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Bioactive compounds in seaweed: functional food applications and legislation

Susan Løvstad Holdt · Stefan Kraan

Abstract Seaweed is more than the wrap that keeps rice together in sushi. Seaweed biomass is already used for a wide range of other products in food, including stabilising agents. Biorefineries with seaweed as feedstock are attracting worldwide interest and include low-volume, high value-added products and vice versa. Scientific research on bioactive compounds in seaweed usually takes place on just a few species and compounds. This paper reviews world-wide research on bioactive compounds, mainly of nine genera or species of seaweed, which are also available in European temperate Atlantic waters, i.e. *Laminaria* sp., *Fucus* sp., *Ascophyllum nodosum*, *Chondrus crispus*, *Porphyra* sp., *Ulva* sp., *Sargassum* sp., *Gracilaria* sp. and *Palmaria palmata*. In addition, *Undaria pinnatifida* is included in this review as this is globally one of the most commonly produced, investigated and available species. Fewer examples of other species abundant worldwide have also been included. This review will supply fundamental information for biorefineries in Atlantic Europe using seaweed as feedstock. Preliminary selection of one or several candidate seaweed species will be possible based on the summary tables and previous research described in this review. This applies either to the choice of high value-added bioactive products to be exploited in an available species or to the choice of seaweed species when a bioactive compound is desired. Data are presented in tables with species, effect and test organism (if present) with examples of uses to enhance comparisons. In addition, scientific experiments performed on seaweed used as animal feed are presented, and EU, US and Japanese legislation on functional foods is reviewed.

Keywords High value-added products · Health promotion · Biorefinery · Nutraceutical · Pharmaceutical · Feed supplement

Introduction

Whilst food has long been used to improve health, our knowledge of the relationship between food components and health is now being used to improve food. Although most foods can be considered "functional", in the context of this review, the term is reserved for foods and food components that have been demonstrated to provide specific health benefits beyond basic nutrition. Widespread interest in select foods that might promote health has resulted in the use of the term "functional foods". Food and nutrition science has moved from identifying and correcting nutritional deficiencies to designing foods that promote optimal health and reduce the risk of disease. Today's science and technology can be used to provide many additional functional foods, and future scientific and technological advances promise an even greater range of health benefits for consumers. Functional foods can provide health benefits by reducing the risk of chronic diseases and enhancing the ability to manage chronic diseases, thus improving the quality of life. Functional foods also can promote growth and development and enhance performance.

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Seaweeds are known for their richness in polysaccharides, minerals and certain vitamins (Arasaki and Arasaki 1983), but they also contain bioactive substances like polysaccharides, proteins, lipids and polyphenols, with antibacterial, antiviral and antifungal properties, as well as many others (Kumar et al. 2008b). This gives seaweed great potential as a supplement in functional food or for the extraction of compounds. Physiologically active substances in marine algae are classified into two types based on the difference in the mechanisms: (1) non-absorbed high-molecular materials like dietary fibres and (2) low-molecular materials, which are absorbed and which affect the maintenance of human homeostasis directly (Murata and Nakazoe 2001).

Nutritional elements

The moisture content of fresh marine algae is very high and can account for up to 94% of the biomass (Table 1). Though, like other plants, marine algae contain nutritional elements such as proteins, lipids, carbohydrates, vitamins and minerals, the content of these elements varies depending on season and the area of production (Connan et al. 2004; Khan et al. 2007; Marinho-Soriano et al. 2006; Murata and Nakazoe 2001; Zubia et al. 2008). Researchers from the Norwegian Institute of Seaweed Research have been studying seasonal variations of the biochemical composition of the large brown seaweed species in particular since the 1950s. The ash content in seaweed is high compared to vegetables (Table 1; Murata and Nakazoe 2001). The ash content includes macro-minerals and trace elements. Ash

content of blades of *Saccharina latissima*, *Laminaria* spp. and *Alaria esculenta* is lowest during September, October and November and highest during spring (February to June); however, it varies only slightly in the stipes over the year. Dry weight was lowest from January to March and highest in July to September for these species (Haug and Jensen 1954; Jensen and Haug 1956). These seasonal and environmental variations in the composition of seaweed make generalisations impossible. Nevertheless, this review summarises scientific data on the biochemical composition and bioactivity of compounds in seaweed, although some data might just provide the concentration as a snapshot and not the seasonal variations, for example.

Polysaccharides

Marine algae contain large amounts of polysaccharides, notably cell wall structural, but also mycopolysaccharides and storage polysaccharides (Kumar et al. 2008b; Murata and Nakazoe 2001). Polysaccharides are polymers of simple sugars (monosaccharides) linked together by glycosidic bonds, and they have numerous commercial applications in products such as stabilisers, thickeners, emulsifiers, food, feed, beverages, etc. (McHugh 1987; Tseng 2001). The total polysaccharide concentrations in the seaweed species of interest range from 4% to 76% of dry weight (Table 2). The highest contents are found in species such as *Ascophyllum*, *Porphyra* and *Palmaria*; however, green seaweed species such as *Ulva* also have a high content, up to 65% of dry weight.

Table 1 Moisture (% of wet weight) and ash content (% dry wt.) in seaweed species of interest in Northwest Europe

	Brown					Green	Red			
	Laminaria and *Saccharina*	*Fucus*	*Ascophyllum*	*Undaria*	*Sargassum*	*Ulva*	*Chondrus*	*Porphyra*	*Gracilaria*	*Palmaria*
Moisture	84–87%[a] (fronds)	68–75%[h]	67–82%[m]	88%[j]	61%[j]	78%[c]	72%[z]	77%[b]	85%[d]	84% (wild and cultured)[cc]
	86%[b]	70–87%[i]	71%[h]			80%[b,f]	72–78%[aa]	86%[c]		
	73–90%[c]	81%[b]	87%[n]					91%[d]		
	94%[d]	84%[j]								
Ash	15–37%[e]	19%[b]	18–27%[o]	27%[p]	14%[r]	11%[t]	21%[l,g]	7%[q]	8%[r]	12–37%[dd]
	16–45%[e] (fronds)	25%[k]		31%[q]	44%[s]	13–22%[c]		8–16%[c]	29%[s]	15%[j]
	21–35%[f]	30%[l,g]		39%[l]		18%[b,u]		9%[b,bb]	17%[d]	15% (wild)[cc]
	38%[g]			40%[g]		26%[v]		18%[d]		27% (cultured)[cc]
	39%[d]					52%[w]		21%[l,g]		
						55%[x,y]				

[a] Horn (2000); [b] Marsham et al. (2007); [c] Foti (2007); [d] Wen et al. (2006); [e] References in Jensen and Haug (1956); [f] Lamare and Wing (2001); [g] Rupérez and Saura-Calixto (2001); [h] Baardseth and Haug (1953); [i] Larsen and Haug (1958); [j] Herbreteau et al. (1997); [k] Rioux et al. (2007); [l] Rupérez (2002); [m] Jensen (1960); [n] Jensen (1966); [o] Jensen (1960); [p] Je et al. (2009); [q] Murata and Nakazoe (2001); [r] Marinho-Soriano et al. (2006); [s] Robledo and Freile-Pelegrín (1997); [t] Ortiz et al. (2006); [u] Ventura and Castañón (1998); [v] Bobin-Dubigeon et al. (1997); [w] Foster and Hodgson (1998); [x] Wong and Cheung (2001b); [y] Wong and Cheung (2000); [z] Simpson and Shacklock (1979); [aa] Holdt (2009); [bb] Arasaki and Arasaki (1983); [cc] Mishra et al. (1993); [dd] Morgan et al. (1980)

Table 2 Content of total polysaccharides (% dry wt.) and structural and dietary fibres (% dry wt.) in seaweed species of interest in Northwest Europe

		Brown					Green	Red			
		Laminaria and *Saccharina*	*Fucus*	*Ascophyllum*	*Undaria*	*Sargassum*	*Ulva*	*Chondrus*	*Porphyra*	*Gracilaria*	*Palmaria*
Polysaccharides	Total	38%[a]	62%[b]	42–64%[b]	35–45%[h,i]	4%[k]	15–65%[l,m,n,o]	55–66%[b]	40%[i]	36%[k]	38–74%[r]
		48%[b]	66%[c]	44%[g]		68%[k]	18%[p]		41%[q]	62%[a]	50%[b]
		58%[c]		70%[c]			42–46%[b]		50–76%[b]	63%[k]	66%[s]
		61%[b]					54%[a]				
Structural and dietary fibres	Total	36%[d]			35–46%[d,j]	49–62%[d,j]	38%[d,j]		35–49%[d,j]		
	Soluble			38%[g]	30%[d,j]	33%[d,j]	21%[d,j]		18%[d,j]		
	Lignin						3%[l]				
	Cellulose	10% in stipe[e]	2–4.5%[f]	2%[f]			9%[l]				
		4.5–9%[f]		3.5–4.6%[e]							
	Hemicelluloses						9%[l]				

See also Tables 4, 5 and 6 for the content of other polysaccharides, including bioactivity

[a] Wen et al. (2006); [b] Morrissey et al. (2001); [c] Rioux et al. (2007); [d] Dawczynski et al. (2007); [e] Horn (2000); [f] Black (1950); [g] Tseng (2001); [h] Je et al. (2009); [i] Murata and Nakazoe (2001); [j] Lahaye (1991); [k] Marinho-Soriano et al. (2006); [l] Ventura and Castañón (1998); [m] Ortiz et al. (2006); [n] Sathivel et al. (2008); [o] Wong and Cheung (2000); [p] Foster and Hodgson (1998); [q] Arasaki and Arasaki (1983); [r] Heo and Jeon (2009); [s] Mishra et al. (1993)

Seaweeds are low in calories from a nutritional perspective. The lipid content is low, and even though the carbohydrate content is high, most of this is dietary fibres and not taken up by the human body. However, dietary fibres are good for human health as they make an excellent intestinal environment (Mouritsen 2009).

The cell wall polysaccharides mainly consist of cellulose and hemicelluloses, neutral polysaccharides, and are thought to physically support the thallus in water. The building blocks needed to support the thalli of seaweed in water are less rigid/strong compared to terrestrial plants and trees. The cellulose and hemicellulose content of the seaweed species of interest in this review is 2–10% and 9% dry weight, respectively. Lignin is only found in *Ulva* sp. at concentrations of 3% dry weight (Table 2).

The cell wall and storage polysaccharides are species-specific, and examples of concentrations are given in Table 3. Green algae contain sulphuric acid polysaccharides, sulphated galactans and xylans, brown algae alginic acid, fucoidan (sulphated fucose), laminarin (β-1,3 glucan) and sargassan and red algae agars, carrageenans, xylans, floridean starch (amylopectin-like glucan), water-soluble sulphated galactan, as well as porphyran as mucopolysaccharides located in the intercellular spaces (Table 3; Kumar et al. 2008b; Murata and Nakazoe 2001). Contents of both total and species-specific polysaccharides show seasonal variations. The mannitol content varied markedly in the fronds of *Saccharina* and *Laminaria* species, with maximum amounts found during summer and autumn, from June to November. Laminaran showed extreme variations during the year, with very small amounts or none at all in February to June and maximum in September to November

(Haug and Jensen 1954; Jensen and Haug 1956). The maximum content of alginic acid in the fronds of *Saccharina* and *Laminaria* was generally found from March to June and the minimum from September to October (Haug and Jensen 1954). However, the highest contents of alginic acid were found during winter in other seasonal studies on *Laminaria* from the same areas in Norway (Jensen and Haug 1956).

Further investigations on the hydrolysates of some brown algae showed complex mixtures of monosaccharides. The components of galactose, glucose, mannose, fructose, xylose, fucose and arabinose were found in the total sugars in the hydrolysates. The glucose content was 65%, 30% and 20% of the total sugars in an autumn sample of 50 individual plants of *Saccharina*, *Fucus* (*serratus* and *spiralis*) and *Ascophyllum*, respectively (Jensen 1956).

Several other polysaccharides are present in and utilised from seaweed, e.g. furcellaran, funoran, ascophyllan and sargassan; however, these are not described in this review. Seaweed polysaccharides are separated into dietary fibres, hydrocolloids, etc. in the following paragraphs, even though the polysaccharides belong to more than just one of the functional groups.

Dietary fibres

The dietary fibres are very diverse in composition and chemical structure as well as in their physicochemical properties, their ability to be fermented by the colonic flora, and their biological effects on animal and human cells (Lahaye and Kaeffer 1997). Edible seaweed contain 33–62% total fibres on a dry weight basis, which is higher than

Table 3 Species-specific polysaccharides and bioactive components (g 100 g^{-1} on dry weight basis)

Seaweed	Alginic acid	Fucoidan	Laminarin	Mannitol	Phorphyran	Floridean starch	Pentoses
Ascophyllum nodosum	28	11.6	4.5	7.5	–	–	
Laminaria digitata	32.2	5.5	14.4	13.3	–	–	
Porphyra umbilicalis	–	–	–	–	47.8	41.8	NA
Palmaria palmate	–	–	–	–	NA	25	46

Free after MacArtain et al. (2007)

NA no data available

the levels found in higher plants, and these fibres are rich in soluble fractions (Lahaye 1991; Dawczynski et al. 2007). The dietary fibres included in marine algae are classified into two types, i.e. insoluble such as cellulose, mannans and xylan, and water-soluble dietary fibres such as agars, alginic acid, furonan, laminaran and porphyran. The total content of dietary fibres is 58% dry weight for *Undaria*, 50% for *Fucus*, 30% for *Porphyra* and 29% for *Saccharina* (Murata and Nakazoe 2001). *Fucus* and *Laminaria* have the highest content of insoluble dietary fibres (40% and 27%, respectively), and *Undaria pinnatifida* (wakame), *Chondrus* and *Porphyra* have the highest content of soluble dietary fibres (15–22%; Fleury and Lahaye 1991).

The undigested polysaccharides of seaweed can form important sources of dietary fibres, although they might modify the digestibility of dietary protein and minerals. Apparent digestibility and retention coefficients of Ca, Mg, Fe, Na and K were lower in seaweed-fed rats (Urbano and Goñi 2002). The seaweed dietary fibres contain some valuable nutrients and substances, and there has been a deal of interest in seaweed meal, functional foods and nutraceuticals for human consumption (McHugh 2003) because, among other things, polysaccharides show anti-tumour and anti-herpetitic bioactivity; they are potent as an anticoagulant and decrease low-density lipid (LDL)-cholesterols in rats (hypercholesterolemia); they prevent obesity, large intestine cancer and diabetes; and they have antiviral activities (Lee et al. 2004; Murata and Nakazoe 2001; Amano et al. 2005; Athukorala et al. 2007; Ghosh et al. 2009; Murata and Nakazoe 2001; Ye et al. 2008; Tables 4, 5 and 6). Moreover, glucose availability and absorption are delayed in the proximal small intestine after the addition of soluble fibres, thus reducing postprandial glucose levels (Jenkins et al. 1978). Water-insoluble polysaccharides (celluloses) are mainly associated with a decrease in digestive tract transit time (see also later chapter on the digestibility of polysaccharides; Mabeau and Fleurence 1993).

Alginates

Alginates were discovered in the 1880s by a British pharmacist, E.C.C. Stanford; industrial production began in California in 1929. Nowadays, the key industrial producers of alginates are the US, Great Britain, Norway, Canada, France, Japan and China; the annual sales volume of alginates in the world is about 26,500 t out of a total volume of 86,000 t hydrocolloids (Bixler and Porse 2010). Production of carbohydrates that dissolve in water is a growing industry. The three major groups of phycocolloids are alginates, carrageenan and agar, and these are used for applications such as thickening aqueous solutions, forming gels and water-soluble films, and stabilising products such as ice cream, tooth paste, mayonnaise, etc. (FAO 2008; Tseng 2001).

Algins/alginates are extracted from brown seaweed and are available in both acid and salt forms. The acid form is a linear polyuronic acid and is referred to as alginic acid, whereas the salt form is an important cell wall component in all brown seaweed, constituting up to 40–47% of the dry weight of algal biomass (Table 4; Arasaki and Arasaki 1983; Rasmussen and Morrissey 2007). Various industries related to food processing, pharmaceuticals, feed and cosmetics use alginic acid extracted from *Saccharina* and *Undaria*. It has been reported that alginic acid leads to a decrease in the concentration of cholesterol, exerts an anti-hypertension effect, can prevent absorption of toxic chemical substances, and plays a major role as dietary fibre for the maintenance of animal and human health (Kim and Lee 2008; Murata and Nakazoe 2001; Nishide and Uchida 2003). These dietary polysaccharides are not found in any land plants. They help protect against potential carcinogens and they clear the digestive system and protect the surface membranes of the stomach and intestine. They absorb substances such as cholesterol, which are then eliminated from the digestive system (Burtin 2003; Ito and Tsuchida 1972) and result in hypocholesterolemic and hypolipidemic responses (Kiriyama et al. 1969; Lamela et al. 1989; Panlasigui et al. 2003). This is often coupled with an increase in the faecal cholesterol content and a hypoglycaemic response (Dumelod et al. 1999; Ito and Tsuchida 1972; Nishide et al. 1993).

Alginates, fucoidans and laminarin extracts were tested against nine bacteria, including *Escherichia coli*, *Staphylococcus*, *Salmonella* and *Listeria*. They appeared to be effective against *E. coli* and *Staphylococcus*. Sodium

Table 4 Bioactivity, source and characteristics of total polysaccharides and alginates in the seaweed families of interests in Northwest Europe

Characteristics	Source and content	Bioactivity
Total polysaccharides	*Saccharina latissima*[a] *Sargassum pallidum*[b,c]	Anti-tumor action[a], in vitro (HepG2, A549 and MGC-803 cells; MMT and DPPH free radical assay)[b] Anti-herpetic[d] Potent anticoagulant[c] Decrease in LDL-cholesterol in rats[e]
Algins/alginic acid Polymer of two different units of uronic acids (D-mannoronic acid and L-glucoronic acid) [o]	*Saccharina latissima*: 17–33%[f], 18%[g] *Laminaria digitata*[h]: 32%[i], 33–46%[f], 30–44%[j] *Laminaria hyperborea*: 17–34%[j], 20–37%[f] *Laminaria* sp.[m,a] *Fucus vesiculosus*: 18–22%[g] *Ascophyllum nodosum*: 28%[i]; 24–29%[l], 26%[g] *Undaria pinnatifida*[a]: 24%[m,a] *Sargassum vulgare*[n] Brown seaweed species: 10–47%[o] *Ulva* sp.[n]	Antibacterial[p] Stimulates reparative processes and prepares wounds for scarring[q,r] Absorbing hemostatic agent[s,t,u], in gauze dressing[v] Protective and coating effects, shielding mucous membranes and damaged skin against irritation from unfavourable environments[w] Anticancer[a] Prevent proliferation of implanted cancer cells[x] Increased (3.5-fold) the ileal viscosity of digesta and their hydration capacity in the ileum and colon in pigs[h] Hypocholesterolemic and hypolipidemic responses due to reduced cholesterol gut absorption[y,z,aa] Reduction of total cholesterol, free cholesterol, tri-glyceride and phospholipid in the liver[cc] Anti-hypertension effect[a,dd] Dietary fibre for maintenance of human health[a] Reduction of glucose absorption balance[bb] and insulin response in pigs[ee] Anti-diabetes[bb] and reduction or prevention of postprandial increase of glucose and insulin [ee,ff] Anti-obesity[bb,gg] Anti-ulcer, treatment of gastritis and gastroduodenal ulcers[hh], prevent gastro-esophageal reflux and to cure epigastric burning[ii] Promotes regeneration of the mucous membranes and suppresses inflammation in the stomach, and restoration of intestinal biocenosis[z] Dietary fibre: increase of faecal microbial fauna, decrease in *Enterobacteriacea. Enterococci* and lecitinase-negative clostridia, decrease of faecal phenol, ρ-cresol, indole, ammonium and skatole and decrease of acetic acid and propionic acid, stimulation of growths of *Bifidobacterium* spp.[jj] Anti-toxic effects on hepatitis[kk] May prevent primordial atherosclerosis[z]
Carrageenan Sulfated polysaccharide. Several types, e.g. *kappa*- and *lambda*-carrageenan	*Chondrus crispus*[ll,mm,nn,oo] 47%[pp], 50%[qq], 58–71%[rr] *Eucheuma cottonii/Kappaphycus alverezii*[ss]: 22%[tt], 88%[uu] *Kappaphycus striatum*: 72%[uu] *Gigartina skottsbergii*[vv] *Stenogramme interrupta*[ww]	Anticoagulant[xx,1] in blood products[g] Reduction of postprandial glycaemic responses[yy] Maybe anti-diabetic[yy] Reduction of plasma cholesterol in chicken[zz] Anti-thrombic in dogs and humans[l] Treatment of diarrhoea, constipation and dysentery[g] Control of ulcers[g] Stimulates the biosynthesis of collagen and the formation of connective tissue[2] Anti-tumour and immunomodulation[ll] in mice[mm] Antiviral: gonorrhoea, genital warts, cervical cancer and the HSV[oo,vv,ww,3], genital herpes in mice[4]

Table 4 (continued)

Characteristics	Source and content	Bioactivity
		Anti-HIV[oo,5] (UV and radioactive counting)[6], but no efficacy on humans[nn]
		Toxicity: inflammatory reaction[8], induces pleurisy and ulceration of the colon[9]
Agar	*Gracilaria* sp.[ss]	Decrease in blood glucose concentration[a]
Consist of agarose and agaropectin (ratio 7:3)	*Gracilaria cornea*: 21–31%[10] *Gracilaria dominguensis*[11] *Gigartina* sp.[ss]	Anti-aggregation effect of red blood cells[a] Anti-tumour: inhibited the transplantation of Ehrlich ascites carcinoma in mice[11]
	Gelidium sp.: 26–42%[14]	Activity against α-glucosidase[12]
		Suppress the production of pro-inflammatory cytokine TNF-α[13]
		Suppress the expression of inducible nitric oxide synthase (iNOS)[13]
		Antioxidant activity (DPPH method)[12]
		Absorption effect of ultraviolet rays[a]

See also Table 2 for total content of polysaccharides and other structural polysaccharides. Concentrations are given in per cent of dry weight

[a] Murata and Nakazoe (2001); [b] Ye et al. (2008); [c] Athukorala et al. (2007); [d] Ghosh et al. (2009); [e] Amano et al. (2005); [f] Haug and Jensen (1954); [g] Morrissey et al. (2001); [h] Kim and Lee (2008); [i] MacArtain et al. (2007); [j] Jensen and Haug (1956); [k] Bartsch et al. (2008); [l] Jensen (1960); [m] Je et al. (2009); [n] Dietrich et al. (1995); [o] Arasaki and Arasaki (1983); [p] Hennequart (2007); [q] Glyantsev et al. (1993); [r] Doyle et al. (1996); [s] Reynolds and Prasad (1982); [t] Katayama et al. (1998); [u] Segal et al. (1998); [v] Savitskaya (1986) and Khotimchenko et al. (2001); [w] Swinyard and Pathak (1985); [x] Doi and Tsuji (1998); [y] Kiriyama et al. (1969), Lamela et al. (1989) and Panlasigui et al. (2003); [z] Slezka et al. (1998); [aa] Tsuchiya (1969) and Ito and Tsuchida (1972); [bb] Kimura et al. (1996); [cc] Nishide and Uchida (2003); [dd] Renn et al. (1994a, b); [ee] Vaugelade et al. (2000); [ff] Torsdottir et al. (1991); [gg] Zee (1991); [hh] Bogentoff (1981), Borgo (1984), Reckitt and Colman Products Ltd. (1999) and Sheth (1967); [ii] Klinkenberg-Knol et al. (1995) and Zeitoun et al. (1998); [jj] Terada et al. (1995) and Wang et al. (2006); [kk] Khotimchenko et al. (2001); [ll] Yan et al. (2004); [mm] Zhou et al. (2006a); [nn] Skoler-Karpoff et al. (2008); [oo] Shanmugam and Mody (2000); [pp] Bruhn et al. (2008); [qq] Chopin et al. (1995); [rr] Chopin et al. (1999); [ss] FAO (2008); [tt] Hayashi et al. (2008); [uu] Rodrigueza and Montaño (2007); [vv] Carlucci et al. (1997); [ww] Caceres et al. (2000); [xx] Hawkins et al. (1962), and Kindness et al. (1979); [yy] Dumelod et al. (1999); [zz] Riccardi and Fahrenbach (1965); [1] Hawkins and Leonard (1963); [2] Robertson and Schwartz (1953); [3] Buck et al. (2006); Luescher-Mattli (2003) and Witvrouw and DeClercq (1997); [4] Zeitlin et al. (1997); [5] Spieler (2002); [6] Vlieghe et al. (2002); [7] Goemar (2010); [8] Dannhardt and Kiefer (2001); [9] Noa et al. (2000); [10] Freile-Pelegrín and Robledo (1997); [11] Fernandez et al. (1989); [12] Chen et al. (2005); [13] Enoki et al. (2003); [14] Mouradi-Givernaud et al. (1992) and Jeon et al. (2005)

alginate seemed to demonstrate a strong antibacterial element. It not only binds but also kills the bacteria. Studies conducted on seaweed extracts found that fucoidan appeared to function as a good prebiotic (a substance that encourages the growth of beneficial bacteria in the intestines). An anti-inflammatory effect from some of the extracts has also been found, and so far, no toxic effects have emerged in use for human health (Hennequart 2007). Furthermore, alginates with molecular weights ≥50 kDa could prevent obesity, hypocholesterolemia and diabetes (Kimura et al. 1996). Clinical observations of volunteers who were 25–30% overweight showed that alginate, a drug containing alginic acid, significantly decreased body weight (Zee et al. 1991). In type II diabetes treatment, taking 5 g of sodium alginate every morning was found to prevent a postprandial increase of glucose, insulin, and C-peptide levels and slowed down gastric transit (Torsdottir et al. 1991). Meal supplemented with 5% kelp alginates decreased glucose absorption balance over 8 h in pigs. Similar studies have been done on rats and humans (Vaugelade et al. 2000). Another health effect is that the binding property of alginic acid to divalent metallic ions is correlated to the degree of the gelation or precipitation in the range of Ba<Pb<Cu<Sr<Cd<Ca<Zn< Ni<Co<Mn<Fe<Mg. No intestinal enzymes can digest alginic acid. This means that heavy metals taken into the human body are gelated or rendered insoluble by alginic acid in the intestines and cannot be absorbed into the body tissue (Arasaki and Arasaki 1983).

