar solvents, by liquid solvent extraction. The solvent disrupts the cell membranes and dissolves lipids, lipoproteins and the membranes of chloroplasts [159, 160]. Special care must be taken in the extraction procedure (e.g. low temperature and being kept in the dark) due to the high instability of fucoxanthin. Alternative methods such as the enzyme-assisted and microwave-assisted extractions and pressurized liquid extraction techniques have been used in an attempt to minimize the degradation of the fucoxanthin [140, 156, 161, 162].

As reported [139-143, 147], the species *Undaria pinnatifida*, *Fucus vesiculosus*, *Sargassum siliquastrum*, *S. fulvellum*, *S. fusiforme*, *Himanthalia elongata*, *Eisenia bicyclis*, *Laminaria digitata*, *Saccharina japonica* and *Ascophyllum nodosum* can be candidates for fucoxanthin extraction. From the reported species, the ones present in

Iberia Peninsula are the *A. nodosum, H. elongata, F. vesiculosus, L. digitata* and *U. pinnatifida* [71].

3.2 Phycobiliproteins

Red algae are rich in phycobiliproteins, i.e., water soluble pigments found in the cytoplasm or in the stroma of the chloroplasts, which are formed by complexes of phycobilins with covalently bound proteins. Chemically, phycobilins are open-chain tetrapyrrole chromophores bearing A, B, C and D rings. These chromophores link to the polypeptide chain at conserved positions either by one cysteinyl thioester linkage through the vinyl substituent on the pyrrole ring A or occasionally, by two cysteinyl thioester linkages through the vinyl substituent on both A and D pyrrole rings [163]. The phycobilins are the main component determining the color of phycobiliproteins. Based on their absorption properties they can be blue (phycocyanobilin), red (phycoerythrobilin), yellow (phycourobilin) or purple (phycobiliviolin). Molecular pigments are organized in supra-molecular complexes (i.e. phycobilisomes) and they exert a fundamental role in the photosynthetic process of the red algae.

R-phycoerythrin (Fig. 8) is the most common phycobiliprotein in many red algae, with levels, on a dry weight basis, of approximately 0.2% for *Polysiphonia stricta* and *Pyropia (Porphyra) yezoensis*, 12% for *Palmaria palmata* and *Gracilaria gracilis* and of 0.5% for *G. tikvahiae* [164-168].

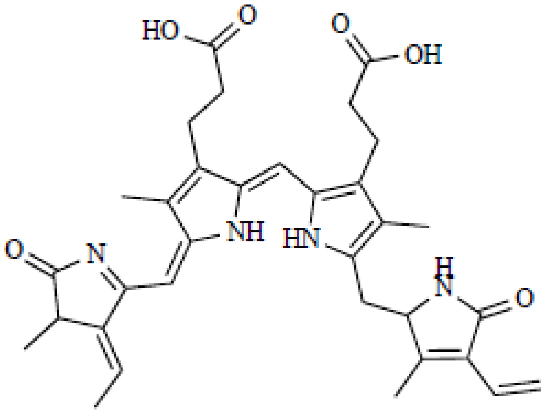

Fig. (8). Chemical structure of R-phycoerythrin [169]

R-phycoerythrin, together with other phycobiliproteins, have been used for decades as natural colorants in foods (e.g chewing gum, ice creams, soft drinks, fermented milk products, milk shakes, desserts, jellies and coated sweet cakes [170, 171]), cosmetic and pharmaceutical products. In general, the colors are very stable and tolerate high temperatures, pH changes and light [171]. Moreover, R-phycoerythrin has specialized applications in analytical techniques such as flow cytometry, cell sorting and histochemistry [30]. C-phycocyanin, R- and B-phycoerythrin are currently used in the cosmetic industry for production of lipsticks, eyeliners and other high value cosmetics [168].

Biological properties of phycoerythrin and/or phycobiliproteins include antioxidant, anti-inflammatory, neuroprotective, immunomodulator, antiviral, antitumor, cardiovascular and liver protection [168, 171-173]. Due to their biological properties, many patents have been established, towards applications of these pigments for nutritional supplements and therapeutic agents [170].