In several countries such as the US, Germany, Japan, Belgium and Canada, the use of alginic acid and its derivatives for the treatment of gastritis and gastroduodenal ulcers, as well as the use of alginates as anti-ulcer remedies, is protected by patents (Bogentoff 1981; Borgo 1984; Reckitt and Colman Products Ltd. 1999; Sheth 1967). Several products of alginate-containing drugs have been shown to effectively suppress postprandial (after eating) and acidic refluxes, binding of bile acids and duodenal ulcers in humans. Examples are "Gaviscon" (sodium alginate, sodium bicarbonate and calcium carbonate), "Algitec" (sodium alginate and cimetidine, an H2 antagonist) and "Gastralgin" (alginic acid, sodium alginate, aluminium hydroxide, magnesium hydroxide and calcium carbonate; Khotimchenko et al. 2001; Washington and

Table 5 Bioactivity, source and characteristics of the polysaccharide fucoidan in seaweed species within the seaweed families of interests in Northwest Europe

Characteristics	Source and content	Bioactivity
Fucoidan ranging from typical fucoidans (major components) to low sulphate-containing hetero-polysaccharide-like fucans (minor components). Fucoidan mainly contains L-fucose, sulphate, and no uronic acid[a,b]	*Laminaria digitata*: 5.5%[c], 2–4% (stipes)[d]	Anticoagulant[a,w,bb] (gel filtration and anion exchange chromatography)[a,tg]
	Laminaria japonica[q,s,bb,dd,jj,nn,qq]	Anti-arteriosclerosis[x,y]
	Laminaria hyperborea: 2–4% (stipes)[d]	Anti-inflammatory agent in mice[z]
	Laminaria sp.[f,g]	Antioxidant[q,t,v,aa,bb], including prevention of Alzheimer and the ageing process[bb]
	Fucus vesiculosus[a,h]: 16–20%[i,iv]	Reduction of contact hypersensitivity reactions in mice[z]
	Fucus sp.	Possible anti-prion (misfolding of proteins) activity[cc]
	Ascophyllum nodosum[j]: 12%[c]; 4–10%[k]	Reduction of neutrophil infiltration and myocardial injury after ischemia/reperfusion[dd]
	Undaria pinnatifida[g,l,u,v,v,uu]; 1.5%[m]	Reduction of interleukin (IL–1) production[ee] and of leukocytes recruitment into cerebrospinal fluid in meningitis model[ff]
	Sargassum horneri[n]	Anticancer[x,g]. In vitro, DPPH and human cancer cell lines[h], direct on human HS-Sultan cells (caspase and ERK pathways)[gg]
	Sargassum vulgare: uronic acid, xylose and fucose accounted for >90% of total sugars[o]	Anti-tumour activity[hh]: L-1210 leukaemia[r], anti-angiogenesis, antiproliferation for and inhibition of tumour cell growth/reduction in tumour size[ii], hepatoma cells[jj], against sarcoma 180 (tissue tumours of mice)[s], and anti-metastatic effect in mice (toxic at high conc.)[kk]
	Sargassum sp.	
	Ulva pertusa[p]	Restrain the development and diffusion of tumour cells[gg]
	Porphyra haitanesis[q]	Kill tumour cells directly[gg] through type 1 Th1 cell and NK cell responses[ll]
	Eisenia bicyclis[r,s]	Inhibits adhesion of tumour cell to various substrata[s]
	Ecklonia kurome[t]	Stimulation of immuno system: innate and adaptive[mm], in mice (acted directly on macrophages and T-lymphocytes)[jj,mn,oo], in irradiated rats through lymphocyte apoptosis[pp], production of interleukin (IL–1) and IFN-γ in vitro[oo], promote primary antibody response to red blood cells in sheep[oo]
	Adenocytis utricularis[u]	
	Stoechospermum marginatum[u]	
	Cystoseira indica[u]	Antiviral[n,g,hh]
	Lessonia sp.	Anti-RNA[mm] and DNA functions[qq]
	Macrocystis sp.	Anti-HIV[rr,ss,tt]
	Cladosiphon sp. *Durvillea* sp.	Anti-hepatitic[ss,tt,l] (methylation analyses and in vitro HSV-1, HSV-2[uu,uu] including Human Herpesvirus 5 (HHV-5)[vv], genital herpes in mice
	Ecklonia sp.	Anti-bovine viral diarrhoea virus[vv]
	Alaria sp. *Padina gymnospora e*[v]	Inhibition og cytopathogenic effect and protect cultural cells from infection of vira: poliovirus III, adenovirus III, ECHO6 virus, coxsackie B3 and A16 virus[qq]
		Potential antiviral against human cytomegalovirus and avian flue (human cytomegalovirus)[uu,tt]
		Potential antiviral (*Cryptosporidium parvum* (parasite) adhesion to the human intestinal cells and on *C. parvum* infection in neontenal mice)[l] Inhibits growth of *C. parvum* in mice[yy]
		Prebiotic[xx]
		Antibacterial properties against *E. coli* and *Staphycococcus*[xx]

See also Table 2 for total content of polysaccharides and other structural polysaccharides. Concentrations are given in per cent of dry weight

[a] Nishino et al. (1994); [b] Matsubara et al. (2005); [c] MacArtain et al. (2007); [d] Jensen and Haug (1956); [e] Xue et al. (2004); [f] Bartsch et al. (2008); [g] Zhuang et al. (1995); [h] Han et al. (2008); [i] Morrissey et al. (2001) and Ruperez et al. (2002); [j] Marais and Joseleau (2001); [k] Jensen (1960); [l] Maruyama et al. (2007); [m] Je et al. (2009); [n] Dietrich et al. (1995); [o] Athukorala et al. (2007); [p] Qi et al. (2005a, b); [q] Zhang et al. (2003); [r] Yamamoto et al. (1984); [s] Liu et al. (2005); [t] Hu et al. (2001); [u] Mandal et al. (2007); [v] Rocha de Souza et al. (2007); [w] Mayer and Hamann (2004); [x] Murata and Nakazoe (2001); [y] Durig et al. (1997), Ying et al. (1997) and Carvalho et al. (2002); [z] Nasu et al. (1997); [aa] Qi et al. (2005a, b), Ruperez et al. (2002) and Xue et al. (2004); [bb] Wang et al. (2008); [cc] Doh-ura et al. (2007); [dd] Omata et al. (1997); [ee] Ostergaard et al. (2000); [ff] Granert et al. (1999); [gg] Aisa et al. (2005); [hh] Chevolot et al. (1999); [ii] Ellouali et al. (1993); [jj] Li et al. (2008a, b); [kk] Alekseyenko et al. (2007); [ll] Maruyama et al. (2006); [mm] Hayashi et al. (2008); [nn] Wang et al. (1994); [oo] Yang et al. (1995); [pp] Wu et al. (2003); [qq] Li et al. (1995); [rr] Schaeffer and Krylov (2000); [ss] Witvrouw and DeClercq (1997); [tt] Iqbal et al. (2000); [uu] Lee et al. (2004); [vv] Hemmingson et al. (2006); [ww] Zeitlin et al. (1997); [xx] Hennequart (2007); [yy] Smit (2004); [l] Gosh et al. (2009)

Denton 1995). Clinical trials showed that sodium alginate promotes the regeneration of the mucous membrane in the stomach, suppresses inflammation, eradicates colonies of *Helicobacter pylori* in the mucous membrane and normal-ises non-specific resistance of the latter in 4- to 15-year-old children. It also promotes restoration of the intestinal biocenosis (Miroshnichenko et al. 1998). Other studies show positive dietary effects of alginates on faecal

Table 6 Bioactivity, source and characteristics of the polysaccharides mannitol, laminaran, phycarine, porphyran, ulvan and floridoside in seaweed species within the seaweed families of interests in Northwest Europe

	Characteristics	Source and content	Bioactivity
Mannitol		*Saccharina latissima*: 2–19%[a], 14%[b] *Laminaria digitata*: 13%[c], 2.5–17%[a], 4–20%[d], 7.5%[b], 2–11% (in stipes)[d] *Laminaria hyperborea*: 4–25%[d], 2–18%[a], 4–20%[d] *Laminaria* sp.[e] *Sargassum mangarevense*: 1–12%[f] *Ascophyllum nodosum*: 7.5%[c], 6.8–10%[g], 5.2–10%[h], 7–11%[g]	Effectively protects the photosynthetic apparatus from low-salinity damage[i,j]
Laminaran/ Laminarin	Branched (soluble) and unbranched (insoluble) polysaccharide: beta 1-3,beta 1-6-glucan[j,k]. 84–94% sugar and 6–9% uronic acid[l] Contains mannitol[m] Only found in brown seaweed[j]	*Saccharina latissima*: 0–33%[a], 16%[b] *Laminaria digitata*: 14%[c], 0–18%[a,d,b] *Laminaria hyperborea*: 0–30%[d], 0.5–24%[a], 0–32%[d] *Laminaria* sp.[e] : 20–30%[m], 99% of total sugars[l] *Fucus vesiculosus*: 84% of total sugars[l] *Ascophyllum nodosum*: 4.5%[c], 1.2–7%[g]; 10%, 90% of total sugars[l] *Undaria pinnatifida*: 3%[n]	Antiviral in agricultural applications[o] Antibacterial[p] Substratum for prebiotic bacteria[q] Dietary fibre[q] Hypocholesterolemic and hypolipidemic responses due to reduced cholesterol absorption in the gut[r] Reduce serum cholesterol levels and total serum lipid[s] Reduction of total cholesterol, free cholesterol, tri-glyceride and phospholipid in the liver[t] Decrease of systolic blood pressure (anti-hypertensive responses)[u] Surgical dusting powder[s] Maybe value as tumour-inhibiting agent[s] Anticoagulant (sulphate ester form)[s,v] Protection against irradiation[s,w], also severe[p] Stimulates immune systems; B and helper T cells[p] Immunostimulating activities in animals and plants; 1→3:1→6-β-D-glucans produced from laminarin[w] Help in wound repair[s]
Phycarine		*Laminaria digitata*[x]	Immune system stimulation of macrophage phagocytosis[x]
Porphyran	Polymer of acidic saccharide containing sulphate groups, β-1,3-xylan[y]	*Porphyra umbilicalis*: 48%[c] *Porphyra* sp.[y,z]	Potential apopototic/programmed cell death activity[y] Anti-blood coagulant[z] Anti-hypercholesterolemia[z] Anti-tumour[z]
Ulvan	Highly branched polymers of soluble dietary fibre and contain rhamnose, glucuronic acid and xylose[aa,bb]. Structurally similar to the mammalian glycosaminoglycans[cc]	*Ulva lactuca*[cc,dd,ee] *Ulva rigida* *Monostroma* sp.[ee]	Modify adhesion and proliferation of normal and tumoural human colonic cells[dd] Treatment of gastric ulcers[ee] Anti-influenza[ee] Cytotoxicity and cytostaticity, HU colon cell line[cc]

Table 6 (continued)

	Characteristics	Source and content	Bioactivity
Floridoside	Floridean starch. Red algae polysaccharide, similar to that of starch amylopectin, but more red iodine reaction[m]	*Porphyra umbilicalis*: 42%[c] *Palmaria palmata*: 25%[c]	

See also Table 2 for the total content of polysaccharides and other structural polysaccharides. Concentrations are given in per cent of dry weight
[a] Haug and Jensen (1954); [b] Morrissey et al. (2001); [c] MacArtain et al. (2007); [d] Jensen and Haug (1956); [e] Bartsch et al. (2008); [f] Zubia et al. (2008); [g] Jensen (1960); [h] Larsen and Haug (1958); [i] Gessner (1971); [j] Lobban and Harrison (1994); [k] Deville et al. (2007); [l] Rioux et al. (2007); [m] Arasaki and Arasaki (1983); [n] Je et al. (2009); [o] Goemar (2010); [p] Hoffman et al. (1995); [q] Deville et al. (2004); [r] Kiriyama et al. (1969), Lamela et al. (1989) and Panlasigui et al. (2003); [s] Miao et al. (1999); [t] Nishide and Uchida (2003); [u] Renn et al. (1994a, b); [v] Shanmugam and Mody (2000); [w] Kuznetsova et al. (1994); [x] Mayer et al. (2007); [y] Plaza et al. (2008); [z] Noda (1993); [aa] Bobin-Dubigeon et al. (1997); [bb] Michel and Macfarlane (1996); [cc] Kaeffer et al. (1999); [dd] Lahaye and Robic (2007); [ee] Nagaoka et al. (2003)

microbial fauna, changes in concentrations of compounds and acids, and prebiotic properties that can promote health (Terada et al. 1995; Wang et al. 2006).

Sodium alginate is often used as a powder, either pure or mixed with other drugs, on septic wounds. The polysaccharide base stimulates reparative processes, prepares the wound for scarring, and displays protective and coating effects, shielding mucous membranes and damaged skin against irritation from unfavourable environments. Calcium alginate promotes the proliferation of fibroblasts and inhibits the proliferation of microvascular endothelial cells and keratinocytes (Doyle et al. 1996; Glyantsev et al. 1993; Swinyard and Pathak 1985). Profound wound healing effects have also been reported for a gelatine–alginate sponge impregnated with antiseptics and antibiotics (Choi et al. 1999).

Alginates absorbing haemostatic effect has also been exploited in surgery. Gauze dressings, cotton, swabs and special materials impregnated with a solution of sodium alginate are produced and used for external use and for application onto bleeding points during abdominal operations on parenchymatous organs (Khotimchenko et al. 2001; Savitskaya 1986). Studies on the effect of alginate on prothrombotic blood coagulation and platelet activation have shown that the degree of these effects depends on the ratio between the mannuronic and guluronic chains in the molecule, as well as on the concentration of calcium. However, a zinc ion containing alginate was shown to have the most profound haemostatic effects (Segal et al. 1998). A "poraprezinc–sodium alginate suspension" has been suggested as a high-performance mixture for the treatment of severe gingivostomatitis (cold sores) complicated by haemorrhagic erosions and ulcers (Katayama et al. 1998). When applied to the tooth surface, alginate fibres swell to form a gel-like substance, a matrix for coagulation. Alginate dressings are used to pack sinuses, fistulas and tooth cavities (Reynolds and Prasad 1982).

Furthermore, the algins have anticancer properties (Murata and Nakazoe 2001), and a bioactive food additive "Detoxal", containing calcium alginate, has antitoxic effects on hepatitis. This drug decreases the content of lipid peroxidation products and normalises the concentrations of lipids and glycogen in the liver (Khotimchenko et al. 2001). Mannuronate surfactants derived from alginate can be applicable in fields as cosmetics, health and agrochemistry (Benvegnu and Sassi 2010).

Carrageenans

Carrageenans are a group of biomolecules composed of linear polysaccharide chains with sulphate half-esters attached to the sugar unit. These properties allow carrageenans to dissolve in water, form highly viscous solutions and remain stable over a wide pH range. There are three general forms (kappa, lambda and iota), each with its own gelling property (Rasmussen and Morrissey 2007). *Chondrus crispus* and *Kappaphycus* sp. contain up to 71% and 88% of carrageenan, respectively (Chopin et al. 1999; Rodrigueza and Montaño 2007). Food applications for carrageenans (E 407) are many, including canned foods, dessert mousses, salad dressings, bakery fillings, ice cream, instant desserts and canned pet foods. Industrial applications for purified extracts of carrageenans are equally diverse. They are used in the brewing industry for clarifying beer, wines and honeys, although less commonly than previously. From a human health perspective, it has been reported that carrageenans have anti-tumour and antiviral properties (Skoler-Karpoff et al. 2008; Vlieghe et al. 2002; Yan et al. 2004; Zhou et al. 2006b). Furthermore, Irish moss or carrageen (*C. crispus* and *Mastocarpus stellatus*) has a large number of medical applications, some of which date from the 1830s. It is still used in Ireland to make traditional medicinal teas and cough medicines to combat colds, bronchitis and chronic coughs. It is said to be particularly useful for dislodging mucus and has antiviral properties. Carrageenans are also used as suspension agents and stabilisers in other drugs, lotions and medicinal creams.

Other medical applications are as an anticoagulant in blood products and for the treatment of bowel problems such as diarrhoea, constipation and dysentery. They are also used to make internal poultices to control stomach ulcers (Morrissey et al. 2001).

New research on the biocide properties shows that applications of carrageenan gels from *C. crispus* may block the transmission of the HIV virus as well as other STD viruses such as gonorrhoea, genital warts and the herpes simplex virus (HSV; Caceres et al. 2000; Carlucci et al. 1997; Luescher-Mattli 2003; Shanmugam and Mody 2000; Witvrouw and DeClercq 1997). In addition, carrageenans are good candidates for use as vaginal microbicides because they do not exhibit significant levels of cytotoxicity or anticoagulant activity (Buck et al. 2006; Zeitlin et al. 1997). Results of sexual lubricant gels raised the possibility that the use of such lubricant products, or condoms lubricated with carrageenan-based gels, could block the sexual transmission of human papillomavirus (HPV) types that can cause cervical cancer and genital warts. However, carrageenan inhibition of herpes simplex virus and HIV-1 infectivity were demonstrated as about 1,000-fold higher than the IC_{50}'s observed for genital HPVs in vitro (Witvrouw and DeClercq 1997; Luescher-Mattli 2003). A carrageenan-based vaginal microbicide called Carraguard has been shown to block HIV and other sexually transmitted diseases in vitro. Massive clinical trials by the Population Council Centre began in two severely affected African countries—Botswana and South Africa—in 2002. Carraguard entered phase III clinical trials involving 6,000 non-pregnant, HIV-negative women in South Africa and Botswana in 2003 (Spieler 2002). This trial showed that the microbiocide Carraguard® was safe for vaginal use, but did not demonstrate that it is effective in preventing male-to-female HIV transmission during vaginal intercourse (Population Council 2008).

Many reports of anticoagulant activity and inhibited platelet aggregation of carrageenan exist (Hawkins et al. 1962; Hawkins and Leonard 1963; Kindness et al. 1979). Among the carrageenan types, λ-carrageenan (primarily from *C. crispus*) has approximately twice the activity of unfractionated carrageenan and four times the activity of κ-carrageenan (*E. cottoni* and *Eucheuma spinosum*). The most active carrageenan has approximately one fifteenth the activity of heparin (Hawkins et al. 1962), but the sulphated galactan from *Grateloupa indica* collected from Indian waters exhibited an anticoagulant activity as potent as heparin (Sen et al. 1994).

The principal basis of the anticoagulant activity of carrageenan appeared to be an anti-thrombotic property. λ-Carrageenan showed greater anti-thrombotic activity than κ-carrageenan, probably due to its higher sulphate content, whereas the activity of the unfractionated material remained between the two. It was found that the toxicity of carrageenans depended on the molecular weight and not the sulphate content. Similar results were obtained with λ-carrageenan of *Phyllophora brodiaei* which gave the highest blood anticoagulant activity (Sen et al. 1994). In addition, the hypoglycaemic effect of carrageenan may prove useful in the prevention and management of metabolic conditions such as diabetes (Dumelod et al. 1999).The use of carrageenan for food applications started almost 600 years ago. Due to its long and safe history of use, carrageenan is generally recognised as safe (GRAS) by experts from the US Food and Drug Administration (21 CFR 182.7255) and is approved as a food additive (21 CFR 172.620). The WHO Joint Expert Committee of Food Additives has concluded that it is not necessary to specify an acceptable daily intake limit for carrageenans (van de Velde et al. 2002). Although carrageenans are used widely as a food ingredient, they are also used in experimental research in animals where they induce pleurisy and ulceration of the colon (Noa et al. 2000). Furthermore, carrageenans can cause reproducible inflammatory reaction and remain a standard irritant for examining acute inflammation and anti-inflammatory drugs. Two test systems are used widely for the evaluation of non-steroidal anti-inflammatory drugs and cyclooxygenase activity: (1) the carrageenan air pouch model and (2) the carrageenan-induced rat paw oedema assay (Dannhardt and Kiefer 2001). The role of carrageenans in the promotion of colorectal ulceration formation is controversial, and much seems to depend on the molecular weight of the carrageenan used. The International Agency for Research on Cancer classified degraded carrageenan as a possible human carcinogen, but native carrageenan remains unclassified in relation to a causative agent of human colon cancer and has GRAS status (Carthew 2002; Tobacman 2001).

Agar

Agar is a mixture of polysaccharides, which can be composed of agarose and agropectin, with similar structural and functional properties as carrageenans. It is extracted from red seaweed such as *Gelidium* spp. and *Gracilaria* spp. (FAO 2008; Rasmussen and Morrissey 2007; Jeon et al. 2005). The agar content in *Gracilaria* species can reach 31% (Table 4). Agar–agar is a typical and traditional food material in Japan and is used for cooking and Japanese-style confectionary. In addition, agar–agar is used in the manufacture of capsules for medical applications and as a medium for cell cultures, etc. It has been reported that agar–agar leads to decreases in the concentration of blood glucose and exerts an anti-aggregation effect on red blood cells. It has also been reported to affect the absorption of

ultraviolet rays (Murata and Nakazoe 2001). Anti-tumour activity was also found in an agar-type polysaccharide from cold water extraction of another *Gracilaria* species, and hydrolysates of agar resulted in agaro-oligosaccharides with activity against α-glucosidase and antioxidant ability (Chen et al. 2005; Fernandez et al. 1989). Agarose can be separated from the agar with a yield of 42%, and the agar content varied seasonally from 26% to 42% in *Gelidium* spp. in another experiment (Mouradi-Givernaud et al. 1992; Jeon et al. 2005). Agaro-oligosaccharides have also been shown to suppress the production of a pro-inflammatory cytokine and an enzyme associated with the production of nitric oxide (Enoki et al. 2003).

Fucoidan/fucans/fucanoids

Fucoidans are a group of polysaccharides (fucans) primarily composed of sulphated L-fucose with <10% of other monosaccharides. They are widely found in the cell walls of brown seaweed, but not in other algae or higher plants (Berteau and Mulloy 2003). Fucoidan is considered as a cell wall-reinforcing molecule and seems to be associated with protection against the effects of desiccation when the seaweed is exposed at low tide. Fucoidans were first isolated by Kylin almost one century ago and have interesting bioactivities (Kylin 1913). *Fucus vesiculosus* contains the highest concentration of fucoidans (up to 20% on a dry weight basis) (Table 5). Fucanoids can make up more than 40% of dry weight of isolated algal cell walls and can easily be extracted using either hot water or an acid solution (Berteau and Mulloy 2003). Fucoidan is viscous in very low concentrations and susceptible to breakdown by diluted acids and bases.

A Tasmanian company, Marinova Pty Ltd., is able to supply commercial volumes of fucoidan extract and their derivates, formulated to purity levels of up to 95%. All fucoidans of *Undaria*, *Lessonia*, *Macrocystis*, *Cladosiphon*, *Durvillea*, *Laminaria*, *Ecklonia*, *Fucus*, *Sargassum*, *Ascophyllum* and *Alaria* are Halal- and Kosher-certified. Marinova has isolated fucoidans from a range of species (species-specific) and can provide characterised fractions for either investigational research or as ingredients for nutraceutical and cosmetic applications. Different therapeutic profiles are primarily due to the molecular structure. The company has developed the Maritech™ cold water extraction process which maintains the integrity of fucoidans and produces nature-equivalent high-molecular-weight molecules with optimal bioactivity. Solvent-based extraction, which is commonly used, causes degradation of fucoidans and limits the activity of these molecules in biological assays (Marinova 2010).

Although the major physiological purposes of fucans in the algae are not thoroughly understood, they are known to possess numerous biological properties with potential human health applications (Berteau and Mulloy 2003). The list of bioactivity of fucoidan for human health is long fucoidan found in seaweed such as *Undaria* and *Laminaria* shows anticoagulant, antiviral and anticancer properties (Table 5; Chevolot et al. 1999; Zhuang et al. 1995).

Fucoidan preparations have been proposed as an alternative to the injectable anticoagulant heparin because fucoidan originates from plant matter and is less likely to contain infectious agents such as viruses (Berteau and Mulloy 2003). No toxicological changes were observed when 300 mg kg^{-1} body wt day^{-1} fucoidan was administered to rats; however, significantly prolonged blood-clotting times were observed when concentrations were increased threefold (Li et al. 2005). The biological activity (e.g. antioxidant and anticoagulant) of sulphated polysaccharides is not only related to molecular weight and sulphated ester content (role in the charge of the molecule), as previously determined, but also to glucuronic acid and fucose content, together with the position of the sulphate groups on the sugar resides (Berteau and Mulloy 2003; Li et al. 2005; Zhao et al. 2008). A large molecular weight is required to achieve anticoagulant activity as fucoidan needs a long sugar chain in order to be able to bind the thrombin (coagulation protein in the blood stream). Some researchers have measured fucoidan's molecular weight at approximately 100 kDa, whilst others have observed a molecular weight of 1,600 kDa (Rioux et al. 2007). The native fucoidan from *Lessonia vadosa* with a molecular weight of 320 kDa showed good anticoagulant activity compared to a smaller depolymerised fraction with a molecular weight of 32 kDa, which presented weaker anticoagulant activity (Li et al. 2008a). Some structural features of fucoidan are most likely required for certain specific activities.

Fucoidan stimulates the immuno system in several ways (Table 5), and the numerous important biological effects of fucoidans are related to their ability to modify cell surface properties (Usov et al. 2001). Oral intake of the fucoidans present in dietary brown seaweed might take the protective effects through direct inhibition of viral replication and stimulation of the immune system (innate and adaptive) functions (Hayashi et al. 2008). Fucoidan has been found to restore the immune functions of immune-suppressed mice, act as an immunomodulator directly on macrophage, T lymphocyte, B cell, natural killer (NK) cells (Wang et al. 1994), promote the recovery of immunologic function in irradiated rats (Wu et al. 2003), induce the production of interleukin 1 (IL-1) and interferon-γ (IFN-γ) in vitro, and promote the primary antibody response in sheep red blood cells in vivo (Yang et al. 1995).

The mechanism of antiviral activities of fucoidan is to inhibit viral sorption so as to inhibit viral-induced syncy-

tium formation (Mandal et al. 2007). Sulphate is necessary for the antiviral activity, and sulphate located at C-4 of (1-3)-linked fucopyranosyl units appears to be very important for the anti-herpetic activity of fucoidan (Mandal et al. 2007). Some antiviral properties of sulphated fucans have also been characterised, for example, inhibition of infection of HIV, HSV (Iqbal et al. 2000; Mandal et al. 2007; Witvrouw and DeClercq 1997), poliovirus III, adenovirus III, ECH06 virus, coxsackie B3 virus, coxsackie A16 (Li et al. 1995), cytomegalovirus and bovine viral diarrhoea virus (Iqbal et al. 2000).

Fucoidan is known to have anti-tumour effects, but its mode of action is not fully understood. A study done by Alekseyenko et al. 2007 demonstrated that when 10 mg/kg of fucoidan was administered in mice with transplanted Lewis lung adenocarcinoma, it produced moderate anti-tumour and anti-metastatic effects (Li et al. 2008a, b). These polyanionic polysaccharides have anti-angiogenesis, antiproliferation for tumour cells, they inhibit tumour growth and reduce tumour size (Ellouali et al. 1993; Li et al. 2008a), inhibit tumour cell adhesion to various substrata (Liu et al. 2005), and have direct anticancer effects on human HS-Sultan cells through caspase and ERK pathways (Aisa et al. 2005).

Besides directly inhibiting the growth of tumour cells, fucoidans can also restrain the development and diffusion of tumour cells through enhancing the body's immuno-modulatory activities because fucoidan mediates tumour destruction through type 1 T-helper (Th1) cell and NK cell responses (Maruyama et al. 2006). In addition, at a dose of 25 mg kg^{-1}, fucoidan potentiated the toxic effect of cyclophosphamide used to treat various types of cancer and some autoimmune disorders (Alekseyenko et al. 2007).

Many studies suggest that fucoidan has potential for use as an anti-inflammatory agent. A study showed that fucoidan treatment led to less severe symptoms in the early stages of *Staphylococcus aureus*-triggered arthritis in mice, but delayed phagocyte recruitment and decreased clearance of the bacterium (Verdrengh et al. 2000). Additionally, injection of fucoidan into sensitised mice before hapten challenge can reduce contact hypersensitivity reactions (Nasu et al. 1997). Furthermore, recruitment of leukocytes into cerebrospinal fluid in a meningitis model is reduced by fucoidan (Granert et al. 1999), as is IL-1 production in a similar model (Ostergaard et al. 2000).

Fucoidan can act as a ligand for either L- or P-selectins, both of which interact with the sulphated oligosaccharides, and this interaction has physiological consequences that could be therapeutically beneficial (Omata et al. 1997). Selectins are a group of lectins (sugar-binding proteins) that interact with oligosaccharides clustered on cell surfaces

during the margination and rolling of leukocytes prior to firm adhesion, extravasation and migration to sites of infection (Lasky 1995).

In addition, fucoidan is an excellent natural antioxidant and presents significant antioxidant activity in experiments in vitro. In recent years, sulphated polysaccharides from the marine algae *Porphyra haitanesis* (Zhang et al. 2003), *Ulva pertusa* (Qi et al. 2005a, b), *F. vesiculosus* (Ruperez et al. 2002), *Laminaria japonica* (Xue et al. 2004) and *Ecklonia kurome* (Hu et al. 2001) have been demonstrated to possess antioxidant activity. There are few reports, however, detailing the relationship between the structure and antioxidant activity of sulphated polysaccharides from marine algae. Fucan showed low antioxidant activity relative to fucoidan (Rocha de Souza et al. 2007), and as mentioned previously, the ratio of sulphate content/fucose and the molecular weight were effective indicators of the antioxidant activity of the samples (Wang et al. 2008). Fucoidan may have potential for preventing free radical-mediated diseases such as Alzheimer's and the ageing process. Previously, fucoidan was extracted from *L. japonica*, a commercially important algae species in China. Three sulphated polysaccharide fractions were successfully isolated through anion exchange column chromatography and had their antioxidant activities investigated employing various established in vitro systems, including superoxide and hydroxyl radical scavenging activity, chelating ability and reducing power (Wang et al. 2008). All fractions were more effective than the unprocessed fucoidan. Two galactose-rich fractions had the most potent scavenging activity against superoxide (generated in the PMS-NADH system) and hydroxyl radicals, with EC$_{50}$ values of 1.7 μg mL^{-1} and 1.42 mg mL^{-1}, respectively. One of these fractions also showed the strongest ferrous ion-chelating ability at 0.76 mg mL^{-1} (Wang et al. 2008). Additionally, fucoidan (homofucan) from *F. vesiculosus* and fucans (heterofucans) from *Padina gymnospora* had an inhibitory effect on the formation of hydroxyl radical and superoxide radical (Rocha de Souza et al. 2007).

Mannitol

Mannitol is an important sugar alcohol which is present in many species of brown algae, especially in *Laminaria* and *Ecklonia*. The mannitol content is subject to wide seasonal fluctuations and varies with environment. Mannitol is the sugar alcohol corresponding to mannose. It usually constitutes <10% of dry weight in both *Ascophyllum nodosum* and *Laminaria hyperborea* stipe. In autumn fronds of *L. hyperborea*, however, the content may be as high as 25% of dry weight (Table 6).

Applications of mannitol are extremely diverse. It is used in pharmaceuticals, in making chewing gum, in the

paint and varnish industry, in leather and paper manufacture, in the plastics industry and in the production of explosives. The US, the UK, France and Japan are the main centres of production. Mannitol can be used in a variety of foods, candies and chocolate-flavoured compound coatings because it can replace sucrose to make sugar-free compound coatings. Sugar-free chocolates are especially popular for people with diabetes, a growing problem in modern society. It is used as a flavour enhancer because of its sweet and pleasantly cool taste. Mannitol can be used to maintain the proper moisture level in foods so as to increase shelf-life and stability because it is non-hygroscopic and chemically inert. Mannitol is the preferred excipient for chewable tablets due to its favourable feel in the mouth. It is non-carcinogenic and can be used in paediatric and geriatric food products as it will not contribute to tooth decay (Nabors 2004).

Laminarin

Laminarin is found in the fronds of *Laminaria/Saccharina* and, to a lesser extent, in *Ascophyllum* and *Fucus* species and *Undaria*. The content varies seasonally and with habitat and can reach up to 32% of dry weight (Table 6).

Commercial applications of the extract have so far been limited, although some progress has been made in France as an antiviral in agricultural applications (Goemar 2010) or as dietary fibre (Deville et al. 2004). Especially the use of laminarin as substratum for prebiotic bacteria seems to have a good commercial application (Deville et al. 2004). Laminarin does not gel or form any viscous solution, and its main potential appears to lie in medical and pharmaceutical uses. It has been shown to be a safe surgical dusting powder and may have value as a tumour-inhibiting agent and, in the form of a sulphate ester, as an anticoagulant (Miao et al. 1999). The presence of anticoagulant activity in brown algae was first reported in 1941, when *Laminaria* showed anticoagulant properties with its active compound being located in the holdfasts (Shanmugam and Mody 2000). There are about 60 brown algal species identified to have blood anticoagulant properties. Laminarin only shows anticoagulant activity after structural modifications such as sulphation, reduction or oxidation. The anticoagulant activity is improved chemically by increasing the degree of sulphation (Shanmugam and Mody 2000).

Preparations containing 1→3:1→6-β-D-glucans, laminarin and fucoidan are manufactured by the health industry and marketed for their beneficial properties on the immune system. The producers of these tablets cite numerous papers discussing the biological activity of these glucans.

Laminarin provides protection against infection by bacterial pathogens and protection against severe irradiation, boosts the immune system by increasing the B cells and helper T cells, reduces cholesterol levels in serum, and lowers systolic blood pressure, among other effects (Table 6; Hoffmane et al. 1995) lower the levels of total cholesterol, free cholesterol, triglyceride and phospholipid in the liver (Miao et al. 1999; Renn et al. 1994a, b). The hypocholesterolemic and hypolipidemic responses are noted to be due to reduced cholesterol absorption in the gut (Kiriyama et al. 1969; Lamela et al. 1989; Panlasigui et al. 2003). This is often coupled with an increase in the faecal cholesterol content and a hypoglycaemic response (Dumelod et al. 1999; Ito and Tsuchida 1972; Nishide et al. 1993). A high level of LDL-cholesterol can lead to plaque forming and clog arteries and lead to cardiovascular diseases and heart attacks or strokes, a major cause of disease in the US. Laminarin as a potential cancer therapeutic is under intensive investigation (Miao et al. 1999).

Ulvan, porphyran and xylans

The name ulvan is derived from the original terms ulvin and ulvacin introduced by Kylin in reference to different fractions of *Ulva lactuca* water-soluble sulphated polysaccharides. It is now being used to refer to polysaccharides from members of the Ulvales, mainly *Ulva* and *Enteromorpha* spp. Ulvans are highly charged sulphated polyelectrolytes composed mainly of rhamnose, uronic acid and xylose as the main monomer sugars and containing a common constituting disaccharide: the aldobiuronic acid, [→4)-D-glucuronic acid-(1→4)-L-rhamnose3-sulphate-(1→]. Iduronic acid is also a constituent sugar. The average molecular weight of ulvans ranges from 189 to 8,200 kDa (Lahaye 1998). The cell wall polysaccharides of ulvales represent 38–54% of dry algal matter (Lahaye 1998). Two major kinds have been identified: water-soluble ulvan and insoluble cellulose-like material.

The mechanism of gel formation is unique among polysaccharide hydrogels. It is very complex and not yet fully understood. The viscosity of ulvan solutions as isolated polysaccharides has been compared to that of arabic gum. Whether ulvans present other functional properties of this gum remains to be established. The gelling properties of ulvans are affected by boric acid, divalent cations and pH. They are thermoreversible without thermal hysteresis. The gelling properties can be of interest for applications where gel formation needs to be precisely controlled (by pH or temperature), like the release of trapped molecules or particles under specific conditions (Percival and McDowell 1990; Lahaye et al. 1998). As already mentioned, highly absorbent, biodegradable hydrocolloid wound dressings limit wound secretions and minimise bacterial contamination. Polysaccharide fibres trapped in a wound are readily biodegraded. In the context

of bovine spongiform encephalopathy (mad cow disease) and other prion contamination diseases, macromolecular materials from algal biomasses such as ulvans can constitute an effective and low-cost alternative to meat-derived products because their rheological and gelling properties make them suitable substitutes for gelatin and related compounds (Choi et al. 1999).

Ulvans are a source of sugars for the synthesis of fine chemicals. In particular, they are a potential source of iduronic acid, the only occurrence to date of this rare uronic acid in plants (Lahaye and Ray 1996). Iduronic acid is used in the synthesis of heparin fragment analogues with anti-thrombotic activities, and obtaining it requires a lengthy synthetic procedure that could be more cost-effectively replaced by a natural source (Lahaye 1998). Oligosaccharides from *Ulva* could be used as reference compounds for analysing biologically active domains of glycosaminoglycan-like heparin. The use of oligo-ulvans as anticoagulant agents could be expected since other, rarer, sulphated polysaccharides, like dermatan sulphate or fucan in brown algae, have shown this anti-thrombinic activity. Regular oligomers from ulvans may provide better-tolerated anti-thrombinic drugs (Paradossi et al. 2002).

Rhamnose, a major component of ulvans, is a rare sugar used as a precursor for the synthesis of aroma compounds. Combinatorial libraries in glycopeptide mimetics are another example of the use of L-rhamnose in the pharmaceutical industry. The production of rhamnose from *Monostroma*, a Japanese species of Codiales, has been patented. Rare sulphated sugars such as rhamnose 3-sulphate and xylose 2-sulphate are also of interest (Lahaye and Robic 2007).

Other potential applications of ulvan oligomers and polymers are related to their biological properties. Recent studies have demonstrated that ulvans and their oligosaccharides were able to modify the adhesion and proliferation of normal and tumoural human colonic cells as well as the expression of transforming growth factors and surface glycosyl markers related to cellular differentiation (Lahaye and Robic 2007). Earlier work demonstrated strain-specific anti-influenza activities of ulvan from *U. lactuca*, and the use of rhamnan, rhamnose and oligomers from desulphated *Monostroma* ulvans has been patented for the treatment of gastric ulcers (Fujiwara-Arasaki et al. 1984; Nagaoka et al. 2003).

Oligomers from seaweed species such as *Laminaria* spp. or *Fucus serratus* have also been studied as plant elicitors. These are natural compounds which stimulate the natural defences of plants. Several products derived from brown algae are already marketed worldwide. The success is because of their size and availability rather than their chemical composition. *Ulva* cell walls bind heavy metals and ulvans are the main contributors with 2.8–3.77 meq g^{-1} polysaccharide. The ion exchange property of ulvans explains why they have been chosen as bioindicators for monitoring heavy metal pollution in coastal waters (Nagaoka et al. 1999).

In red algae, the fibrillar network is made of low crystalline cellulose, mannan or xylan and represents only about 10% of cell wall weight. It can also contain minor amounts of sulphated glucans, mannoglycans and complex galactans. Most of our current knowledge of red algal cell wall polysaccharides is on the gelling and thickening water-soluble galactans, agars and carrageenans used in various applications. Unlike most red seaweed generally studied, *P. palmata* does not produce matrix galactans, but instead (10/4)- and (10/3)-linked-b-D-xylan together with a minor amount of fibrillar cellulose and b-(10/4)-D-xylan. Xylans can be 35% of the dry weight of *Palmaria* (Lahaye et al. 2003). Xylans have not yet been of economic interest, and only few applications are known.

Species of *Porphyra* contain a sulphated polysaccharide called porphyran, a complex galactan. Porphyran is a dietary fibre of good quality and chemically resembles agar. A powder consisting of 20% nori mixed with a basic diet given orally to rats prevented 1,2-dimethylhydrazine-induced intestinal carcinogenesis. Porphyran showed appreciable anti-tumour activity against Meth-A fibrosarcoma. In addition, it can significantly lower the artificially enhanced level of hypertension and blood cholesterol in rats (Noda 1993).

Digestibility of polysaccharides

The majority of edible seaweed fibres are soluble anionic polysaccharides which are little-degraded or not fermented by the human colonic microflora (Lahaye and Kaeffer 1997). The amount of dietary fibres in marine algae not digested by the human digestive tract is higher than that of other food materials (Murata and Nakazoe 2001). Most of the total algal fibres disappeared after 24 h (range 60–76%) in in vitro fermentation of, e.g. *Laminaria digitata* and *U. pinnatifida* using human faecal flora. However, unlike the reference substrate (sugar beet fibres), the algal fibres were not completely metabolised to short-chain fatty acids (SCFA; range 47–62%). Among the purified algal fibres, disappearance of laminarins was approximately 90% and metabolism to SCFA was approximately 85%, in close agreement with the fermentation pattern of reference fibres. Sulphated fucans were not degraded. Sodium alginates (Na alginates) exhibited a fermentation pattern quite similar to that of the whole algal fibres, with a more pronounced discrepancy between disappearance and production of SCFA: disappearance was approximately 83%, but metabolism was only approximately 57%. Laminarin seemed to be a modulator of the intestinal metabolism by its effects on mucus composition, intestinal pH and short-chain fatty acid production, especially butyrate. The characteristic fermentation pattern of the total fibres from the brown algae

investigated was attributed to the peculiar fermentation of alginates (Michel et al. 1996; Deville et al. 2007).

Phycolloids are more or less degraded following adaptation of the human microflora, but none of the seaweed polysaccharides have been shown to be metabolised, although some may be partly absorbed. Nothing is known about the fate of other algal polysaccharides in the human digestive tract, except that they cannot be digested by human endogenous enzymes. Results of fermentation in vitro with human faecal bacteria indicate that brown seaweed fibres exhibit an original fermentation pathway (Mabeau and Fleurence 1993). Carrageenan is a good source of soluble fibre (Burtin 2003). Rats excrete carrageenan quantitatively in the faeces if it is administered in the diet at levels of 2–20%, and it therefore has no direct nutritive value (Hawkins and Yaphe 1965). Weight gain was significantly reduced, especially at higher levels. Furthermore, food efficiency showed interference with utilisation of other nutrients in the diet. Only 10–15% appeared digestible from faecal examination (Hawkins and Yaphe 1965). An experimental feeding with L. digitata seaweed extract in pig resulted in a higher production of butyric acid in the caecum and colon compared to the control group (Reilly et al. 2008). Butyrate is a beneficial metabolite for intestinal bacteria because it is quickly metabolised by colonoyctes and accounts for about 70% of the total energy consumption of the colon (Reilly et al. 2008). Therefore, it is desirable to promote butyrate production in the colon by laminarin fermentation.

The particular chemical structure of ulvan (and of Ulva) is responsible for the resistance of this polysaccharide to colonic bacterial fermentation. Consumption of dietary fibres from Ulva sp. could be expected to act mainly as bullring agents with little effect on nutrient metabolism due to colonic bacterial fermentation products (short-chain fatty acids; Bobin-Dubigeon et al. 1997). All soluble fibre fractions of P. palmata consisted of linear beta-1,4/beta1,3 mixed linked xylans containing similar amounts of 1,4 linkages (70.5–80.2%). The insoluble fibres contained essentially 1,4-linked xylans with some 1,3-linked xylose and a small amount of 1,4-linked glucose (cellulose). Soluble fibres were fermented within 6 h by human faecal bacteria into short-chain fatty acids (Lahaye et al. 1993).