Typically, extraction of phycobiliproteins comprises the disruption of cells and a primary isolation from the algae by chemical and physical techniques. The extraction yield can be improved by the addition of other processes such as freezing, sonication and homogenization, or the use of enzymes (e.g. lyzozymes) [168]. Phycobiliproteins are then purified, usually by chromatographic methods [170], or by the use of novel techniques such as immuno-absorption and genetic recombination.

From the reported data, *Corallina elongata*, *Gracilaria gracilis*, *Grateloupia turuturu* and *Palmaria palmata* are present on the Iberian Peninsula and hence, can be considered potential candidates for the extraction and applications of phycobiliproteins [4].

4. PROTEINS

Besides the commercial applications of phycobiliproteins, macroalgae have other proteic compounds which have a promising potential for exploitation. Indeed, macroalgae (in particular certain of the green and reds) have relatively high protein contents, ranging from 9-26% (w⁄w) dry weight (green) or reaching up to 47% (w⁄w) dry weight (red) [174]. Some of these contents are even higher than those found in high-protein conventional foods, e.g. eggs, beans or fish [174, 175]. According to the literature, the levels of seaweed proteins are determined by seasonality, with the highest contents in general being observed for the winter period [174, 176].

Additionally, the majority of seaweeds contain all the essential amino acids. In particular, isoleucine and threonine can be found at similar levels (e.g. in *Palmaria* *palmata*) to those found in legumes, while histidine levels (e.g. in *Ulva pertusa*) can be as high as those found in egg proteins [174]. Some seaweeds (mainly browns) may also have high levels of acidic amino acids, i.e. aspartic acid and glutamic acid [174]. The latter have much interest in flavor development processes and in particular, glutamic acid (mainly responsible for the taste sensation of ‘umami’) is presently being used as a food additive in the form of its sodium salt (E-621) [177]. The combined glutamic acid and aspartic acid levels account for 22-44% wet weight of the total amino acid fraction in *Fucus* sp. and 39-41% in *Sargassum* spp., whilst both amino acids together represent 18% of the total amino acid content in *L. digitata* proteins [26].

Likewise, certain macroalgae produce several useful enzymes, from which haloperoxidases are probably of major relevance. Haloperoxidases are rare enzymes that catalyse the oxidation of a halide (i.e., chloride, bromide, or iodide) by hydrogen peroxide, a process that results in the concomitant halogenation of organic substrates [178]. These enzymes are crucial in the synthesis of compounds of biological importance that are difficult to be synthesized by the conventional methods of organic chemistry [178]. Haloperoxidases also have powerful applications in qualitative and quantitative diagnostic assays (e.g. glucose, uric acid and cholesterol), as it generates intense colored products with appropriate subtrates.

In addition, some macroalgal protein hydrolysates and their associated peptides might exert important bioactive properties, providing them with commercial prospects as functional foods. The main beneficial properties of protein of macroalgal origin were recently reviewed by Harnedy and FitzGeral [8]. These include ACE-inhibitory, antihypertensive, antioxidant, antitumor, antityrosinase, anticoagulant, calcium-precipitation-inhibitory, antimutagenic, plasma- and hepatic-cholesterol reducing, blood-sugar-lowering, and superoxide dismutase (SOD)-like activities.

The main seaweeds with high protein content from the Iberian Peninsula are: *Porphyra (Pyropia) umbilicalis* (i.e. Atlantic nori), *Palmaria palmata* (Rhodophyta), and *Himanthalia elongata*, *Saccharina latissima*, *Undaria pinnatifida* (Phaeophyceae), and *Ulva compressa* (Chlorophyta) [5, 30]. "Atlantic nori" from the Iberian Peninsula is, for now, a wild seaweed (as compared to Japanese equivalent species which have been cultivated since the XV century). Note that nori is one of the most appreciated and highly commercially valued algae, due to its high content in minerals and proteins, together with intense flavor, aroma and smooth texture.

5. PHLOROTANNINS

Chemically, phenolic compounds are organic compounds characterized by an aromatic ring with one or more hydroxyl groups that can occur in different chemical structures [179-181] varying between simple phenolic molecules to complex high-molecular weight polymers (126-650 kDa) [182]. Phlorotannins consist of oligomers or polymers of phloroglucinol (Fig. 9), which are known to be located in special vesicles (i.e. physodes) of the cells [26, 110].

Phlorotannins are only found in the brown algae and have been identified in distinct families, including: the Alariaceae, Fucaceae and Sargassaceae. In particular, the species *Eisenia bicyclis*, *Ishige okamurae*, *Sargassum thunbergii*, *S. fusiforme*, *Undaria pinnatifida* and *Saccharina japonica*, as well as algae belonging to the genera *Cystophora* and *Ecklonia*, are recognized as good sources of phlorotannins [183]. Relevant phlorotannins encountered in *Ecklonia cava* [184], *E. stolonifera* [185], *Eisenia bicyclis* and *Fucus vesiculosus* [186] are represented in Fig. 10 and comprise: phloroglucinol, tetrafucol A, fucophlorethol A, fucodiphloroethol G, phlorofucofuroeckol A, 7-phloroeckol, eckol, dieckol and triphlorethol-A.

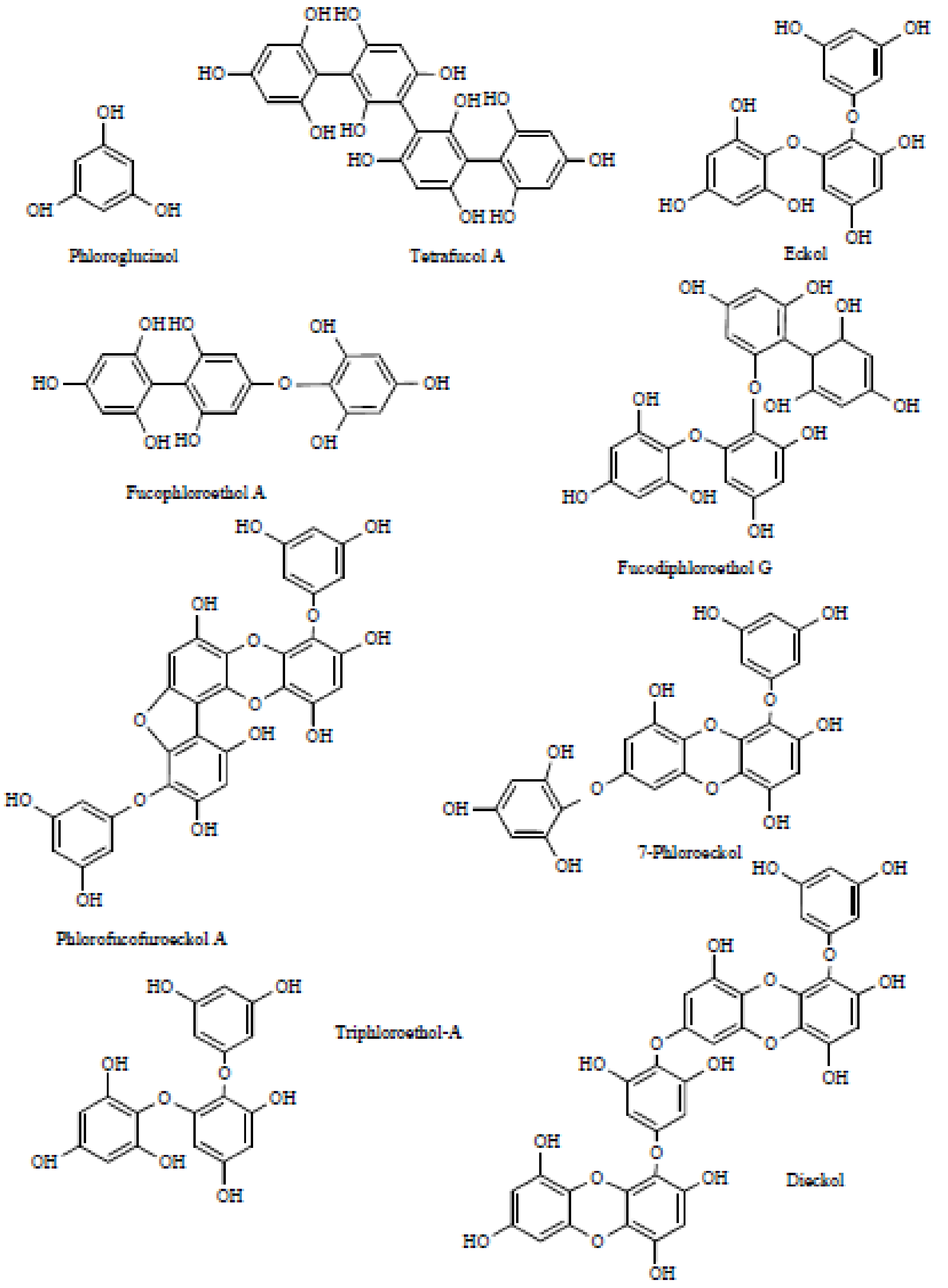

Fig. (9). Chemical structure of phlorotannins (adapted from [185])

The levels of phlorotannins varies greatly between different taxonomic groups and geographical areas. Variations also occur in the same species and depending on factors such as plant size, age, tissue type and environmental factors such as nutrient, light, salinity, water depth and season [187].

The interest in phlorotannins has increased in the last decade due to their potential biological activities, as described by several authors. In more detail, the compounds eckol, doxinodehydroeckol and dieckol from *E. bicyclis* have been shown to have interesting deodorizing effects [168]. Moreover, phlorotannin compounds identified in different *Ecklonia* species were reported to possess important antimicrobial activities against several pathogens [188], as well as an antidiabetic effect in *in vitro* and *in vivo* models [189], antioxidant [183], hypnotic [190], hepatoprotective [191], anti-inflammatory [192] and for lowering blood pressure [193] capacities. Overall, these claimed effects for phlorotannins render these metabolites with many potential future applications in several industries.

Traditionally, phlorotannins have been extracted using ethanol, methanol or aqueous acetone as a solvent [139, 186], while additional purification is commonly achieved by chromatographic techniques [194, 195]. Due to the low stability of phlorotannins, the extracts are frequently obtained with nitrogen or by adding $K_2S_2O_5$ or ascorbic acid in order to prevent oxidation [196, 197].

6. MINERALS

Marine algae are known to contain a wide variety and high levels of certain minerals (this may vary form 8-40% of algal dry weight (DW) and have therefore been employed as mineral additives to feed and food supplements [198]**.** Their high mineral content is related to their capacity to retain inorganic marine substances [199] due to the ionic and exchange capacity features of their cell surface polysaccharides [200].