Proteins, peptides and amino acids

Although the structure and biological properties of seaweed proteins are still poorly documented, the amino acid compositions of several species have been known for a long time (Murata and Nakazoe 2001).

The non-protein nitrogen is thought to be an intermediate or final product of nitrogen metabolism in plant tissue, and this fraction consists of amino acids, peptides, amines, and nucleotides and accounts for 10–20% of the nitrogen in seaweed (Arasaki and Arasaki 1983). Investigations found the biochemical composition of total nitrogen to be 57% in F. vesiculosus, of which 7–8% were the total nitrogen peptides and 10% free amino acids (Smith and Young 1953).

Habitat and especially seasonal variation have an effect on proteins, peptides and amino acids in seaweed (Arasaki and Arasaki 1983; Haug and Jensen 1954).

Proteins

The protein fraction of seaweed varies with the species, but is generally small in brown seaweed. Undaria has the maximal content of 24% dry weight, followed by several species (Sargassum, Fucus and Laminaria/Saccharina) with maxima around 17–21% and with Ascophyllum with the lowest content (maximum 10% of dry weight; Table 7). Higher protein contents are recorded for green and red seaweed. Proteins can represent up to 35%, 44% and 44% of dry matter in P. palmata (dulse), Porphyra tenera (nori) and Ulva spp., respectively. These levels are comparable to those found in high-protein vegetables such as soybeans, in which proteins make up 40% of the dry mass (Murata and Nakazoe 2001). The protein content in the fronds of Saccharina and Laminaria species and A. esculenta showed a pronounced maximum during the period from February to May, the young parts of the Saccharina and Laminaria species fronds being considerably richer than the old parts (Haug and Jensen 1954; Jensen and Haug 1956).

Most seaweed species contain all the essential amino acids and are a rich source of the acidic amino acids, aspartic acid and glutamic acid (Fleurence 2004). Whilst threonine, lysine, tryptophan, sulphur amino acids (cysteine and methionine) and histidine have been perceived as limiting amino acids in algal proteins, their general levels in algal proteins are higher than those found in terrestrial plants (Galland-Irmouli et al. 1999). The proteins from P. tenera exhibit an amino acid composition close to that of ovalbumin (Mabeau and Fleurence 1993). The combined glutamic acid and aspartic acid level accounts for 22–44% wet weight of the total amino acid fraction in Fucus sp. and 39–41% in Sargassum sp., whilst both amino acids together represent 18% wet weight of the total amino acid content of L. digitata proteins. An analogous result was reported for A. nodosum (Augier and Santimone 1978; Fleurence 2004; Munda 1977). Brown seaweed proteins have also been described as being a rich source of threonine, valine, leucine, lysine, glycine and alanine, with amino acids such as cysteine, methionine, histidine, tryptophan and tyrosine

Table 7 Total protein content (% of dry weight) in seaweed of Northwestern Europe

	Laminaria and Saccharina	Fucus	Ascophyllum	Undaria	Sargassum	Ulva		Chondrus	Porphyra	Graciliaria	Palmaria
Total protein	3–14%[a]	1.4%[f]	1.2%[f]	24%[n]	9%[r]	4–9%[t]		6–7%[s]	7%[t]	5%[s]	8–35%[z]
	5–20% (fronds)[b]	5–10%[i]	3.2% (total N)[k]	11–24%[o]	16%[s]	6%[u]		13–18%[n]	9–16%[s]	21%[h]	17%[aa]
	7–13% (stipes)[b]	6.2%[e]	4.8–9.8%[l]	13%[p]	20%[e]	6.3% total amino acids[v]		21%[x]	28%[h]	23%[s]	12–22%[bb]
	7.5%[c]	17%[g]	4.0–9.7%[m]	15%[q]		74% AA of PC[w]		27%[y]	30–50%[d]		
	10%[d]	57% (total N)[j]	5–10%[l]	16%[e]		7%[t,v]		29%[g]	34%[o]		
	11%[e]		5–12%[i]	20%[c]		24%[n]			39%[q]		
	12%[f]					28%[e]			44%[g]		
	16%[g]					31%[c]					
	21%[h]					34%[s]					
						39%[q]					
						44%[g]					

AA of PC: Amino acids of protein concentrate

[a] Jensen and Haug (1956); [b] Haug and Jensen (1954); [c] Dawczynski et al. (2007); [d] McHugh (2003); [e] Rupérez and Saura-Calixto (2001); [f] Rioux et al. (2007); [g] Marsham et al. (2007); [h] Wen et al. (2006); [i] Morrissey et al. (2001); [j] Smith and Young (1953); [k] Pavia et al. (1997); [l] Jensen (1960); [m] Larsen and Haug (1958); [n] Plaza et al. (2008); [o] Arasaki and Arasaki (1983); [p] Je et al. (2009); [q] Murata and Nakazoe (2001); [r] Robledo and Freile-Pelegrín (1997); [s] Marinho-Soriano et al. (2006); [t] Barbarino and Lourenço (2005); [u] Foster and Hodgson (1998); [v] Wong and Cheung (2000); [w] Wong and Cheung (2001c); [x] Ventura and Castañón (1998); [y] Ortiz et al. (2006); [z] Morgan et al. (1980); [aa] Mishra et al. (1993); [bb] Galland-Irmouli et al. (1999)

recorded at lower levels (Augier and Santimone 1978; Dawczynski et al. 2007; Fujiwara-Arasaki et al. 1984).

Red seaweed proteins in general, as with other seaweed groups, possess high quantities of the acidic amino acids, glutamic acid and aspartic acid, whilst basic amino acids are less dominant. However, some reports have shown that red algae in general appear to contain lower quantities of glutamic acid and aspartic acid compared to the other two algal groups (Fleurence 2004). Quantities range from 7.9% of total amino acids in *C. crispus*, 14% in *P. tenera* and up to 28% in *P. palmata* (Fujiwara-Arasaki et al. 1984; Galland-Irmouli et al. 1999; Young and Smith 1958). *Ulva armoricana* contains high levels of the amino acid proline (approximately 5–11%) of total amino acids, whilst *U. pertusa* is reported to have an arginine content of 15% (Fujiwara-Arasaki et al. 1984; Fleurence et al. 1995).

Bioactive lectins are found in macroalgal species such as *Ulva* sp., *Eucheuma* spp. and *Gracilaria* sp. (Table 8). Lectins are a structurally diverse group of carbohydrate-binding proteins of non-immune origin found in a wide range of organisms (Hori et al. 2000). Lectins purified from the green marine algae *Codium fragile* subsp. *tomentosoides* have been produced and sold commercially (Smit 2004). Lectins interact with specific glycan structures linked to soluble and membrane-bound glycoconjugates. It is these protein–carbohydrate interactions that are responsible for lectin involvement in numerous biological processes such as host–pathogen interactions, cell–cell communication, induction of apoptosis, cancer metastasis and differentiation, as well as recognising and binding carbohydrates (Hori et al. 2000). Furthermore, lectin has been found to increase the agglutination of blood cells (erythrocytes) and is also useful in the detection of disease-related alterations of glycan synthesis, including infectious agents such as viruses, bacteria, fungi and parasites (Bird et al. 1993; Cardozo et al. 2007; Murata and Nakazoe 2001). Other bioactive properties exhibited by marine algal lectins include antibiotic, mitogenic, cytotoxic, anti-nociceptive, anti-inflammatory, anti-adhesion and anti-HIV activities (Bird et al. 1993; Mori et al. 2005; Smit 2004). Lectins from three *Eucheuma* species, *E. serra*, *E. amakusaensis* and *E. cottonii* have shown strong mitogenic activity on mouse and human lymphocytes, whilst a marine glycoprotein *E. serra* agglutinin (ESA) derived from *E. serra* exhibits a cytotoxic effect against several cancer cell lines, such as colon cancer Colo201 cells and cervical cancer HeLa (Kawakubo et al. 1997, 1999; Sugahara et al. 2001). It was also reported that ESA-2, a lectin isolated and characterised from *E. serra*, suppressed colonic carcinogenesis in mice when orally administered and exhibited growth inhibition of 35 human cancer cell lines (Hori et al. 2007). This phycolectin was found to inhibit adenosine diphosphate and collagen-induced human platelet aggregation in a dose-dependent manner.

Antibacterial lectins have also been isolated from *E. serra* and *Galaxaura marginata* (Liao et al. 2003). These carbohydrate-binding proteins exhibit antibacterial activity against the fish pathogen *Vibrio vulnificus*. Aggregation and immobilisation of *V. vulnificus* cells were observed following incubation of the cells with glycoprotein molecules because lectins recognise and bind to complementary

Table 8 Source species and bioactivity of proteins, peptides and amino acids from seaweed

	Characteristics	Source and content	Bioactivity
Protein total	Total	22 different species[a]	Stimulates mitogenesis in human lymphocytes[a]
			Agglutinates erythrocytes in bacteria, rabbits and sheep[a]
Protein	Lectin	*Ulva* sp.	Antibiotic[f]
		Gracilaria sp.	Antibacterial against the fish pathogen *Vibrio vulnificus*[c]
		Codium fragile, subsp. *tomentosoides*	Host–pathogen interactions[g]
			Anti-inflammatory[f]
			Cell–cell communication[g]
		Eucheuma serra[b,c]	Anti-nociceptive[f]
		Eucheuma amakusaensis[b]	Mitogenic[f] effect on mice an human lymphocytes[b]
			Induction of apoptosis, metastasis and differentiation[g]
		Eucheuma cottonii[b]	Recognising and binding of carbohydrates[g], including viruses, bacteria, fungi and parasites[h,a]
		Galaxaura marginata[c]	Anti-HIV[f,d]
		Griffithsia sp.[d]	Anti-adhesion[f]
		Hypnea japonica[e]	Cytotoxic[f]
			Inhibit human platelet aggregation[e]
	Agglutinin glycoprotein	*Soleria robusta*[i]	Mitogenic on mice spleen lymphocytes[i]
		Eucheuma serra[i,b]	Cytotoxic[i] against several cancer cell lines (incl. Colo201 and HeLa)[b]
			Anticancer: inhibited growth of mice leukaemia cells (L1250) and FM3A tumour cells[i], suppressed colonic carcinogenesis in mice and growth inhibition of 35 human cancer cell lines[i]
	Mycin-binding agglutinin	*Hypnea cervicornis*[j]	Anti-inflammatory activity[j]
Peptides	Depsipeptide (Kalahide F)	*Bryopsis* sp.[f]	Anticancer[f]
			Anti-tumour[f]
			Anti-AIDS[f]
	Hexapeptide (SECMA 1)	*Ulva* sp.[k]	Mitogenic[k]
			Involved in the modulation of cell proliferation-associated molecules, proteoglycans and glycosaminoglycans, in human foreskin fibroblasts[k]
	Cyclic pentapeptid (Galaxamide)	*Galaxaura filamentous*[l]	Anticancer: anti-proliferative activity against human renal cell carcinoma GRC-1 and human hepatocellular carcinoma HepG2 cell lines[l]
	Dipeptide	*Undaria pinnatifida*[m,n]	Reduced blood pressure in rats[m,n]
			Inhibitory activity on angiotensin-converting enzyme[n]
	Oligopeptide	Red algae[o]	Analogue action of that of neurotransmitter γ-aminobutyric acid[o], which can reduce migratory activity in SW 480 colon carcinoma cell[p]
			Proposed applications diagnosis and therapy of certain brain and central nervous system disorders[q] like epilepsy[p]
	Peptides	*Porphyra yezoensis*[r]	Inhibitory activity on angiotensin-converting enzyme[s,r]
		Hizikia fusiformis[r]	Reduction in plasma and hepatic cholesterol in rats[s]
		Ecklonia cava[s]	Improvement of hepatic function in rats[s]
		Acanthophora delilei[t]	Reduction in plasma glucose levels[s]
			Antioxidant[t] and superoxide dismutase-like activity in a linoleic acid system[s]
Amino acids	Taurine (not a true amino acid)		Anti-hypertensive[u,v]
			Hypocholesterolemic[u] in serum and liver of rats[v]
			Anti-diabetic[v]
			Preventive effect of vascular diseases[v]
			Preventive effect of chronic hepatitis[v]
			Antioxidant properties[u]
	Laminine (trimethyl (5-amino-5-carboxypentyl) ammonium oxalate)	*Laminaria angustata*[w] *Chondria armata*[w]	Hypertensive effect[w]
			Depress contraction of smooth muscles[w]

Characteristics	Source and content	Bioactivity
Kanoids (kainic and domoic acid)	*Digenia simplex*[f,w,x]	Insecticidal properties[x]
	Chondria armata[f,w,x]	Anthelmintic properties[f,w,x]
	Palmaria palmata[y]	Neuroexcitatory properties[x]
		Research on effect of Alzheimer's and Parkinson's disease and epilepsy[f]

[a] Bird et al. (1993); [b] Kawakubo et al. (1997, 1999) and Sugahara et al. (2001); [c] Liao et al. (2003); [d] Mori et al. (2005); [e] Matsubara et al. (1996); [f] Smit (2004); [g] Hori et al. (2000); [h] Cardozo et al. (2007) and Murata and Nakazoe (2001); [i] Hori et al. (1988); [j] Bitencourt et al. (2008); [k] Ennamany et al. (1998); [l] Xu et al. (2008); [m] Sato et al. (2002); [n] Suetsuna et al. (2004); [o] Morse (1991); [p] Joseph et al. (2002); [q] Aneiros and Garateix (2004); [r] Suetsuna (1998a, b); [s] Cha et al. (2006); [t] Arasaki and Arasaki (1983) and Shiu and Lee (2005); [u] Lourenço and Camilo (2002), Militante and Lombardini (2002), Zhang et al. (2003) and Houston (2005); [v] Mochizuki et al. (1999); [w] Bhakuni and Rawat (2005); [x] Parsons (1996); [y] Lüning (2008)

carbohydrates or glycoproteins on either the cell walls or plasma membranes of the associated bacteria cells. As a result, the microorganisms are immobilised and further growth and multiplication is prevented (Liao et al. 2003).

Mucin-binding agglutinin and isoagglutinin glycoproteins isolated from two different species of red algae possessed anti-inflammatory activity and showed mitogenic activity on mouse spleen lymphocytes, and they inhibited the growth of mouse leukaemia cells L1210 and mouse FM3A tumour cells (Bitencourt et al. 2008; Hori et al. 1988).

Phycobiliproteins are described later.

Peptides

The light-harvesting complex fucoxanthin, from brown algae, has been found to contain four 20-kDa polypeptides. The gene coding sequences for these polypeptides (*lhcf* genes) show homology to those found in *Macrocystis pyrifera* and *L. digitata* (two *Laminariales*) and indicate that these proteins are probably similar in all brown algae (Douady et al. 1994; Martino et al. 2004). Eisenine is isolated from *Eisenia bicyclis*; octaglutamic acid and L-pyrrolidonoyl-L-glutamyl-L-glutamine are isolated from *Pelvetia canaliculata*; carnosine in *Acanthophora delilei* and many peptides, including glutamic and aspartic acid, are found in *L. japonica* (Arasaki and Arasaki 1983). The two antioxidant peptides, carnosine and glutathione, that are generally present in high concentrations in animal muscle have also been found in marine macroalgae (Arasaki and Arasaki 1983; Shiu and Lee 2005).

The depsipeptide kahalalide F from *Bryopsis* sp. is active in the treatment of lung cancer, tumours and AIDS (Smit 2004). In addition, ten dipeptides from hot water extracts of *U. pinnatifida* reduced blood pressure in spontaneously hypertensive rats and showed angiotensin-converting enzyme (ACE) inhibitory activity (Sato et al. 2002; Suetsuna et al. 2004). Peptides with ACE inhibitory activity have been isolated from *Porphyra yezoensis* and *Hizikia fusiformis* (Suetsuna 1998a, b). Aqueous extracts of ten green algae and 19 brown algae extracted at 70°C also exhibited

ACE inhibitory activity, with the highest activity associated with *Ecklonia cava* (Cha et al. 2006). In addition, plasma and hepatic cholesterol-reducing actions were observed when feed containing hydrolysates was administered to rats. This feed was also shown to improve rat hepatic function and reduce plasma glucose levels. Furthermore, fractions of the pepsin hydrolysates were reported to have superoxide dismutase (SOD)-like and antioxidant activity in a linoleic acid system.

A mitogenic hexapeptide, SECMA 1, has been isolated from *Ulva* sp. This peptide was shown to be involved in the modulation of cell proliferation-associated molecules, proteoglycans and glycosaminoglycans in human foreskin fibroblasts (Ennamany et al. 1998). In addition, a rare cyclic pentapeptide, Galaxamide, obtained from the marine alga *Galaxaura filamentous* has been shown to exhibit anti-proliferative activity against human epithelial cancer cell lines (Xu et al. 2008).

A number of oligopeptides that act like analogues of the neurotransmitter γ-aminobutyric acid (GABA) have been discovered in red algae. These analogue compounds bind to GABA sub(A) receptors, and some are even more active than GABA itself. The proposed applications for these oligopeptides are in both the diagnosis and therapy of certain brain and central nervous system disorders caused by the malfunction of systems controlled by GABA (Aneiros and Garateix 2004).

Free amino acids

The free amino acid fraction of seaweed is mainly composed of alanine, amino butyric acid, taurine, ornithine, citruiline and hydroxyproline. Levels differ according to the species. The characteristic taste of nori is caused by the large amounts of the three amino acids: alanine, glutamic acid and glycine. In *P. tenera*, alanine amounting to about 25% of the total free amino acids probably accounts for the faintly sweet taste (McHugh 2003).

Ulva contains large amounts of cysteinolic acid, cysteic acid, praline, glutamic acid and chondrine, and *Undaria*

contains abundant alanine, glycine and praline, whereas the arginine content is high in *Gracilaria*. In addition, such amino acids as citrulline, praline, taurine, arginine and ornithine accumulate in cells (Arasaki and Arasaki 1983). Certain species have a high level of arginine (*U. pertusa, U. pinnatifida* and *P. tenera*) or glycine (*P. tenera*). The major amino acids in *C. crispus* are arginine (34%) and amide N (10% of total N). Furthermore, citrulline and ornithine (6% and 7% of total N, respectively) have been established as occurring both in the free state and in simple and complex peptides in *C. crispus*, but not in the insoluble protein (Table 9; Young and Smith 1958).

The eight essential amino acids (cystine, isoleucine, leucine, lysine, methionine, phenylalanine, tyrosine and valine) cannot be synthesised by animals, nor can they be replaced by other "less valuable" building blocks. Generally, the first limiting amino acid in most of the proteins of marine algae is lysine, one of the essential amino acids (Murata and Nakazoe 2001), and the various edible seaweed exhibit similar essential amino acid patterns (Mabeau and Fleurence 1993). All essential amino acids were detected in some brown and red seaweed species, and red species featured uniquely high concentrations of taurine when compared to brown seaweed varieties (Dawczynski et al. 2007). Taurine is mostly found in fish, shellfish and seaweed. The taurine content is at a level of 400 mg g^{-1} dry weight in *S. latissima* and *P. tenera*, which is also the case in lobster, crab, shellfish and squid (Murata and Nakazoe 2001). Taurine is not a true amino acid due to the lack of a carboxyl group, but contains a sulfonated acid group instead. This amino acid is not used as building blocks in proteins but is found in, e.g. the gall bladder, where it works as an emulsifier which binds and eases the uptake of lipids. Taurine is important for the formation of bile by which cholesterols are bound. Taurine thereby facilitates reduction of cholesterol content in the blood of humans (Mouritsen 2009). In addition to its requirement for a number of biological and physiological functions, taurine has been identified as having a number of health-promoting properties, e.g. anti-hypertensive, hypocholesterolemic and antioxidant properties, to name but a few (Lourenço and Camilo 2002). Taurine leads to decreases in the concentration of cholesterol in both the serum and liver of rats, prevention effect of vascular diseases, chronic hepatitis and diabetes (Mochizuki et al. 1999).

In addition to taurine, other bioactive amino acids such as laminine, kainoids and mycosporine-like amino acids have been found in marine macroalgae. Laminine, a choline-like basic amino acid, has been isolated from *Laminaria angustata* and *Chondria armata* (Bhakuni and Rawat 2005). This amino acid was reported to depress the contraction of excited smooth muscles, whilst laminine monocitrate was shown to exert a transitory hypotensive

effect (Bhakuni and Rawat 2005). The kainoid amino acids, kainic and domoic acids have also been found in numerous algal species, but extracted from *Digenea simplex* and commercialised (Smit 2004). Several preparations of kainic acids are available, and these include 'Digenin' and 'Helminal' (Bhakuni and Rawat 2005). Kainoids are a unique group of unusual amino acids which are related structurally to, and have similar functions to, the acidic amino acids aspartic acid and glutamic acid. They have attracted considerable interest due to their high insecticidal, anthelmintic and neuroexcitatory properties (Parsons 1996). Moreover, *D. simplex* and *C. armata* extracts containing domoic and kainic acid have been used as anthelmintic agents for centuries in Japan for the treatment of ascariasis (a disease in humans caused by the parasitic roundworm; Bhakuni and Rawat 2005; Parsons 1996; Smit 2004). These compounds are currently being used in research associated with neurophysiological disorders such as Alzheimer's and Parkinson's disease and epilepsy (Smit 2004).

Nutritional value and digestibility of seaweed proteins

The nutritional value of proteins referred to as "amino acid score" is evaluated based on the composition of essential amino acids. The amino acid score of the proteins of the marine algae ranges from 60 to 100, a value higher than that of the proteins in cereal and vegetables. The amino acid score of proteins in *Porphyra* and *Undaria* was 91 and 100, respectively, the same as that of animal foods (Murata and Nakazoe 2001).

The in vivo digestibility of seaweed proteins is not well documented, and available studies about their assimilation by humans have not provided conclusive results. However, several researchers have described a high rate of seaweed protein degradation in vitro by proteolytic enzymes such as pepsin, pancreatin and pronase, with pronase as the most digestive enzyme. For instance, the digestibility in vitro of proteins from *P. tenera, U. pinnatifida* and *U. pertusa* is 78%, 87% and 95%, respectively (Fleurence 1999). Digestibility of *U. lactuca* protein concentrates was 86%, determined by a multi-enzyme method using different trypsins and peptidases (Wong and Cheung 2001c). However, for brown seaweed species, the high phenolic content might limit protein availability in vivo and thus moderate in vitro figures. This situation is probably not found for the green and red seaweed which possess low levels of phenols and higher protein content (Mabeau and Fleurence 1993).

Lipids

Lipids are a broad group of naturally occurring molecules which includes fats, waxes, sterols, fat-soluble vitamins

Table 9 Proximate amino acids (% of total N or % of total protein N) in seaweed of Northwestern Europe

Amino acids (AA)	Laminaria and Saccharina % of total AA[a]	Fucus % of total N[b]	Undaria % of total AA[o] or protein[c]	Sargassum % of total N[b] or protein[d]	Ulva % of total AA[a,c] or protein[e]	Chondrus % of total N[f] % of total AA[a]	Porphyra % of total protein[g]	Gracilaria % of total N[h]	Palmaria % of total AA[a] or protein[i]
Alanin	8.0–9.0[a]	5.4	1.3[o] 4.8[c]	6.2[b] 6.9[d]	8.5[a] 1.8[e] 6.1[c]	3.8[f] 6.4[a]	7.4[c]		7.5[a] 6.7[i]
Arginine	5.0–5.9[a]	9.4	0.52[o] 7.5[c]	10[b] 2.6[d]	5.1[a] 3.0[e] 15[c]	34[f] 6.8[a]	16[g] 16[c]		6.2[a] 5.7[i]
Aspartic acid	9.6–9.8[a]	9.0	1.3[o] 5.6[c]	7.6[b] 13[d]	9.2[a] 6.5[c]	3.8[f] 8.5[a]	7.0[g] 7.0[c]		9.3[a]
Citrulline						5.8[f]			
Cystine[j]	0.6–1.3[a]	+	0.11[o] 0.5[c]	3.7[b] 0.0[d]	2.2[a] 1.2[c]	2.6[a]	0.3[g] 0.3[c]		1.3 0[i]
Glutamic acid	11–13[a]	11	2.1[o] 5.1[c]	3.7[b] 17[d]	10[a] 3.2[e] 6.9[c]	4.1[f] 9.9[a]	7.2[g]		13[a] 9.9[i]
Glycine	6.5–7.0[a]	5.4	0.6[o] 4.4[c]	0.6[b] 6.3[d]	7.0[a] 2.2[e] 5.2[c]	3.5[f] 7.3[a]	7.2[g]		7.2[a]
Histidine	2.3–2.4[a]	1.6	1.3[o] 2.7[c]	4.1[b] 1.4[d]	1.8[a] 4.6[e] 4.0[c]	0.9[f] 2.1[a]	1.4[g]		2.1[a] 13[i]
Hydroxyproline		–		3.4[b]					2.3[i]
Isoleucine[j]	5.5–5.8[a]	3.0	0.5[o] 2.9[c]	4.7[d]	6.1[a] 2.8[e] 3.5[c]	1.8[f] 5.7[a]	4.0[g]	3.0	5.3[a]
Leucine[j]	8.7–9.2[a]	5.0	0.9[o] 5.1[c]	0.4[b] 7.8[d]	9.2[a] 5.0[e] 6.9[c]	2.9[f] 7.8[a]	8.7[g]	4.5	7.8[a] 7.1[a]
Lysine[j]	6.5–7.3[a]	6.0	0.6[o] 4.3[c]	6.9[b] 5.8[d]	6.3[a] 17[e] 4.5[c]	4.9[f] 8.1[a]	4.5[g]	3.2	8.2[a] 3.3[i]
Methionine[j]	1.9–2.2[a]	0.4	0.32[o] 2.2[c]	0.0[b] 0.9[d]	1.8[a] 19[e] 1.6[c]	0.5[f] 1.5[a]	1.7[g]	+cysteine >1.3	1.9[a] 2.7[i]
Ornithine	n.d.[a]				n.d.[a]	7.1[f] 2.1[a]			n.d.[a]
Phenylalanine[j]	5.7–6.2[a]	2.6	0.6[o] 3.7[c]	0.4[b] 4.3[d]	6.3[a] 13[e] 3.9[c]	1.5[f] 5.2[a]	3.9[g]	+tyrosine 5.6	5.2[a] 5.1[i]
Proline	4.8–4.9[a]	3.3	0.6[o] 2.8[c]	9.5[b] 4.4[d]	5.2[a] –[e] 4.0[c]	1.9[f] 4.7[a]	6.4[g]		4.4[a]
Serine	3.8–3.9[a]	3.5	0.5[0] 2.8[c]	5.5[d]	4.0[a] 5.4[e] 3.0[c]	2.2[f] 3.9[a]	2.9[g]		4.6[a] 6.3[i]
Threonine	4.6–5.0[a]	3.3	2.4[c]	6.0[d]	4.6[a] 5.6[e] 3.1[c]	2.2[f] 4.2[a]	4.0[g]	3.0	4.5[a] 3.6[i]
Tryptophan		–	0.8[c]	1.9[b] nd[d]	0.3[c]		1.3[g]		
Tyrosine[j]	4.0–4.3[a]	1.2	1.6[c]	1.8[b] 3.9[d]	5.0[a] 2.6[e] 1.4[c]	1.0[f] 6.3[a]	2.4[g]		4.5[a] 3.4[i]

Table 9 (continued)

Amino acids (AA)	*Laminaria* and *Saccharina* % of total AA[a]	*Fucus* % of total N[b]	*Undaria* % of total AA[o] or protein[c]	*Sargassum* % of total N[b] or protein[d]	*Ulva* % of total AA[a,c] or protein[e]	*Chondrus* % of total N[f] % of total AA[a]	*Porphyra* % of total protein[g]	*Gracilaria* % of total N[h]	*Palmaria* % of total AA[a] or protein[i]
Valine[j]	6.9[a]	3.0	4.1[c]	8.3[b] 3.4[d]	7.7[a] 5.6[e] 4.9[c]	2.7[f] 7.0[a]	6.4[g]	3.0	7.3[a] 6.9[i]
Amide N						10[f]			
Ammonia		15		11[b]					
Total amino acids			13[o]						36[a]
Lys-Met-Cys-Trp-Thr-score	0.7[k]		0.9[k]	0.7[k]			1.0[k]		
Amino acid score (AAS)	31[k]		100[l] 61[k]	82[l] 40[k]			91[l] 62–64[k]		
Essential amino acid index (EAAI)	66[k]		96[k]	40[d] 81[k]	37[m] 39[n]		90–91[k]		

N nitrogen

[a] Mai et al. (1994); [b] Smith and Young (1953); [c] Arasaki and Arasaki (1983); [d] Wong and Cheung (2001a); [e] Wahbeh (1997); [f] Young and Smith (1958); [g] Mabeau and Fleurence (1993); [h] Wen et al. (2006); [i] Galland-Irmouli et al. (1999); [j] Essential amino acid; [k] Dawczynski et al. (2007); [l] Murata and Nakazoe (2001); [m] Wong and Cheung (2000); [n] Wong and Cheung (2001c); [o] Je et al. (2009)

(such as vitamins A, D, E and K), mono-, di- and triacylglycerols, diglycerides, phospholipids, and others. Lipids account for about 40% of the total calories in most industrialised countries; they reduce the bulk of the diet because of the concentrated source of energy and are indispensable from the human diet as they form the major sources of essential fatty acids and contain fat-soluble substances like vitamins and carotenoids. Vegetable oils contribute 70% of the dietary lipids, whilst marine oils contribute about 2% of the global oil production, with the remainder coming from fats from land animals. The per capita consumption of marine oils is approximately 1 g day^{-1}. Vegetable oils usually consist of saturated and unsaturated fatty acids with 16- and 18-carbon chain lengths (C16 and C18), whilst marine oils mainly consist of C14–C22 fatty acids (Narayan et al. 2006).

Murata and Nakazoe (2001) state that phospholipids are the main source of lipids in marine algae, contrary to Le Tutour (1990), Bhaskar et al. (2004) and Khotimchenko (2005) who claim that the glycolipids are the major lipid class in all seaweed, followed by neutral and phospholipids. Besides fatty acids, the unsaponifiable fraction of seaweed contains carotenoids, such as β-carotene, lutein and violaxanthin in red and green algae and fucoxanthin in brown algae, as well as tocopherols and sterols (Table 10; see also later chapters; Jensen 1969b). Lipids represent up to 4.5% of the seaweed on a dry weight basis, and this content is lower than that of other marine organisms. Their contribution as a food energy source thus appears to be low (Table 11; Mabeau and Fleurence 1993; Murata and Nakazoe 2001). Like other biochemical components, the fatty acid content

Table 10 Composition of lipids in seaweed related to total lipids extract and (in parentheses) amount of pigments in the fraction (% of total lipids; Khotimchenko 2005; Le Tutour 1990)

	Neutral lipids Triacylglyceride	Glycolipids Monogalactosyldiacylglycerides Diagalactosyldiacylglycerides Sulfoquinovosyldiacylglycerides	Phospholipids Phosphatidylcholines Phosphatidylglycerines Phosphatidylinosites Phosphatidylethanolamines Inositephosphoceramides
Fucus vesiculosus	18.0 (26.7)	33.5 (3.9)	4.7 (1.9)
Fucus serratus	18.3 (45.4)	30.1 (~0)	2.7 (3.5)
Ascophyllum nodosum	38.7 (23.1)	32.6	4.7 (1.5)
Gracilaria verrucosa	5.5	63.3	31.2

Table 11 Fatty acid profiles of the seaweed species of interest in Northwestern Europe

	Common name	Brown					Green	Red			
		Laminaria and *Saccharina*	*Fucus*	*Ascophyllum*	*Undaria*	*Sargassum*	*Ulva*	*Chondrus*	*Porphyra*	*Gracilaria*	*Palmaria*
Total		0.3–1.8%[a] 0.5%[b,c] 0.6% (stipe)[d,a] 0.7–2.9%[d] 1%[e,c] 1.8%[f] 2%[g] 2.1%[h]	0.5–1.5%[i] 0.5–2%[c] 1.4[h] 1.8%[b] 3.1%[j,i]	1.2%[h] 1.9–4.8%[k] 2–4%[c]	1%[l] 2.4%[j,m] 3.2%[n] 4.5%[e]	0.5%[o] 1.4%[e] 2.6–3.8%[c] 3.9%[j]	0.3%[m-p] 0.5%[b] 0.6–0.7%[q] 0.6–1%[c] 1.6%[r]	0.7%[s] 1–3%[c]	0.12–2.5%[c] 0.6%[f] 0.7%[b,t,q] 1.0%[l] 1–2.8%[e] 1.9%[n]	0.4%[o] 0.9%[f] 1.5%[u] 2.6%[v]	0.2–3.8%[w] 0.7–3%[c] 2.0%[x]
Sterols								0.02%[s]			
C10:0	Capric acid					16%[j]					
C12:0	Lauric acid	0.06%[e]	0.1%[j]		n.d.[e]	n.d.[e] 0.03%[j]	0.14%[m] 1.3%[y]		0.06%[e]		
C14:0	Myristic acid	2.9%[e]	14%[j]		2.3%[e] 3.2%[l] 4.5%[j]	0.30%[e] 5.2%[j]	1.1%[m] 1.5%[y]	1.0%[s]	3.4%[e] 0.53%[l]	5.1%[v] 4.6%[u]	6.4%[x]
C15:0		0.40%[e]			0.21%[e]	0.17%[e]	0.20%[m] 1.1%[y]		0.41%[e]	0.8%[v]	
C16:0	Palmitic acid	23–36%[e,n]	10%[j] 24%[i] 24%[i]		11–14%[e,n] 17%[l] 25%[j]	27%[e] 24%[j]	14%[m] 3.2%[y]	12%[s]	23–34%[e,n] 63%[l]	30%[v] 33%[u] 33%[f]	23%[x]
C17:0		0.16%[e]			0.20%[e]	0.04%[e]			0.19%[e]		
C18:0	Stearic acid	1.5–2.3%[e,n]	1.0%[j]		0.86–1.1%[e,n] 0.69%[l] 3.0%[j]	0.76%[e] 1.0%[j]	8.4%[m] 1.4%[y]	3.5%[s]	0.7–1.3%[e,n] 1.2%[l]	3.3%[v] 2.0%[u] 6.8%[f]	1.1%[x]
C20:0		0.28%[e]			0.39%[e]	0.04%[e]	0.19%[m] 6.5%[y]		0.33%[e]		
C22:0		n.d.[e]			n.d.[e]	0.01%[e]	0.27%[m]		0.21%[e]		
C24:0		n.d.[e]			n.d.[e]	n.d.[e]	9.5%[m]		0.09%[e]		
C14:1(n5)		n.d.[e]			n.d.[e]	n.d.[e]			0.03%[e]		
C14:1 (n9)							4.8%[y]				
C16:1(n7)	Palmitoleic acid	1.7%[e]	1.2%[j]		0.44%[e] 3.7%[l]	0.15%[e] 8.0%[j]	1.9%[m] 3.6%[y]	6.1%[s]	2.0%[e] 6.2%[l]	2.7%[v] 2.2%[u] 1.6%[f]	5.2%[x]
C16:1(n5)											1.2%[x]
C16:1trans										0.3%[v] 0.4%[u]	
C16:2 (n-6)							20.3%[y]				
C16:3 (n-4)					2.3%[l]				1.56%[l]		
C16:3 (n-6)							0.5%[y]				
C16:4 (n-3)							6.1%[y]				
C17:1(n7)		0.13%[e]			0.12%[e]				0.2%[e]		
∑C18:1		13–28%[e,n]			5.0–6.0%[e,n]	7.7%[e]			3.1–11%[e,n]		
C20:1(n9)		1.6%[e]			n.d.[e]	4.09%[e]	2.1%[y]		1.5%[e] 4.7%[l]		
C22:1(n11)		0.02%[e]			n.d.[e]	n.d.[e]			1.5%[e]		
C22:1(n13)		0.96%[e]			n.d.[e]	0.64%[e]			0.58%[e]		
C18:1(n9cis)	Oleic acid		22%[i] 25%[j] 22%[i]		6.8%[l] 19%[j]	8.5%[j]	27%[m] 6.9%[y]	9.4%[s]	6.7%[l]	7.3%[v] 8.4%[u] 31%[f]	2.8%[x]
C18:1 (n7)					–	–			1.29%[l]		5.2%[x]
C18:1 (n5)							1.3%[y]				
C18:2 (n-6)	Lineoleic acid	5.5–7.9%[e,n]	12%[j]		6.1–7.4%[e,n] 6.1%[j]	3.6%[e] 8.1%[j]	8.3%[m] 9.7%[y]	1.6%[s]	1.8–5.5%[e,n] 1.17%[l]	2.1%[v] 1.3%[u]	1.4%[x]

Table 11 (continued)

	Common name	Brown					Green	Red			
		Laminaria and Saccharina	Fucus	Ascophyllum	Undaria	Sargassum	Ulva	Chondrus	Porphyra	Graciliaria	Palmaria
					6.2%[l]					22%[f]	
C18:2 (n9)							9.4%[y]				
C20:2 (n-6)		0.87%[e]			0.12%[e]	0.97%[e]	3.0%[y]		0.71%[e]		
C18:3(8t,10t,12c)		n.d.[e]			0.34%[e]	0.56%[e]			0.53%[e]		
C18:3 (n-3)	Linolenic acid (n-3)	0.8–3.9%[e,n]	3.4%[j]		2.8%[j]	0.41%[e]	4.4%[m]	4.3%[s]	0.2–3.3%[e,n]	0.5%[v]	
					11–12%[e,n]	2.2%[j]	7.1%[y]			1.0%[f]	
					12%[l]				0.23%[l]		
C18:3 (n-6)	Gamma linolenic acid (n-6)	1.6%[e]	1.1%[j]		1.7%[e]	0.42%[e]	5.6%[y]		1.18%[e]	0.3%[v]	1.1%[x]
					2.2%[j]						
C20:3 (n-6)			1.2%[e]		0.57%[e]	3.2%[e]			1.1%[e]	2.6%[v]	
										2.8%[u]	
C20:3 (n-3)		0.01%[e]			0.14%[e]	0.09%[e]			0.10%[e]		
C18:4 (n-3)	Octadecatetraenoic acid	1.2–3.9%[l,n]	4.3%[j]		15%[j]	n.d.[e]	0.41%[m]	6.6%[s]	2.4–3.9%[e,n]		2.2%[x]
					26-up to 40%[e,z,n]	3.2%[j]	Up to 40%[z]		0.24%[l]		
					23%[l]		4.6%[y]				
C20:4 (n-3)		0.5%[n]			0.8%[n]				0.8%[n]		
					0.70%[l]				0.07%[l]		
C20:4 (n-6)	Arachidonic acid	11–12%[e,n]	14%[i]		12–13%[e,n]	5.3%[e]	0.34%[m]	20%[s]	4.6–8.9%[e,n]	37%[v]	2.6%[x]
			24%[j]		16%[l]	19%[j]			6.8%[l]	41%[u]	
			14%[i]		19%[j]					2.72%[f]	
C20:5 (n-3)	Eicosapentanoic acid (EPA- ω3)	5.4–16%[e,l,n]	3.6%[j]		13–15%[e,n]	42%[e]	1.0%[m]	35%[s]	6.0–54%[e,l,n]	1.0%[v]	47%[x]
					9.4%[l]	2.5%[j]				0.5%[u]	
					2.9%[j]				6.0%[l]	2.8%[f]	
					present[aa]						
C22:5n-3 (n-3)		n.d.[e]			n.d.–15%[e,n]	0.09%[e]			0.05%[e]		
C22:6n-3 (n-3)	Docosahexaenoic acid (DHA)	n.d.[e]			n.d[e,n]	n.d.[e]	0.8%[m]		None[e,n]		
						1.8%[j]					
Other										7.0%[v]	1.1%[x]
										3.8%[u]	
PUFA (ω3)		25%[bb]			present[aa]		6.6%[m]	68%[s]	7.2%[l,bb]		26%[bb]
					45%[l,bb]						
PUFA (ω6)		21%[bb]			22%[bb]				8.0%[bb]	45%[u]	2.1%[bb]
15-HETE, 13-HODTA, and 13-HODE [u]		100–1,000 μg/g dw[cc]									
Saturated FA					20%[l]		34%[m]		65%[l]	39%[u]	
Monosaturated FA					11%[l]				19%[l]	11%[u]	
Ratio n-6/n-3		1.3[e]			0.5[e,l,bb]	0.3[e]	1.3[m]		0.6–1.8[e]		0.1[bb]
		0.81[bb]							1.2[l,bb]		

Fatty acid content (total) and composition given in mean (% of dry weight and % of total fatty acid, respectively)

[a] Jensen and Haug (1956); [b] Marsham et al. (2007); [c] Morrissey et al. (2001); [d] Haug and Jensen (1954); [e] Dawczynski et al. (2007); [f] Wen et al. (2006); [g] McHugh (2003); [h] Rioux et al. (2007); [i] Kim et al. (1996); [j] Herbreteau et al. (1997); [k] Jensen (1960); [l] Plaza et al. (2008); [m] Ortiz et al. (2006); [n] Murata and Nakazoe (2001); [o] Marinho-Soriano et al. (2006); [p] Foster and Hodgson (1998); [q] Indergaard and Minsaas (1991); [r] Wong and Cheung (2000); [s] Tasende (2000); [t] Arasaki and Arasaki (1983); [u] Khotimchenko (2005); [v] Khotimchenko and Levchenko (1997); [w] Morgan et al. (1980); [x] Mishra et al. (1993); [y] Wahbeh (1997); [z] Ishihara et al. (2000); [aa] Khan et al. (2007); [bb] MacArtain et al. (2007); [cc] Rasmussen and Morrissey (2007)

varies with the season and other environmental factors. It is generally known that algae can accumulate polyunsaturated fatty acids (PUFAs) when there is a decrease in the environmental temperature (Khotimchenko 1991). Aquatic species that live in colder waters generally contain larger quantities of PUFAs (Narayan et al. 2006), and the maximum content of lipids in the fronds of Saccharina, Laminaria species and A. esculenta was generally found in winter (Haug and Jensen 1954). However, the total lipids of Fucus sp. were most abundant in summer, with highest levels recorded in August. A attached specimen of Graciliaria accumulated twice as much lipid compared to the unattached form, but with no difference in fatty acid composition (Khotimchenko and Levchenko 1997; Kim et al. 1996).

Induction of omega-3 fatty acid production has been reported in seaweed. Cell suspension cultures in photo-bioreactors of *S. latissima* produced three sulphate fatty acids deriving from an *n*-6 lipoxygenase oxidation (15-hydroxy-5,8,11,13-eicosatetraenoic acid (15-HETE), 13-hydroxy-6,9,11,15-octadecatetraenoic acid (13-HODTA), and 13-hydroxy-9,11-octadecadienoic acid (13-HODE). The yields of 15-HETE, 13-HODTA and 13-HODE ranged from 100 to 1,000 μg product g^{-1} dry biomass, but addition of linoleic and γ-linolenic acid in the medium increased the yield of all three sulphate fatty acids by up to 400% (Rorrer et al. 1997).

The lack of studies of the bioavailability of algal lipids currently limits their nutritional evaluation (Mabeau and Fleurence 1993).

Fatty acids

Marine-based long-chain PUFAs (LC-PUFA) have 20 or more carbons with two or more double bonds from the methyl (omega) terminus. The omega-3 LC-PUFAs (*n*-3 LC-PUFA) have the first double bond located in the third carbon from the methyl terminus and can contain up to six double bonds. They are of particular interest in respect to functional food (Rasmussen and Morrissey 2007). PUFAs are occasionally classified into two families because of their metabolic connections. One is the linoleic acid family (*n*-6 fatty acid) and the other is the α-linolenic acid family (*n*-3 fatty acid; Table 11). Marine lipids contain substantial amounts of LC PUFAs, with *n*-3 fatty acids as the significant component and mono-unsaturated fatty acids. Eicosapentaenoic acid (EPA; 20:5 *n*-3) and docosahexae-noic acid (DHA; 22:6 *n*-3) are the two important fatty acids of marine lipids, along with the precursor α-linolenic acid (ALA; 18:3 *n*-3) and docosapentaenoic acid (22:5 *n*-3). Both EPA and DHA are basically derived from ALA through elongation and desaturation (Narayan et al. 2006). These LC-PUFAs EPA and DHA have been shown to cause significant biochemical and physiological changes in the body. The main effects of *n*-3 fatty acids on human health can be divided into three main categories: (1) their essentiality as structural components of cell and organelle membranes; (2) their significant role in lowering blood lipids; and (3) their role as precursors for mediating biochemical and physiological responses. Humans have to directly intake the ALA, EPA and/or DHA to obtain physiological effects of EPA and DHA. The major sources of EPA and DHA in human diets are marine products. Terrestrial plants can produce small to moderate amounts of ALA; however, the mammalian system cannot synthesise ALA. Major sources of EPA and DHA are unicellular phytoplankton and seaweed. EPA and DHA are accumu-lated in fish and other marine animals that consume algae and get passed on to other species through the food chain. It was found that individuals consuming a normal diet had low tissue levels of EPA and DHA, whilst those who consumed fish had higher levels in their tissue (Narayan et al. 2006). Generally, the marine *n*-3 polyunsaturated fatty acids exert anti-arteriosclerosis, anti-hypertension, anti-inflammation, immunoregulation effects, etc. (Khan et al. 2007; Maeda et al. 2005; Plaza et al. 2008).

The predominant fatty acid in various seaweed products is EPA (C20:5, *n*-3), which is at concentrations as high as 50% of the total fatty acid content (Dawczynski et al. 2007; Murata and Nakazoe 2001). Marine algae also contain the *n*-3 PUFA 18:4 *n*-3, which is not included in other organisms. Notably, red seaweed species contain significant quantities of polyunsaturated fatty acids such as EPA and arachidonic acid (20:4). The green algal species are unusual in containing 16:4 varying from 4.9% to 23.1% of the total fatty acids; 16:0, 18:1 and 18:3 acids have also been found in high amounts. Unsaturated fatty acids predominate in all the brown seaweed studied and saturated fatty acids in the red seaweed, but both groups are balanced sources of *n*-3 and *n*-6 acids. Even though seaweed is processed (canned and dried), the products are left with substantial nutritional value of protein, ash, and *n*-3 and *n*-6 fatty acid contents (Mabeau and Fleurence 1993; Sanchez-Machado et al. 2004a). Algae are therefore a good source of EPA *n*-3 (Plaza et al. 2008) and an important source of supply of *n*-3 PUFAs for the maintenance of health (Murata and Nakazoe 2001). It is suggested that algal 18:4 *n*-3 affects the immune system in humans (Ishihara et al. 1998). In accordance with Table 11, *Palmaria* and *Sargassum* have the best *n*-6/*n*-3 ratio (0.1 and 0.3, respectively) and also some of the highest total lipid contents of 3.8% and 3.9% respectively. *Gracilaria*, *Ulva* and *Fucus* have the highest contents of oleic acid (31%, 27% and 25%, respectively).