Nevertheless, the mineral composition of macroalgae varies according to phylum and even amongst species [201] as well as many other factors such as environmental and physiological variations, geographic harvesting site, seasonality and wave exposure. Moreover, it is also a result of seaweed’s oceanic residence time and type of processing [202].

The value of edible seaweeds in human nutrition is based, among others (e.g., dietary fiber, vitamins, etc.), on their high content in several (essential) minerals, namely: Na, Mg, P, K, I, Fe, and Zn [202]. Seaweeds also contain large amounts of trace elements [198] that are scarce in vegetables and hence, algal-based supplements can provide to humans the daily requirements of these minerals [203].

Seaweeds have higher mineral content than edible terrestrial plants and animals. Indeed, mean ash (and thereby mineral) content of most traditional vegetables is frequently much lower than that of seaweeds (e.g. 10.4% in potatoes, 2.6% in sweet corn, 7.1% in carrots and in tomatoes) [202]. Only the higher values observed in spinach (20%) are comparable to those of seaweeds [202]. Rupérez [198] also showed that ash content of many algae was elevated and higher in brown (i.e. 30.1-39.3%) rather than in red (20.6-21.1%) seaweeds.

Most algae display higher Na and K values than those reported in vegetables. However, their Na/K ratios are usually low [204]. Additionally, most edible algae have higher levels of Mg (500-1,000 mg.100g^{-1} DW) than terrestrial plants and animals [205]. Ca is one of the major elements in algae and is present at concentrations of about 400-2000 mg.100g^{-1} DW (table V). The Ca and P contents of certain seaweeds are higher than those of apples, oranges, carrots, and potatoes. High Ca/P ratio in algae (3:5) could compensate the deficit of Ca in several foods, such as cereals and meats [201]. Iodine (I) can reach high levels in certain brown algae [206], whereas green algae present low or nonexistent values (Table 5). Members of the genus *Laminaria* are the strongest iodine accumulators among all living systems (the accumulation can be up to 30,000 times greater than the surrounding sea water, and brown algal tissue can represent a major source of this element [207]. The uptake of dietary iodide by the human and animal thyroid leading to thyroid hormone formation, is a well-established phenomenon. *L. digitata* is widely used as a health supplement for myxoedema and for the treatment of goiter [208]. It has been reported that *U. pinnatifida* (or its equivalent iodine content) inhibited tumorogenesis in rats with carcinogen-induced mammary tumors, although the mode of action is not understood [209].