Phospholipids

Phospholipids (PLs) consist of fatty acids and a phosphate-containing compound attached to glycerol or the amino alcohol sphingosine, resulting in compounds with fat-soluble and water-soluble regions. Cell membranes utilise the dual hydrophilic and hydrophobic characteristic of PLs to maintain structure and transport materials. Glycerol-containing PLs include phosphatidic acid, phosphatidyl-choline (PC), phophatidylethanolamine (PE), phophatidyli-nositol and phosphatidylserine. Sphingomyelin (SPH), the other major PL, consists of sphingosine and PC. Phospho-lipids contribute to lipoprotein formation in the liver, nervous system conduction and protection, memory storage and muscle control. Choline, a major component of PC and SPH, functions as a methyl donor and a precursor to the neurotransmitter acetylcholine (Miraglio 2009).

The amount of phospholipids in various red seaweed species varies from 10% to 21% of the total lipid (0.5–2.6 mg g^{-1} dry weight). The major phospholipids appear to be PC (62–78%) and PG (10–23%). The presence of unidentified polar phospholipids vary from 2.7% to 10%, and PE and DPG are found as minor phospholipids (Dembitsky and Rozentsvet 1990). The major phospholipids in *F. vesiculosus* and *A. nodosum* are phosphatidylethanolamine, but these represent <10% of the total acyl lipids (Jones and Harwood 1992).

Phospholipids in diet act as natural emulsifiers and as such facilitate and ease the digestion and absorption of fatty acids, cholesterol and other lipophilic nutrients. A producer of marine phopholipids explains that these phospholipids have many advantages compared with fish oils because they are much more resistant to oxidation (rancidity), have much higher contents of the physiologically important EPA and DHA, provide these fatty acids with much better bioavailability and have much better spectrum of health benefits for humans and animals (Sørensen 2009).

Glycolipids

Glycolipids are carbohydrate-attached lipids. Their role is to provide energy and also serve as markers for cellular recognition because of their association with cell membranes.

The red algae contained almost equal quantities of mono-glycosyldiacylglycerol (MGDG), diglycosyldiacylglycerol (DGDG) and sulphaquinovosyldiacyl-glycerol, with some exceptions. MGDG and DGDG were the major glycolipids in green seaweed. Glycolipid contents of total lipid extracts of red seaweed range from 16 to 32 μmol g^{-1} dry weight, whilst those in green algae vary from 11 to 32 μmol g^{-1} dry weight. Examination of the composition of glycolipids in some brown algae showed that MGDG content varied from 26% to 47%, DGDG content from 20% to 44% and sulphaquinovosylglycerol content from 18% to 52% of total glycolipids (Dembitsky et al. 1990, 1991). Glycolipid content in two *Fucus* species made up 14% of the ester-soluble lipids (Dembitsky et al. 1990)

The major acyl lipids in *F. vesiculosus* and *A. nodosum* are monogalactosyldiacylglycerol, digalactosyldiacylglycerol, sulphoquinovosyldiacylglycerol and trimethyl-beta-alaninediacylglycerol (Jones and Harwood 1992). The highest concentration of saturated and mono-unsaturated fatty acids was found in sulfoquinovosyldiacylglycerides for species of *Palmaria*, *Undaria* and *Ulva* (Khotimchenko 2003).

Sterols

Sterols occur naturally in plants, animals and fungi, with the most familiar type of animal sterol being cholesterol. Cholesterol is vital to cellular function where it affects the fluidity of the animal cell membrane and serves as a secondary messenger in developmental signalling. Furthermore, cholesterol is a precursor to fat-soluble vitamins and steroid hormones. Content and type of sterols vary with the seaweed species. Green seaweed species contain 28-isofucocholesterol, cholesterol, 24-methylene-cholesterol and β-sitosterol, whilst brown seaweed contains fucosterol, cholesterol and brassicasterol. Red seaweed contains desmosterol, cholesterol, sitosterol, fucosterol and chalinasterol (Sanchez-Machado et al. 2004b; Whittaker et al. 2000). The predominant sterol, fucosterol, in the brown seaweed (*Laminaria* and *Undaria*) makes up 83–97% of total sterol content (662–2,320 μg g^{-1} dry weight) and desmosterol in red seaweed (*Palmaria* and *Porphyra*), 87–93% of total sterol content (87–337 μg g^{-1} dry weight). However, the red seaweed *C. crispus* has cholesterol as its major sterol (Kumar et al. 2008b; Sanchez-Machado et al. 2004b).

It is reported that plant sterols such as β-sitosterol and fucosterol lead to the decrease of the concentration of cholesterol in the serum in experimental animals and humans (Whittaker et al. 2000).

Pigments

Chlorophylls

Chlorophylls are green lipid-soluble pigments found in all algae, higher plants or cyanobacteria that carry out photosynthesis. Chlorophyll *a* is essential in the reaction centre of the thylakoid, light-harvesting structures in which photosynthesis is carried out (Lobban and Harrison 1994; Rasmussen and Morrissey 2007). Chlorophyll is known to be converted into pheophytin, pyropheophytin and pheophorbide in processed vegetable food and following ingestion by humans. These derivates show anti-mutagenic effect and may play a significant role in cancer prevention. The cellular uptake and inhibition of myeloma cell multiplicity were found to be greater for pheophorbide than for pheophytin. Calculated on the amount of cell-associated chlorophyll derivative, however, pheophytin was more cytostatic/cytotoxic than pheophorbide (Chernomorsky et al. 1999).

The pigment content (violaxanthin, fucoxanthin, carotene and chlorophyll *a*) in *Ascophyllum* was high in March to June (peak in May) and with minimum levels in July to November. This seasonal variation was not so distinct in *F. serratus*, although it showed somewhat lower levels during autumn (Jensen 1966). Preliminary studies on chlorophyll showed that the content was three times higher in seaweed growing in harbour districts compared to seaweed from an open sea locality (Larsen and Haug 1958). The chlorophyll

a content was 565–2,000 mg kg^{-1} on a dry weight basis in the brown species reported (Table 12).

Carotenoids

Carotenoids are nature's most widespread pigments, and they are present in all algae, higher plants and many photosynthetic bacteria. They represent photosynthetic pigments in the red, orange or yellow wavelengths. Carotenoids are linear polyenes that function both as light energy harvesters and as antioxidants that inactivate reactive oxygen species formed by exposure to light and air (von Elbe and Schwartz 1996). Carotenoids are tetraterpenes, carotenes are hydrocarbons, and xanthophylls contain one or more oxygen molecules (Table 12; Lobban and Harrison 1994). Green seaweed species include β-carotene, lutein, violaxanthin, neoxanthin and zeaxanthin, whilst red seaweed species contain mainly α- and β-carotene, lutein and zeaxanthin. β-carotene, violaxanthin and fucoxanthin are present in brown seaweed species (Haugan and Liaaen-Jensen 1994).

Some carotenoids also function as vitamins that are classified by their biological and chemical activity, not their structure, and each "vitamin" may therefore refer to several vitamer compounds. Vitamers are often interconverted in the body. Vitamins have diverse biochemical functions, including function as hormones, antioxidants, and mediators of cell signalling and regulators of cell and tissue growth and differentiation.

The β-carotene (with provitamin A activity) content ranges from 36 to 4,500 mg kg^{-1} (or ppm) dry weight, with *Porphyra* with the highest content and *P. palmata* with the second highest of 456 ppm according to Table 12. The carotenes in *Palmaria* show seasonal variations, with the highest content in summer (420 ppm) and lowest in winter (37 ppm; Yuan 2008).

The antioxidant properties of the algal carotenoids have also been shown to play a role in preventing man pathologies linked to oxidative stress (Okuzumi et al. 1993, Yan et al. 1999). Furthermore, experimental studies strongly suggest that β-carotene could prevent the onset of cancers, especially lung cancer (Astorg 1997). However, other studies suggest that β-carotene could induce lung cancer in smokers. Recent studies have shown the correlation between a diet rich in carotenoids and a diminishing risk of cardiovascular disease, cancers (β-carotene, lycopene), as well as opthalmological diseases (lutein, zeaxanthin; Hosokawa et al. 1999).

Fucoxanthin is a xanthophyll and has a unique structure, including an unusual allenic bond and 5,6-monoepoxide in its molecule (Maeda et al. 2008b). Fucoxanthin is one of the most abundant carotenoids in nature. The content in seaweed varies during season and life cycle. It is quite

stable in the presence of organic ingredients, apart from surviving the drying process and storage at ambient temperature. In pure form, fucoxanthin is vulnerable to oxidation (Haugan and Liaaen-Jensen 1994). The total carotenoid content of *F. serratus* was found to be aproximately 0.08% of the dried extracted cells, and fucoxanthin comprises about 70% of the total carotenoid (Chapman 1970; Haugan and Liaaen-Jensen 1989). In accordance with Table 12, the fucoxanthin content ranges from 172 to 720 mg kg^{-1} dry weight in the brown seaweed species, with maximal concentration in *F. serratus*.

Waste parts of cultivated *L. japonica* (kombu) are a good biosource for fucoxanthin extraction. Discards from processing (stipe, holdfast and blade material) can be used as a source for fucoxanthin extraction. These discards have similar content of fucoxanthin (178–196 mg kg^{-1} fresh weight). The recovery ratio of fucoxanthin has been shown to reach 82%, and a total of 1,490 g of fucoxanthin was obtained from 10 t of kombu waste. The fucoxanthin obtained was stable and reduced by only 2% at 4°C in 6 months of storage (Kanazawa et al. 2008). Fucoxanthin from fresh *Undaria* is mostly found as the geometrical isomer all-*trans* (~88%). *Trans* forms are more stable; however, *cis* forms of fucoxanthin were found to exert a higher inhibitory effect compared to their *trans* counterparts on human leukaemia (HL-60) cells and colon cancer (Caco-2) cells. Uptake and incorporation of the *trans* form of fucoxanthin into cellular lipids were faster compared to *cis* counterparts (Nakazawa et al. 2009). Fucoxanthin is easily converted to fucoxanthinol in human intestinal cells and in mice (suggesting that the active form of fucoxanthin in a biological system would be fucoxanthinol; Sugawara et al. 2002).

Experiments have shown that fucoxanthin from brown seaweed *Undaria* significantly reduces the viability of human prostate cancer cells and significantly reduces the percentage of tumour-bearing mice and the average number of tumours per mouse when given in the drinking water (Table 12; Kotake-Nara et al. 2001; Okuzumi et al. 1993). Other studies demonstrated anticancer effects, including inhibition of the proliferation of human leukaemia cell line (HL-60), and induced their apoptosis (Hosokawa et al. 1999; Miyashita and Hosokawa 2008).

Maeda et al. (2005) demonstrated a reduction in white adipose tissue (storage tissue for fat) in rats and obese and diabetic model mice when fed with fucoxanthin extracted from brown seaweed. Furthermore, the diet containing fucoxanthin suppressed body weight gains in mice and induced the expression of the thermogenesis protein, uncoupling protein 1 (UCP1), in white adipose tissue.

Purified fucoxanthin inhibited the cytoplasmic lipid accumulation in 3T3-L1 that can be induced by, e.g. insulin, and in a dose-dependent manner significantly

attenuated the expression of lipid metabolic genes in 3T3-L1 adipocytes. These results suggest that fucoxanthin is an effective natural food constituent to prevent obesity (Miyashita and Hosokawa 2008).

Tocopherol is another strong antioxidant and part of the carotenoid family, and the content can fluctuate strongly, e. g. in *L. digitata*. The concentration ranges from trace levels in winter to 2% of dry weight in summer. *Porphyra* also contains high contents of vitamin E (tocols), followed by *Ulva*, *Ascophyllum* and *Fucus* species (Table 13). Vitamin E includes α-, β- and δ-tocopherol (Kumar et al. 2008b). The species of tocols in some seaweed species are given in Table 13.

Phycobiliproteins

Unlike chlorophylls and carotenoids, phycobiliproteins are water-soluble and form particles (phycobilisomes) on the surface of the thylakoids rather than being embedded in the membranes. Phycobiliproteins consist of pigmented phycobilins, which are linear tetrapyrroles. Different combinations of the two principal phycobilins—phycoerythrobilin (red) and phycocyanobilin (blue)—which absorb different regions of wavelengths give different absorption spectra (Lobban and Harrison 1994). Besides the phycoerythrin and phycocyanin, phycobiliproteins can also be divided into allophycocyanin and phycoerythrocyanin. Within phycobilisomes, phycobiliproteins play an important role in the photosynthetic process of the three types of algae—Rhodophyta, Cyanophyta and Cyptophyta (Aneiros and Garateix 2004; Chronakis et al. 2000). The additional photosynthetic pigments make light harvesting possible in deep waters as surface light wavelengths for some colours are almost completely absorbed below 10 m (Voet et al. 1999).

Phycobiliproteins, in particular phycoerythrin, can constitute a major proportion of the red algal cell proteins, with levels of 1.2% and 0.5% of dry weight reported for *P. palmata* and *Gracilaria tikvahiae*, respectively (Chronakis et al. 2000; Wang et al. 2002). Phycobiliproteins are currently being used as natural colourants for food and cosmetic applications and are used in foods such as chewing gum and dairy products in addition to lipsticks and eyeliners (Sekar and Chandramohan 2008). Niohan Siber Hegner Ltd. and Dainippon Ink & Chemical Inc. are two companies in Tokyo that market the phycobiliprotein phycocyanin as a natural food colourant (Houghton 1996). Different phycobiliproteins have been shown to exhibit antioxidant, anti-inflammatory, neuroprotective, hypocholesterolemic, hepatoprotective, antiviral, anti-tumour, liver-protecting, atherosclerosis treatment, serum lipid-reducing and lipase inhibition activities (Sekar and Chandramohan 2008).

Iodine

Marine algae are known to be high in mineral content and are used as feed and food supplements to supply minerals. As mentioned previously, marine algae have 10–100 times higher mineral content than traditional vegetables (Arasaki and Arasaki 1983; Nisizawa 2002). Ash and thereby the mineral content of the species of interest reaches levels of up to 55% on a dry weight basis (Table 1). Ash content in most land vegetables is usually much lower than in seaweed. For example, sweet corn has a content of 2.6%, whilst spinach has an exceptionally high mineral content of 20% (Rupérez 2002). Some of the minerals are necessary for our health, whilst some are toxic in varying degrees. The mineral composition varies according to phylum as well as various other factors such as seasonal, environmental, geographical and physiological variations. Nevertheless, this review will not focus on the contents of all minerals and vitamins despite their importance in human health. However, the important mineral iodine needs some attention in this review as the concentration of iodine can reach very high levels in certain brown algae. Generally, the iodine content reached up to 1.2% of dry weight in these species (Table 14).

Laminaria japonica is an excellent source of iodine, and it has been used in China for centuries as a dietary iodine supplement to prevent goitre (underactive thyroids, myxoedema) and has also been used for medical and food purposes for over 1,500 years in China, Japan and Korea. Most of the kombu is dried and eaten directly in soups, salads and tea or used to make secondary products with various seasonings (sugar, salt, soy sauce; Lobban and Harrison 1994). Furthermore, kelps were used as raw material for the extraction of iodine in Ireland during the seventeenth century (Morrissey et al. 2001).

The results of a study on the feasibility of naturally iodised salt indicated that the level of iodine in seaweed is constant, consumer-acceptable and of equal bioavailability (Mabeau and Fleurence 1993). Species of the genus *Laminaria* are the strongest iodine accumulators among all living systems, and the accumulation can be up to 30,000 times larger than the surrounding evironment (Table 14; Bartsch et al. 2008). The uptake of dietary iodide by the human and animal thyroid glands 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 goitre (Müssig 2009). An anti-tumourogenic role of *U. pinnatifida* has been reported (Funahashi et al. 1999; Maruyama et al. 2003; Takahashi et al. 2000). This Asian kelp species or its equivalent iodine content inhibited tumourogenesis in rats with carcinogen-induced mammary tumours, although the mechanism of action is not understood (Funahashi et al.

2001). It has also been suggested that the high dietary seaweed content may account for the relatively low prevalence of breast cancer in Japanese women (Cann 2006). Nevertheless, too much iodine in sensitive persons can trigger a hyperactive thyroid gland and may cause goitre, similar to the myxoedema reaction. Excessive seaweed consumption was found to be frequently associated with goitre, hypothyroidism and Hashimoto's thyroiditis in countries where marine algae are traditionally used as food, whereas iodine-induced thyrotoxicosis following consumption of seaweed or seaweed-containing dietary supplements appears to be rare (Cloughley et al. 2008).

Phenols and other phorotannins

Phenols, sometimes called phenolics, are a class of chemical compounds consisting of a hydroxyl group (–OH) bonded directly to an aromatic hydrocarbon group. The simplest of the class is phenol, the parent compound used as a disinfectant and for chemical synthesis. Polyphenols from terrestrial plants are derived from gallic and ellagic acid, whereas the algal polyphenols are derived from polymerised phloroglucinol units (1,3,5-trihydroxybenzene). Phlorotannins are a group of phenolic compounds. Phlorotannins constitute an extremely heterogeneous group of molecules (structure and polymerisation degree heterogeneity) providing a wide range of potential biological activity (Table 15; Burtin 2003). Phlorotannins are localised in physodes which are membrane-bound cytoplasmic vesicles, and the fusion of physodes with cell membranes results in a secretion of phlorotannins (Bartsch et al. 2008; Li et al. 2009; Lüder and Clayton 2004). The size of the physodes is about 2,500 μm in F. serratus and L. hyperborea, and appearance does not differ much. The reducing power (up to 3.0 meq g^{-1} dry weight) increased with increasing physode volume (3–11% of the volume of the entire seaweed tissue of F. serratus, F. vesiculosus and A. nodosum; Baardseth 1958). Reducing power also correlated positively with the dry matter content (correlation coefficient of 0.73; Larsen and Haug 1958).

Green and red seaweed have low concentrations of phenols (Mabeau and Fleurence 1993) compared to brown seaweed species, which have high concentrations of the phenol group phlorotannin. Phenol content varies from <1% to 14% of dry seaweed biomass, with Ascophyllum and Fucus as the species with the highest content (14% and 12%, respectively; Table 15). Concentrations of polyphenols exhibit seasonal variations, but also vary within the different parts of thalli, such as old versus new thalli, basal part or frond (Johnson and Mann 1986). Polyphenol content shows a significantly temporal correlation with the

reproductive state of the algae. The polyphenol content in Ascophyllum is at a minimum (~9–10% of dry weight) during the period of maximal fruit body shedding (May) and reaches a maximum (~12–14%) during the "winter season". In F. vesiculosus, the minimum (~8–10%) is 1–2 months later, just before the period of maximum fertility. Thereafter, the content rises to a maximum (~11–13%) during the period of sterility (August to March; Ragan and Jensen 1978). This does not, however, correspond to the seasonal phenolic content shown in another study by Connan et al. (2004). In that study, the highest phenolic content in F. vesiculosus is during summer. Seasonal variations in phenolic content are more pronounced in some seaweed species like F. vesiculosus and Himanthalia elongata (sea spaghetti) compared to that of L. digitata (Connan et al. 2004). Seasonal studies on the bromophenol content of U lactuca showed that the levels increased dramatically at the end of the summer whilst they decreased during the rest of the year. The bromophenols may protect the seaweed from strong light intensities experienced during the summer (Pedersen et al. 1996; Flodin et al. 1999). The main phenolic compound of marine origin is bromophenol as it is found at high levels in various types of seaweed such as Polysiphonia urceolata (Li et al. 2007).

The levels of antioxidants present in algae can also be affected by a number of other parameters such as location and salinity. Sampath-Wiley et al. (2008) examined the effect of sun exposure and emersion on Porphyra umbilicalis and found that seaweed located in upper intertidal regions during the summer contained higher levels of antioxidants than submerged seaweed. Submersion protected against environmental stresses caused by moisture loss and exposure (Sampath-Wiley et al. 2008). The reducing power of polyphenols was ten times higher in species of Ascophyllum from open coast localities than from specimens from fjords near river outlets, probably because of differences in salinity (Baardseth 1958; Larsen and Haug 1958).

Preliminary studies of polyphenols in seaweed species collected in Denmark show that species of Fucus showed the highest antioxidative activity compared to other brown algal species, e.g. Sargassum and Laminaria. The antioxidant activity was tested with four methods: in vitro established systems such as antioxidant activity in liposome model systems; 1,1-diphenyyl-2-picrylhydrazyl (DPPH) radical scavenging activity; reducing power; and metal chelating activity. Water extracts had the highest antioxidant activity compared to ethanol extracts. Extracts were made from freeze-dried seaweed samples (Farvin et al. 2010).

Drying has no influence on the reducing power of the Fucaceae, but this is not the case for Laminaria and Ascophyllum species. In these species, the reducing power

is usually markedly lower in dry samples (Haug and Larsen 1958). Antioxidants from the red seaweed *K. alvarezii* were extracted and a phenolic content of approx. 2% was found in the chloroform/methanol (2:1) extracts using the Folin–Ciocalteau method (Kumar et al. 2008c). The ethanol extract had the best DPPH scavenging ability (IC_{50} = 3.03 mg mL^{-1}) and most potent inhibitory effect against lipid peroxidation, whereas the methanol extract exhibited the best metal ion-chelating ability (IC_{50} = 3.08 mg mL^{-1}) and also had the greatest reducing power. Li et al. (2007) extracted four bromophenol compounds from a red alga *P. urceolata*; each was found to have DPPH-scavenging ability, with one compound displaying an IC_{50} value of 9.67 μM.

Polyphenols (fucol, fucophlorethol, fucodiphloroethol G and ergosterol) and the phenolic compound phlorotannin are abundant in brown macroalgae, such as *Sargassum*, *Fucus* and *A. nodosum*, and have strong antioxidant effects (Table 16).

Investigations on crude extracts and phenol content show that the reducing power and hydroxyl radical scavenging activity of some seaweed species (*Eucheuma*, *Kappaphycus* and *Turbinaria conoides*) are found to be higher compared to standard antioxidant (a-tocopherol). In several experiments, the total phenol content of several seaweed species was significantly different in three out of six seaweed species tested. The in vitro antioxidant activities of methanol extracts of all six species tested exhibited dose dependency and increased with increasing concentration of the extract (Ganesan et al. 2008; Kumar et al. 2008a). Studies have shown that there is a synergistic effect with vitamin E (tocopherol; Le Tutour 1990).

Polyphenols are of cosmeceutical and pharmacological value because of their antioxidative activity, and they have also shown other effects such as radiation protective, antibiotic and antidiabetic. Several of these effects were tested in bacteria, cell cultures, rodents and even in humans with regard to sexual performance and desire (Table 16). Certain polyphenols work as preventative medicines for problems such as cardiovascular diseases, cancers, arthritis and autoimmune disorders by helping to protect tissues against oxidative stress (Garbisa et al. 2001; Maliakal et al. 2001; Kang et al. 2003). In addition, polyphenols are found as anti-inflammatory agent and have anti-allergic effect and antibacterial activity (e.g. anti-*Staphylococcus* activity) together with other broad therapeutic perspectives (Table 16; Li et al. 2009; Zubia et al. 2008; Sailler and Glombitza 1999).

Oral tests on rats and humans with a commercially available sample containing 30% polyphenols and 70% dietary fibres indicated good oral absorption of the compounds and fast binding to the luminal surface of the blood vessels (Kang et al. 2003). Polyphenols have been traditionally thought of as having low bioavailability, but some studies have noted a significant increase in the antioxidant capacity of plasma following ingestion of these compounds in foods and beverages (Arts et al. 2001; Kalt et al. 2000). Epidemiological studies also note an association between a high intake of dietary polyphenols and lowered incidence of various chronic diseases (Arts et al. 2001). Therefore, it could be suggested that phlorotannins would be potential candidates for the development of unique natural antioxidants for further industrial applications as functional foods, cosmetics and pharmaceuticals (Li et al. 2009).

Besides phloroglucinol, there are many other flavenoids and their glycosides present in green, brown and red algae, such as catechin and epicatechin (up to 4.77 mg g^{-1} dry weight) or the flavonol glycoside rutin (up to 11.4 mg g^{-1} dry weight) in *Porphyra*. The flavone glycoside hespiridin is present in green, brown and red seaweeds and is especially high in certain green algae at 117 mg g^{-1} dry weight.

Halogenated compounds

Halogenated compounds are produced naturally, mainly by red and brown seaweed, dispelling the widespread notion that these chemicals are only of man-made origin (Butler and Carter-Franklin 2004; Flodin et al. 1999). Halogenated compounds are dispersed in several different classes of primary and secondary metabolites, including indoles, terpenes, acetogenins, phenols, fatty acids and volatile halogenated hydrocarbons (e.g. bromoform, chloroform, dibromomethane; Butler and Carter-Franklin 2004; Dembitsky and Srebnik 2002; Flodin et al. 1999). In many cases, they possess biological activities of pharmacological interest, including antibacterial (Vairappan et al. 2001) and anti-tumoural (Fuller et al. 1992). The most notable producers of halogenated compounds in the marine environment belong to the genus *Laurencia* (Rhodophyta; Faulkner 2001; Wright et al. 2003). The compounds are predominantly derivates of esquiterpenes diterpenes, triterpenes, acetogenins, fatty acids and brominated indoles. In addition to antimicrobial and cytotoxic properties, *Laurencia* compounds may also play multifunctional ecological roles such as acting as a feeding defendant (Brito et al. 2002; Flodin et al. 1999; Iliopoulou et al. 2002; Suzuki et al. 2002).

Polyhalogenated monoterpenes from red algae of the genera *Plocamium* and *Chondrococcus* exhibit a wide range of pharmacological activities, including antimicrobial, antitubercular and anticancer activities (Blunt et al. 2003; Darias et al. 2001; Flodin et al. 1999; Fuller et al. 1992; Knott et al. 2005). Brominated fatty acids are synthesised by *Aspara-*

Table 12 Pigments (mg kg^{-1} of dry weight (=ppm)) in seaweed, their possible usage in industry, source and bioactivity

Pigments		Use	Source	Effect
Carotenoids Linear polymer Tetraterpenes Light energy harvester Lipid-soluble	β-carotene	Natural colouring of, e.g. margarine and fish	*Laminaria digitata*: 63[a], 336[b] *Fucus serratus*: 80[c], 105[d], 102–173[a] *F. vesiculosus*: 95[d], 80[a] *Ascophyllum nodosum*: 35–80[b], 47–84[e], 50[d], 42–98[a] *Sargassum* sp.: 36–60[b] *Ulva* sp.: 310[b] Chondrus crispus: 84[d] *Porphyra* sp: 85[d], 4,500[b] *Palmaria palmata*: 456[b], 37–420[f]	Provitamin A activity[g] Cancer prevention[g,h] Antioxidant[i,j] Antioxidant effect and retinoid-dependent signalling, stimulation of gap junctional communications, impact on the regulation of cell growth and induction of detoxifying enzymes, such as cytochrome P450-dependent monooxygenases[k] Diminish risk of cardio-vascular disease[h]
	Astaxanthin	Orange-red pigment in aquatic animals and pink colour in salmoid fish	Usually found in species of microalgae	Antioxidant activity up to 10 times stronger than other carotenoids[l]
	Fucoxanthin Has an unique structure including an unusual allenic bond and 5,6-monoepoxide in its molecule[m,n] Fucoxanthin is converted to fucoxanthinol before uptake in the digestive tract[o]. Fucoxanthinol is the deacetylated product of fucoxanthin[o]		*Laminaria digitata*: 468[a] *Laminari japonica*: 178–213 mg kg^{-1} ww[p] *Ascophyllum nodosum*[q]: 660[r], 172–272[a] *Undaria pinnatifida* (not destroyed by cooking)[s,t,u] *Fucus serratus*[q]: 495–720[a] *F. vesiculosus*[q]: 340[a] *Sargassum siliquastrum*[v]	Anti-obesity effect[o,m] and increase the metabolism[s] Weight reduction in white adipose tissue in rats and mice with 0.5% and 2% added to feed[m,w,x] Induced expression of thermogenesis UCP1 in white adipose tissue[w] Attenuation of lipid metabolic gene expression and inhibition of cytoplasmic lipid accumulation (3T3-L1 adipocytes)[y] Reduced blood glucose and plasma insulin in rats and mice[o] Increased the level of hepatic docosahaxaenoic acid (DHA) in rats and mice[o] Antioxidant activity[q] Protective effect on UV-B induced cell injury in human fibroblast[v] Preventive effect on cerebrovascular diseases[s] Beneficial effect on cerebrovascular diseases in stroke-prone rats (SHRSP), independent of hypertension[u] Inhibits chemical carcinogenesis[j] and decreased growth of leukaemia and prostate cancer cells[m] Preventive function against cancer and metabolic syndrome without side effects[p] Anticancer effect on cells[y] Inhibitory effect on colon cancer (Caco-2) cells[t] and human leukaemia (HL-60) cells[t,h], and induces their apoptosis Significantly attenuated neuronal cell injury in hypoxia and re-oxygenation[u] Possible preventive effect against neuronal cell death sean in SHRSP with stroke[u]
	Violaxanthin	A major xanthophyll in brown seaweed	*Laminaria digitata*: 110[a] *Ascophyllum nodosum*[r] : 64–129[a] *Fucus serratus*: 129–198[a] *Fucus vesiculosus*: 162[a]	
	Zeaxanthin and lutein	Both pigments are the predominant carotenoids of the retina in the human eye	*Ascophyllum nodosum*: up to 100 mg/kg at storage[r]	Diminish the risk of opthalmological diseases[h]
	Tocopherol (vitamin E=tocols)	See details in Table 13	*Laminaria/ Saccharina*: 8.9[b], 20[aa], 34[bb] *Fucus* sp.: 200–600[cc] *Ascophyllum*: 3.6[bb], 250–500[cc], 8.9[b] *Undaria*: 40[dd] *Ulva*: 9.1[b], 1070[ee] *Porphyra*: 17[aa], 57[dd], 330[b] *Gracilaria*: 10[aa]	Antioxidant[ff]

Table 12 (continued)

Pigments	Use	Source	Effect
Phycobiliproteins Tetrapyrroles Water-soluble	Natural colouring: chewing gums, dairy products, cosmetics etc.[gg]	*Palmaria palmata*: 12% of ww[hh] *Gracilaria tikvahiae*: 0.5% ww[hh]	Form stable conjugates with, e.g. biotin and antibodies[i] Antioxidant[gg] Anti-inflammatory[gg] Antiviral[gg] Anti-tumour[gg] Liver-protecting[gg] Neuroprotective[gg] Hypocholesterolemic[gg] Atherosclerosis treatment[gg] Serum lipid-reducing[gg] Lipase inhibition activity[gg] Hepatoprotective[l,gg]
Chlorophylls Tetrapyrroles Lipid-soluble	Chlorophyll *a*	Food and beverages	*Laminaria digitata*: 1,250[a] *Ascophyllum nodosum*: 830[a], 565–1,030[a] *Fucus serratus*: 1,572–2,000[a]	Anticancer activity[ii]
	Chlorophyll *b*, *c* and *d*		

[a] Jensen (1966); [b] Morrissey et al. (2001); [c] Haugan and Liaaen-Jensen (1989); [d] Haug and Larsen (1957); [e] Larsen and Haug (1958); [f] Yuan (2008); [g] Astorg (1997); [h] Hosokawa et al. (1999); [i] Rasmussen and Morrissey (2007); [j] Okuzumi et al. (1993) and Yan et al. (1999); [k] Stahl et al. (2002) and Stahl and Sies (2005); [l] Miki (1991); [m] Maeda et al. (2008b); [n] Maeda et al. (2008a); [o] Sugawara et al. (2002); [p] Kanazawa et al. (2008); [q] Le Tutour et al. (1998); [r] Jensen (1969b); [s] Plaza et al. (2008); [t] Nakazawa et al. (2009); [u] Ikeda et al. (2003); [v] Heo and Jeon (2009); [w] Maeda et al. (2005); [x] Weinberger (2007); [y] Miyashita and Hosokawa (2008); [z] Le Tutour et al. (1998); [aa] Wen et al. (2006); [bb] MacArtain et al. (2007); [cc] Jensen (1969a); [dd] Tititudorancea (2009); [ee] Ortiz et al. (2006); [ff] References in Plaza et al. (2008); [gg] Sekar and Chandramohan (2008); [hh] Chronakis et al. (2000) and Fleurence (2004); [ii] Chernomorsky et al. 1999

gopsis and *Bonnemaisonia* (Dembitsky and Srebnik 2002). The presence of halogen atoms (F, Cl, Br or I) in the fatty alkyl chain causes significant changes in their physicochemical characteristics, increasing their reactivity and changing the conformation of biological membranes (Dembitsky and Srebnik 2002).

Extracts or powder of seaweed

Various extraction methods have been used to release identified and unidentified bioactive substances from marine algae. Powder derived from dried seaweed has also been tested.

Antioxidant effect

The result of 16 lipophilic extracts suggests that seaweed can be considered as a potential source for the extraction of lipophilic antioxidants, which might be used as dietary supplements or in production in the food industry. The results indicated an increase in antioxidative property with increasing content of unsaturated fatty acid (Huang and Wang 2004). *Sargassum* species might be a valuable source of natural antioxidants containing both water- and fat-soluble antioxidative components, preventing oxidative

damage of food oils (Siriwardhana et al. 2003, 2004). Further antioxidative effects of compounds from macro-algae with potential in applications in human health and nutrition are described by Cornish and Garbary (2010).

Zaragoza et al. (2008) investigated the antioxidant behaviour of two extracts from brown seaweed *F. vesiculosus* using either 30–35% ethanol or 50–70% ethanol. The 30–35% ethanol extract exhibited more potent antioxidant behaviour than the 50–70% ethanol extract, showing superior DPPH, superoxide, peroxyl and ABST radical scavenging ability. The 50–70% ethanol extract was found to increase the reducing power and superoxide scavenging ability in the plasma of laboratory rats. The 50–70% ethanol extract was also found to stimulate the immune system of the animals tested by increasing the Cu–Zn SOD activity by approx. 32% (Dembitsky and Srebnik 2002).

Peroxidation of fatty acids

Addition of 1% or 2% *Undaria* powder to rat diets decreased liver and serum triglycerol levels, respectively, compared to control. It is known that the synthesis and oxidation of fatty acids by the liver control the concentration of triacylglycerol in the serum and liver. The enzyme activities involved in the synthesis or the oxidation of fatty acids show changes in rats with *Undaria* powder in diets.

Addition of 5–10% *Undaria* powder decreased glucose-6-phosphate dehydrogenase activity; however, 10% wakame increased several activities of other enzymes and co-enzymes. These results indicate that the decrease in concentration of triacylglycerol in serum and liver by dietary *Undaria* powder in rats is due to the promotion of fatty acid oxidation in rat liver. Therefore, *Undaria* may play a role in the prevention and treatment of arteriosclerosis. In addition, since the decrease in concentration of triacylglycerol in the serum and liver by dietary *Undaria* is associated with the promotion of oxidation of fatty acids in the liver, *Undaria* may become a food material for the prevention of obesity (Table 17; Murata et al. 1999). Furthermore, fish oil in rat diets was found to decrease the concentration of triacylglycerols in serum and liver significantly compared to control, but this decrease became even more conspicuous in a diet with both fish oil and *Undaria* powder (Murata et al. 2002). Methanol extract from the brown algae *Sargassum* inhibits oxidation in rat liver homogenates (Kumar et al. 2008b; Mori et al. 2003).

Other effects

Extracts of seaweed with different solvents such as water, ethanol, dichloromethane and chloroform have shown antibacterial, anti-inflammatory and anti-pathogenic effects (Table 17).

The antibacterial effect of seaweed extracts was seen in several Gram-negative bacteria strains, and the extracts were non-toxic against non-targeted larvae (Andersson et al. 1983; Zubia et al. 2008). Anti-inflammatory effect was seen in oedema and erythema of mice, but there was also decreased motor activity in rodents when seaweed extract was added to their diet (Andersson et al. 1983). Another study on rodents improved the survival of stroke-prone hypertensive rats when given 5% seaweed powder in the diet (Ikeda et al. 2003). Similarly, *Undaria* powder supplement in rat diet (5% wet weight) attenuated the development of hypertension and its related diseases and improved survival rates (Ikeda et al. 2003). Methanol or enzymatic extracts of *Sargassum* species were furthermore preventive against DNA damage (Cho et al. 2007; Park et al. 2005). The latter effect was also seen by enzymatic extracts of other brown seaweed (Heo et al. 2005). Seaweed extract stimuli in plant science and agriculture is described in recent publications such as Fan et al. (2011) and the comprehensive review by Craigie (2010).

Feed supplement

Animals such as sheep, cattle and horses that live in the coastal areas are known to actively graze seaweed from the shore. Today, seaweed is dried and milled to a fine seaweed meal, in particular from *A. nodosum* due to the harvesting history of this species. Analyses show that it contains useful amounts of minerals (K, P, Mg, Ca, Na, chlorine and S), trace metals and vitamins. Because most of the carbohydrates and proteins are not digestible, the nutritional value of seaweed has traditionally been assumed to be in its contribution of minerals, trace elements and vitamins to the diet of animals. The feeding value has been assessed in Norway as having only 30% of the value of grains. Feeding trials with added *Ascophyllum* meal to poultry and pigs showed an increase in the iodine content of the eggs from the poultry, and no effect was observed in pigs. However, positive results were reported with increases in milk production in dairy cows, whilst sheep were able to maintain weight better during winter feeding, with increases in lambs' birth weight and greater wool production (McHugh 2003; Hertz 2008, personal communication on the birth weight of lambs).

Recent research on seaweed used as animal feed supplement of either protein, polysaccharides or enriched with PUFAs has given promising results. Moreover, fish-meal protein can be supplemented with no effect or even with a beneficial effect on growth, feed conversion ratio and flesh colour if supplemented with seaweed (Table 18). Soler-Vila et al. (2009) have shown that *Porphyra dioica* can effectively be included in diets for rainbow trout at up to 10%, without significant negative effects on weight gain and growth performance. The positive pigmentation effect of the fish flesh by adding the *Porphyra* meal to the feed is of considerable interest to the organic salmon-farming industry. Other research showed that when *Ulva* meal replaced 5% of the diet lipids, the growth performance, feed efficiency, nutrient utilisation and body composition of Nile tilapia were improved (Ergün et al. 2008). In addition, seaweed meal elevated body weight gain of sea bream and tended to increase feed efficiency and muscle protein deposition. Algae-fed groups were higher in liver glycogen and triglyceride accumulation in muscle. Feeding *Porphyra* showed the most pronounced effects on growth and energy accumulation, followed by *Ascophyllum* and *Ulva*. The results suggest the practical efficacy of using algae as a feed additive for the effective use of nutrients in cultured sea bream (Mustafa et al. 1995).

Many experiments have been performed on seaweed additions in the diets of pigs (including weanling and grower-finisher). When piglets move from suckling to a solid diet, stomach-soling and intestinal problems often appear. Seaweed extracts fed to pigs have been shown to provide a dietary means to improve gut health and potentially reduce pathogen carriage in finishing pigs. However, the effect on growth performance in healthy animals was negative (Gardiner et al. 2008).

Table 13 Vitamin E (tocols) content (mg kg^{-1} of dry weight, or based on the lipid content) and effect and variations in some of the seaweed genera of interest in Northwest Europe

Compound	Effect and variations	Laminaria (mg kg^{-1} dw)	Fucus (mg kg^{-1} dw)	Ascophyllum (mg kg^{-1} dw)	Ulva (mg kg^{-1} lipid)
Tocols (total)	Seasonal variations; highest content in autumn and winter[a]			250–500[a]	1,071[b]
α-Tocopherol (stable to heat and acids, unstable to alkali)	Antioxidant[c] Highest content in oldest part	0.1[d]	38–73[d]	125[e] 92 (average of 10)[a] 195[a] 34[d]	9[b]
α-Tocotrienol					33[b]
β-Tocopherol					14[b]
gamma-Tocopherol		0.1[d]	14–29[d]	70[e] 12[d]	26[b]
gamma-Tocotrienol					964[b]
δ-Tocopherol			19–37[d]	110[e] 17[d]	25[b]

[a] Jensen (1969a); [b] Ortiz et al. (2006); [c] References in Plaza et al. (2008); [d] Le Tutour (1990); [e] Jensen (1969b)

Undesirable compounds

Heavy metals

Besides health-promoting and stimulating compounds in seaweed, other metals, minerals and bioactives may pose a negative effect on health. Not only desireable minerals but also metals in toxic concentrations, heavy metals and other compounds are concentrated in seaweed. For example, lead (Pb), mercury (Hg) cadmium (Cd), copper (Cu), manganese (Mn), zinc (Zn) and the explosive compound trinitrotoluene that may be present in the ambient environment (Besada et al. 2009; Cruz-Uribe et al. 2007; Greger et al. 2007; Mehta and Gaur 2005; Ronnberg et al. 1990; Sandau et al. 1996). Concentration factors of 10^3–10^4 for the above heavy metals and even up to 10^6 can be reached for chromium (Cr; references in Lobban and Harrison 1994). This accumulating effect present in seaweed can also be exploited to remediate for undesired compounds in sea and wastewater or in the use of seaweed as a bioindicator (Boubonari et al. 2008; Cruz-Uribe et al. 2007; Mehta and Gaur 2005). However, undesired metals and compounds should be taken into account and tested if seaweed species are to be used as a feed and food product. The concentrations of, e.g., heavy metals depend on the surrounding environment, and variations can be very local.

Inorganic arsenic (As) accumulation in seaweed is an example of another problem because it has an effect on the human nervous system. Marine organisms take up the inorganic arsenic, but usually, the biological system transforms it into an organic and non-toxic form of arsenic. Arsenic concentrations are generally considerably higher in brown seaweed than in red or green (Francesconi and Edmonds 1996). In most species of seaweed, the concentrations are below 54 mg kg^{-1} dry weight, and 5-10% of the total arsenic is organic, primarily in the form of various arseno-sugars (Table 19; Almela et al. 2002; Francesconi and Edmonds 1996). Fucus readily accumulates arsenate and transforms it into several arsenic compounds depending on the exposure concentration and other major arsenic species. Arsenite, methylarsonate and dimethylarsinate can be transformed to e.g. arsenosugars (Geiszinger et al. 2001). However, the seaweed species Sargassum fusiforme (and possibly other species in the Sargassum family) concentrate large amounts of the inorganic form (88 mg kg^{-1} dry weight, up 72% of total As content; Table 19). This edible brown seaweed, S. fusiforme (former Hizikia fusiformes), is sold as Hijiki or Hiziki from Japan, and the S. muticum may only contain 38–75% of their arsenic in organic forms (Almela et al. 2002; Shinagawa et al. 1983; Yasui et al. 1978). Arsenic in Sargassum is removed by 89–92% (wet weight) by the cooking process, or effectively removed just by soaking edible brown seaweed. These experiments were tested on mice (Ichikawa et al. 2006). However, this effect has not been observed in vegetables where cooking is only of a very limited value as a means of reducing metal concentrations (arsenic, cadmium, mercury and lead; Perelló et al. 2008). Figures of these compounds in seaweed sold as food or in coastal seaweed in Ireland are shown in Table 19.

Kainic acid

Kainic acid is a neurotoxin that is similar to domoic acid (a neurotoxin which causes amnesic shellfish poisoning), an amino acid associated with certain harmful algal blooms. This acid is a natural marine acid present in some seaweed, and it is a potent central nervous system stimulant. Kainic acid was originally isolated from the seaweed called "Kainin-sou" or "Makuri" (D. simplex) in Japan in 1953.

Table 14 Iodine content (mg 100 g^{-1} of dry weight) in the seaweed species of Northwest Europe

	Laminaria and Saccharina	Fucus	Ascophyllum	Undaria	Sargassum	Ulva	Chondrus	Porphyra	Gracilaria	Palmaria	RDI
I (iodine)	23–211[a]	73[a]		6–10[a]	43[a]			17–18[a]			0.150
	200–1,000[b]			25[b]		2.0–25[b]				10–100[b]	
	250–1,150[c]										
	304[d]		70–125[e]				3.6[d]		426[d]		
	193–471[f]		91[g]	18–35[f]	300[f]		1.1[f]	0.5[f]			
	150–1,200[h]										
	80–500[i]	50[i]	70–120[i]		3[i]	24[i]	20–30[i]	15–55[i]		15–55[i]	

RDI recommended daily intake

[a] van Netten et al. (2000); [b] Mabeau and Fleurence (1993); [c] Haug and Jensen (1954) and Rupérez (2002); [d] Wen et al. (2006); [e] Jensen (1960); [f] Arasaki and Arasaki (1983); [g] MacArtain et al. (2007); caculated from dw/ww ratio of 1:5 given in Vadas et al. (2004); [h] Jensen and Haug (1956); [i] Morrissey et al. (2001)

"Kainin-sou" is used as an anthelmintic in Japan. Moreover, it has been developed as the prototype neuroexcitatory amino acid for the induction of seizures in experimental animals, at typical doses of 10–30 mg kg^{-1} in mice. Because of recent supply shortages, the price of kainic acid has risen significantly (Ramsey et al. 1994). Three different companies quote prices ranging from US $3 mg^{-1} to US $12 mg^{-1} for 99% pure kainic acid (glutamate-free). *P. palmata* var. *sarniensis* seems to have some levels of kainic acid which, after metabolite extraction, produced 0.72% kainic acid. Kainic acid can be extracted from these sources by treatment with a mixture of chloroform and methanol (1:2, *v/v*).

The concentration of kainic acid was higher in wild-harvested populations of *P. palmata* (12 and 130 mg kg^{-1} dry weight in Ireland and France, respectively) compared to cultivated material (2.5 mg g^{-1} dry weight). Experiments have shown that this neurotoxin is not transferred to abalone fed on *Palmaria* (Lüning 2008).