Table 5. Mineral composition of some Iberian Peninsula, edible seaweeds (g.100 g^{-1} DW^{a} or mg. 100 g^{-1} DW^{b}). Adapted from [5].

Species	**Na^{a}**	**K^{a}**	**P^{a}**	**Ca^{a}**	**Mg^{a}**	**Fe^{b}**	**Zn^{b}**	**Mn^{b}**	**Cu^{b}**	**I^{b}**
Green seaweed										
Caulerpa racemosa	2.6	0.32	29.7	1.9	0.38 – 1.6	30 – 81	1 – 7	4.91	0.6 – 0.8	-
Ulva lactuca		-	0.14	0.84	-	66	-	-	-	-
U. rigida	1.6	1.6	0.21	0.52	2.1	283	0.6	1.6	0.5	-
Brown seaweed										
Fucus vesiculosus	2.5 – 5.5	2.5 – 4.3	0.32	0.72 – 0.94	0.67 – 1.0	4 – 11	3.71	5.50	<0.5	14.5
Himanthalia elongata	4.1	8.3	0.24	0.72	0.44	59	-	-	-	14.7
Laminaria digitata	3.8	11.6	-	1.0	0.66	3.29	1.77	<0.5	<0.5	-
Undaria pinnatifida	1.6 – 7.0	5.5 – 6.8	0.24 – 0.45	0.68 – 1.4	0.41 – 0.69	1.54 – 30	0.94	0.33	0.19	22 – 30
Red seaweed										

Chondrus crispus	1.2 – 4.3	1.4 – 3.2	0.14	0.42 – 1.1	600 – 732	4 – 17	7.14	1.32	<0.5	24.5
Gracilaria spp.	5.5	3.4	-	0.40	565	3.65	4.35	-	-	-
Palmaria palmata	1.6 – 2.5	7.0 – 9.0	0.24	0.56 – 1.2	170 – 610	50	2.86	1.14	0.376	10 – 100
Porphyra umbilicalis	0.94	2.0	0.24	0.33	370	23	-	-	-	17.3

Na – sodium; K – potassium; P – phosphorus; Ca – calcium; Mg – magnesium; Fe – iron; Zn – zinc; Mn – manganese; Cu – copper; I – iodine.

One negative aspect of seaweed consumption could involve the potential health risks associated with high algal concentrations of heavy metals (i.e. As, Cd, Cu, Hg, Pb, and Zn) [210], as algal fibers may act as a powerful cation exchanger [211]. Organic values reported for brown algae are especially high (i.e. 200 – 500 times greater than the levels found in terrestrial plants). Nevertheless, metal values in macroalgae are generally below the maximum concentrations permitted for human consumption in most countries [205]. Moreover, it has been shown that organic As is less toxic than the inorganic form [212]. In contrast, marine fish may contain high concentrations of Hg, but this element is found in low, even trace, amounts in algae [213].

7. CONCLUSION

Presently, seaweeds are used in many countries for a multituide of very different purposes. The majority of seaweeds are still used for direct human consumption, while a minor portion is for industrial exploitation of seaweed-derived products. Nevertheless, recent investigations point to seaweed-derived products (e.g. polysaccharides, proteins, lipids and polyphenols) as novel bioactive products and/or biomaterials/biopolymers which have great potential in many areas, opening a framework for future research and development.

The Iberian Peninsula is located in the warm temperate Mediterranean-Atlantic region and is under unique influences receiving climatic effects from the North Atlantic Ocean and the Mediterranean Sea. This coast is a home to a great diversity of seaweeds, albeit only a few of these species are currently being exploited. The present manuscript is intended to raise and alert to the potential applications of seaweed-derived products, as well as to the seaweeds diversity in Iberian Peninsula, hoping to contribute to boost their industrial utilization.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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