Legislation, bioactive molecules and seaweed as food

Seaweed species and their components must meet certain consumer safety regulations. The seaweed species authorised for human consumption have been defined in France (Table 20). Moreover, maximum allowed levels of toxic minerals (lead, cadmium, tin, mercury, mineral arsenic and iodine) have been defined for all edible seaweed. These low levels are considered a high guarantee of food safety; in fact, heavy metal norms for certain fish and shellfish are much higher (e.g. 1 mg kg^{-1} dry weight for mercury in tuna in the USA; 0.7 mg kg^{-1} in France; Mabeau and Fleurence 1993).

No legislation regarding contaminants in algae food products is currently present in Spain. Some samples analysed from legal seaweed food products did, however, reveal cadmium and inorganic arsenic levels higher than those permitted by legislation in other countries (Table 21). Given the high concentrations of inorganic arsenic found in *S. fusiforme*, a daily consumption of 1.7 g of the product would reach the Provisional Tolerable Weekly Intake recommended by the WHO for an average body weight of 68 kg (Almela et al. 2002). The maximal content of neurotoxins (not specified) is 20 ppm on a fresh weight basis for mussels, but no limits seem to be mentioned for seaweed, e.g. kainic acid in *Palmaria* sp. (Lüning 2008).

Seaweed species are not subject to particular regulations in other European countries, but are considered as food if put on market as food or food ingredient and consumed to a significant degree before May 15 1997, and therefore not considered as novel food. However, other specific legislation may restrict the placing on the market in some Member States. As an example, *Fucus serratus* and *Ulva* sp. would be considered novel food in Denmark (European Commission 1997). Algal products have to comply with the upper level limits given in Table 21.

International legislation on food supplements, fortified and functional foods

Functional foods are continuing to grow in popularity around the world, but there is currently no universal definition of the category. Functional food is a category recognised by the industry only and is a virtual category in legal terms in that there is no specific "functional food" legislation. Authorisation and labelling of "functional food" falls under existing legislation that governs all food.

Functional foods originated in the Far East as an effort to reduce increasing health costs in the public sector. Industrial functional foods have blossomed, first in Japan and then in the US, and these contries have the majority of the value; only a modest increase has been achieved in the EU of eight billion euros. The key reason for this is the incoherent EU legislation because no European legislation exists specifically for the health benefits (efficacy and health claims). The combined US, Western European and

Table 15 Phenolic (or when mentioned phlorotannin) content of seaweed genera of interest in Northwest Europe

Seaweed genera	Concentration
Laminaria/Saccharina	0.2–2.6%[a]
	~0.2%[b]
	<0.4%[c]
	1.3–3.1%[d]
	Up to 5.3%[e]
Fucus	<0.4%[c]
	0.7–8.5%[f]
	1.0–12.2%[f]
	>2% (2–6%)[b]
Ascophyllum	0.5–14%[e]
	4–13%[f] (phlorotannin)
	4–13%[g]
	5%[a,h] (phlorotannin)
Undaria	<0.4%[c]
Sargassum	Yes with rapid rates of turnover[i]
	1.1–2.3%[j]
	2–3%[k]
	5.1% of GAE[l]
	6%[a]
	12.7%[m]
Ulva	0.9% of GAE[n]
Chondrus	less than 0.4%[c]
Porphyra	less than 0.4%[c]
Gracilaria	1.6% of GAE[o]

Figures are given in percentage of dry weight

GAE gallic acid equivalents

[a] Connan et al. (2006); [b] Connan et al. (2004); [c] Rupérez and Saura-Calixto (2001); [d] Hammerstrom et al. (1998); [e] References in Horn (2000); [f] Haug and Larsen (1958); [g] Pavia and Åberg (1996); [h] Pavia et al. (1997); [i] Arnold and Targett (2000); [j] Wong and Cheung (2001a); [k] Zubia et al. (2008); [l] Lim et al. (2002); [m] Cho et al. (2007); [n] Wong and Cheung (2001c); [o] Ganesan et al. (2008)

Asia Pacific functional food and drink market are worth US $72.3 billion, and the market is forecast to grow at a compound annual growth rate of 5.7% between 2007 and 2012. Asia will remain the largest functional food market, and it is forecast to continue to outperform the US and European markets in the foreseeable future. The buoyant growth throughout the sector is being driven by consumers who are increasingly looking for products that offer a solution to both long-term and short-term health problems (Gruenwald 2008; Korver et al. 2008).

The situation in the EU contrasts with Japan and the US. An American company deals only with one regulatory body, the Food and Drug Administration (FDA), and the same applies for Japan. In Europe, however, a variety of national regulators have to be dealt with. The European and US markets are quite different in structure, market positioning, consumer and reseller attitudes and expectations, regulations, labelling and claims, value chain, and even product specifications and packaging. Furthermore, there is no GRAS protocol in Europe, and many functional foods have to obtain "novel foods" approval, a potentially lengthy and expensive process with no guarantee of success.

Europe

The European Commission Concerted Action on Functional Food Science in Europe regards a food as functional if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease. In this context, functional foods are not pills or capsules, but must remain foods, and they must demonstrate their effects in amounts that can normally be expected to be consumed in the diet (EAS 2008).

United States

The US FDA does not provide a legal definition for the term 'functional foods', and the term is currently used primarily as a marketing idiom for the category. The FDA is still reviewing comments on how functional foods should be regulated before considering further actions (Heller 2009). Comments filed with the FDA follow a public hearing held in 2006 designed to examine whether the current regulatory framework is suitable for the overview of functional foods or whether the FDA needs to change the way it regulates this new category. At the public hearing, the agency took into account recommendations from the Government Accountability Office, the International Life Sciences Institute, the Institute of Food Technologists (IFT) and a citizen's petition from advocacy group Center for Science in the Public Interest. The FDA is currently in the process of evaluating all comments submitted on this issue, and once it has done this, the FDA will consider further action, if necessary. However, no timeline has been issued (Heller 2009). A number of working definitions have been developed though, by different organisations, including the American Dietetic Association (ADA), the International Food Information Council (IFIC), and the IFT. ADA classifies all foods as functional at some physiological level because they provide nutrients or other substances that furnish energy, sustain growth or maintain/repair vital processes. However, functional foods move beyond necessity to provide additional health benefits that may reduce disease risk and/or promote optimal health. The IFIC considers functional foods to include any food or food component that may have health benefits other than basic nutrition. These substances provide essential nutrients, often beyond quantities necessary for

normal maintenance, growth and development, and/or other biologically active components that impart health benefits or desirable physiological effects.

"Medical foods" and "foods for special dietary use" are considered to be two subcategories of functional foods in the US.

Medical foods are defined by the Orphan Drug Act. "A food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognised scientific principles, are established by medical evaluation".

Foods for special dietary use are defined by the Federal Food, Drug, and Cosmetic Act (Section 411(c)(3)) as "a particular use for which a food purports or is represented to be used, including but not limited to the following: 1. Supplying a special dietary need that exists by reason of a physical, physiological, pathological, or other condition….; 2. Supplying a vitamin, mineral, or other ingredient for use by humans to supplement the diet by increasing the total dietary intake. 3. Supplying a special dietary need by reason of being a food for use as the sole item of the diet…". Examples of such include infant foods, hypoallergenic foods such as gluten-free and lactose-free foods, and foods offered for reducing weight (Heller 2009).

Canada

Health Canada defines functional foods as "similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions".

Japan

Japan is the only country that recognises functional foods as a distinct category, and the Japanese functional food market is now one of the most advanced in the world. Known as "foods for specified health use", these are foods composed of functional ingredients that affect the structure and/or function of the body and are used to maintain or regulate specific health conditions, such as gastrointestinal health, blood pressure and blood cholesterol levels (EAS 2008).

Food supplements

Ireland

The 2003 Irish food supplements regulation (S.I. No. 539) lays down specific rules for the use of vitamins and minerals in food supplements. Herb and other substances are not specifically covered at this stage (EAS 2008). The Irish regulation lists the vitamin and mineral substances permitted for use in food supplements, in line with those listed in Annex II of the EU Food Supplement Directive. The Irish Food Safety Authority (FSAI) has granted derogations for 210 substances until the end of 2009. No minimum or maximum levels have been set in the 2003 regulations; however, the Irish authorities indicate that the level should not exceed $1\times$ the recommended daily intake as listed in the 2005 nutrition labelling for foodstuffs regulations (S.I. No. 65 of 2005). Bioactive substances are evaluated on a case-by-case basis and classified as foods or medicines by the Irish Medicine Board (IMB). When substances are to be considered safe, the FSAI generally does not object to their use as a food supplement. To this purpose, the IMB also communicates ingredient/product classification decisions to the FSAI. The FSAI may ask the IMB for an opinion, in case of doubt. According to IMB guidelines, amino acids may only be used at levels usually present in a normal diet. This is, however, not enforced, except for tryptophan (EAS 2008).

The regulations require a food supplement product to be notified by forwarding a completed notification form, a model of the label and any relevant references. This requirement applies when the product is manufactured and is being placed on the Irish market for the first time. Once notification has taken place, food products can be placed on the market and sold through a variety of outlets, such as supermarkets, pharmacies, drugstores and health food stores.

Fortified and functional foods

European Union

The new EU Regulation 1925/2006 on the addition of vitamins and minerals and certain other substances to food came into force in Ireland in July 2007. The legislation currently provides clear rules for the addition of vitamins and minerals to food, whilst herbal ingredients and other substances are not explicitly mentioned in the Regulation. There is currently no additional national legislation on food fortification or functional foods (EAS 2008). With regard to functional foods, amino acids, fish oil and lactic bacteria can generally be used in foods as long as the resulting product is safe. There is no notification requirement for foods with added substances, and products can be sold via all outlets.

The underlying principle of all legislative developments is that the food manufacturer must be able to substantiate every health claim on any functional food that is marketed. The question of "what is sufficient scientific evidence?" remains a problem (Korver et al. 2008). Although the safety aspects of new functional

Table 16 Effects, source species and test system of phlorotannins found in genera of seaweed of interest in Northwest Europe

Effects	Source	Test system
Antioxidant[a,b,c,d,e,f,g,h,i,j,k,l,m,o,p]	*Laminaria setchelli*[b]	In vitro[o,l]
	Fucus spiralis[c]	ESR cellular systems in vitro[p]
	Ascophyllum nodosum[m]	HeLa cells[b,n]
	Sargassum mangarevense[g]	Solvent partition and NMR experiments[c]
	S. siliquastrum[f]	Improved blood antioxidant activity[m]
	Ulva lactuca[j,k]	Inhibition of red blood cells hemolysis[f]
	Porphyra umbilicalis[i]	Supression of lipid peroxidation using rat brain
	Kappaphycus alvarezii[d]	homogenates[f]
	Polysiphonia urceolata[h]	Scavenging activity of superoxide radicals[f]
	Palmaria palmata[b,n]	DPPH scavenging ability[d,h]
Radiation protection[o,n,e]	*Palmaria palmata*[n]	In vitro, ascorbic acid calibration curve[n]
	Ascophyllum nodosum[e]	Absorption in UV-B range which leads to protection against UV-B radiation[e]
Anti-proliferative activities[b,v,n]	*Laminaria setchellii*[b]	In vitro, HeLa cells[b,n]
	Palmaria palmata[b]	
Antibiotics[q,r,g,s]	*Ulva lactuca*[q]	Bacteria and epifauna[r]
	Sargassum natans[r]	Anti-*Staphylococcus* activity[g,s]
	S. fluitans[r]	Strong antibacterial activity against the fish pathogens
	S. mangarevense[g]	*Vibrio parahemolyticus* and *Edward tarda*[s]
	Sargassum sp.[s]	
	Eisenia bicyclis[s]	
Anti-diabetes[m,o]	*Ascophyllum nodosum*[m]	In vivo, rats and mice: inhibits intestinal a-glycosidase, stimulates basal glucose uptake, decreases blood total cholesterol and glycated serum protein levels, normalises the reduction in liver glycogen level[m]
Sexual performance and desire[e]		Human respons to oral absorption[e]
Anticancer[o,u]		
Anti-HIV[o]		
Hepatoprotective effects[u]		
Anti-allergic[o]		
Anti-plasmin inhibition[v]		
Photo chemoprevention[v]		
Antibacterial activity[w,x]		
Anti-inflammatory[u]		
Preventive against cardiovascular diseases[u]		
Preventive against arthritis[u]		
Preventive against autoimmune disorders[u]		

[a] Plaza et al. (2008); [b] Yuan and Walsh (2006); [c] Cérantola et al. (2006); [d] Kumar et al. (2008a); [e] Kang et al. (2003); [f] Lim et al. (2002); [g] Zubia et al. (2008); [h] Li et al. (2007); [i] Sampath-Wiley et al. (2008); [j] Flodin et al. (1999); [k] Pedersen et al. (1996); [l] Nakamura et al. (1996); [m] Zhang et al. (2007); [n] Yuan et al. (2005); [o] Li et al. (2009); [p] Zou et al. (2008); [q] Murata and Nakazoe (2001); [r] Sieburth and Conover (1965); [s] Kim and Lee (2008); [u] Maliakal et al. (2001) and Garbisa et al. (2001); [v] Li et al. (2008b); [w] Sailler and Glombitza (1999); [x] Nagayama et al. (2003)

foods are covered in the EU Novel Foods legislation (258/97/EC as amended by 1829/2003/EC and 1882/2003/EC), no European legislation exists specifically for the health benefits (efficacy and health claims). Until there is such legislation, EU Member States will each continue to have their own set of rules and regulations. A proposal was submitted by the European Commission in 2003 on nutrition and health claims to better inform the consumer and harmonise the market. It was hoped that this would transpose into law by 2005 (Korver et al. 2008). Negotiations between EU Member States about a legislative framework for health claims have been going on for many years. At the crux of the problem are the different views on functional foods in various EU countries. For instance, in some countries, especially in Southern Europe, the attitude on functional foods is generally fairly positive

Table 17 Effects of extracts from the seaweed species or genera of interest in Northwest Europe

Effect	Species	Detail on effect or extract
Anti-fungicidal[a,b,m]	Laminaria digitata[b,m]	Seaweed conditioned seawater had antifungal effect on fungal-specific PCR primers[m]
Anti-ulcerative activity[a]		
Antioxidation[c,d,n,o]	Laminaria digitata[d,n]	Synergistic effect as antioxidant with vitamin E at given concentration[n]
		Intermediate antioxidant activity [d]
	Sargassum fusiforme[o]	Heat- and UV light-resistant antioxidants[o]
Antibacterial[b,e,f,g,h,m,p]	Saccharina latissima[h]	Petroleum ether and methanol extract active against Escherichia coli[h]
	Laminaria digitata[b,m,h]	Chloroform extract active against Proteus vulgaris[h]
		Seaweed conditioned seawater reduced the community composition of bacteria (bacteria-specific PCR primers)[m]
	Laminaria orchroleuca[p] Chondrus crispus[p]	Ethanolic extract antibacterial and non-toxic against non-targeted larvae[p]
	Ascophyllum nodosum[p]	Ethanolic and dichloromethane extract antibacterial. The first non-toxic against non-targeted larvae[p]
	Fucus serratus[h]	Petrolium extract active against Streptococcus pyogenes[h]
	Sargassum muticum[p]	Ethanolic and dichloromethane extract. Both non-toxic against non-targeted larvae[p]
	Sargassum mangarevense[e]	Against Staphylococcus[e]
	Palmaria palmata[p]	Dichloromethane extract antibacterial and non-toxic against non-targeted larvae[p]
Anti-pathogenic bacterial[i,j,g,q,r]	Laminaria digitata[g]	Strong fish pathogenic bacterial activity at 31 mg dw/mL[g]
	Gracilaria chilensis[j]	Agar degrading microorganisms[j]
	Gracilaria cornea[q]	Against Vibrio anguillarum and Pseudomonas anguilliseptica[q]
	Ulva pertusa[r]	Against E. coli and Pasteurella piscicida with 5% Ulva feed supplement[r]
Anti-inflammatory[k]	Undaria pinnatifida[k] Ulva linza[k]	Mice edema and erythema[k]
Lipid peroxidation[o,s]	Sargassum fusiforme[o]	
	Sargassum micracanthum[s]	Better than vitamins A and E[s]
Preventive against DNA damage[l]	Sargassum thunbergii[l]	
Reactions in rodents[h,v,t]	Laminaria digitata[h]	Chloroform extract inhibited the contractions of the stimulates guinea pig ileum at a concentration of 100 μg/mL and water extract decreased motor activity, weak loss of screen grip, enophthalmus and cyanosis with death occuring several hours later[h]
	Fucus serratus[h]	Water extract decreased motor activity and pilomotor erection in the hippocratic screening of mice[h]
	Ascophyllum nodosum[h]	Water extract decreased motor activity and pilomotor erection in the hippocratic screening of mice and induced fearful behaviour[h]
	Undaria pinnitifida[t]	5% powder (wet wt of diet) significantly delayed the development of stroke signs and significantly improved the survival rates of stroke-prone hypertensive rats[t]

[a] Plaza et al. (2008); [b] Lam et al. (2008); [c] Murata and Nakazoe (2001); [d] Huang and Wang (2004); [e] Zubia et al. (2008); [f] Freile-Pelegrín and Morales (2004); [g] Plouguerne et al. (2008); [h] Andersson et al. (1983); [i] Dubber and Harder (2008); [j] Weinberger (2007); [k] Khan et al. (2008); [l] Park et al. (2005); [m] Lam et al. (2008); [n] Le Tutour (1990); [o] Siriwardhana et al. (2004); [p] Hellio et al. (2001); [q] Bansemir et al. (2006); [r] Satoh et al. (1987); [s] Mori et al. (2003); [t] Ikeda et al. (2003)

Table 18 Seaweed species used as feed supplement or replacement

Test organism	Species	Replacement of feed (%)	Effect	Reference
Sea bass juveniles	*Gracilaria bursa-pastoris*	Protein 10%	No negative consequences on growth performance, nutrient utilisation or body composition	Valente et al. (2006)
	Gracilaria cornea	Protein 5%	No negative consequences on growth performance, nutrient utilisation or body composition	Valente et al. (2006)
	Ulva rigida	Protein 10%	No negative consequences on growth performance, nutrient utilisation or body composition	Valente et al. (2006)
Sea bream	*Ascophyllum nodosum* *Porphyra yezoensis* *Ulva pertusa*		Increased body weight, feed efficiency and muscle protein deposition	Mustafa et al. (1995)
	Porphyra>*Ascophyllum*>*Ulva*		Growth and energy composition	Mustafa et al. (1995)
	Ascophyllum nodosum	0%, 2.5%, 5%	Increased muscle protein in response to the algae level	Nakagawa et al. (1997)
			Response to air-dipping and recovery time from anaesthesia with 2-phenoxyethanol	
	Ulva pertusa	Lipid Up to 5%	No effect on growth	Nakagawa and Kasahara (1986)
			Accumulated triglycerides	
			Low fatty acid composition	
			Activated lipid mobilisation	
			Suppressed protein breakdown	
	Ascophyllum nodosum *Undaria pinnatifida*	5%	Improved growth and feed efficiency	Yone et al. (1986)
Nile tilapia	*Ulva* sp.	Lipid 5%	Increased specific growth rate (SGR)	Kotake-Nara et al. (2001)
			Increased feed conversion ratio (FCR)	
			Increased protein efficiency ratio (PER)	
	Ulva sp.	Protein 5%	Increased growth, specific growth rate, FCR and PCR	Ergün et al. (2008)
Rainbow trout	*Porphyra dioica*	Protein and lipid Up to 10%	No difference in weight gain and growth performance Increased pigmentation	Soler-Vila et al. (2009)
Sea urchin	*Sargassum linearifolium*		Feeding stimulant Increase protein and energy consumption	Dworjanyn et al. (2007)
Pigs	*Palmaria palmata* (Pp) *Laminaria digitata* (Ld)	Dietary fibres Alginate	Pp no effect Ld increased the ileal viscosity of digesta and their intestinal hydration capacity	Hoebler et al. (2000)
Weanling pigs	*Laminaria hyperborea* *Laminaria digitata*	Contained laminaran and fucoidan	Decrease in intestinal bacteria Reduction in intestinal ammonia concentration	Reilly et al. (2008)
			Marginal effect on immune response	
	Laminaria sp.	Contained laminaran and fucoidan	May alleviate use for high-lactose diets Alleviate some of the common problems that occur post weaning	Gahan et al. (2009)
	Ascophyllum nodosum	Extract Iodine	Reduction in intestinal *E. coli* Increases iodine concentration in several tissues	Dierick et al. (2009)
Grower-finisher pigs	*Ascophyllum nodosum*	Extract	Reduced daily weight gain, but no effects on feed intake, FCR, or carcass characteristics Change in intestinal bacterial communities	Gardiner et al. (2008)
Sheep	*Ascophyllum nodosum*	2%	Lowered body temperature during transport Suppressed antibody titre, which could leave animals susceptible to bacterial infection	Archer (2005)
	Ascophyllum nodosum	35 g	Less body weight reduction of ewes Increased number of lambs born per ewe and increased growth rate of lambs	Sæter and Jensen (1957)
			Increased wool production (20%), prevented moulting	
Cattle	*Ascophyllum nodosum*	158 g	Higher milk yield (6%) and no influence on fat content of milk Increase in iodine content of milk (100 in control to 600 μg/L in test)	Jensen et al. (1968)
			Less body weight gain during barn feeding periods	
			No difference in reproduction performance and the weight of new-born calves	
			Less incidence of mastitis	
	Ascophyllum nodosum	>2%	Main effect: increasing the shelf life of meat	Gravett (2000)
Chicken	*Porphyridium* sp.	Polysaccharides PUFA and EPA	No difference in body weight, egg number and egg weight Consumed less food (10%)	Ginzberg et al. (2000)
		5% and 10%	Lower cholesterol level (decrease of 28%)	
			Reduced cholesterol but increased fatty acids and darker colour of egg yolk	

Species of the genera available in Northwest Europe are included. Percentage replaced by seaweed according to the reference compound. Effects of seaweed on test organism are described

Table 19 Total arsenic, inorganic arsenic, lead, cadminum and mercury in seaweed

Phyllum	Species	Description of product	Total As	Inorg. As	Pb	Cd	Hg
Green	*Enteromorpha* sp.	Green nori flakes (dried edible algae)	2.3±0.1	0.37±0.07	1.33±0.03	0.03±0.01	20.6±0.4
	Ulva sp.	Irish coast	6.39±0.59				
	Ulva pertusa	AO nori (dried edible algae)	5.17±0.05	0.36±0.06	0.93±0.02	0.17±0.01	18±2
Red	*Porphyra* sp.	Irish coast	11.5±9.75	<0.15			
	Porphyra tenera	Nori (dried edible algae)	23.7±0.5	0.57±0.04	0.31±0.06	0.35±0.01	14±2
		Nori (dried edible algae)	28.3±0.5	0.19±0.02	0.289±0.004	0.18±0.02	4±1
		Toasted nori (dried edible algae)	30±1	0.314±0.005	0.29±0.02	0.38±0.01	11.3±0.4
	Palmaria palmata	Atlantic dulse (dried tender Japanese algae)	7.56±0.02	0.44±0.06	1.1±0.2	0.70±0.03	10.5±0.4
		Irish coast	12.8±0.46				
Brown	*Eisenia bicyclis*	Ise wild arame (dried tender Japanese algae)	23.8±0.5	0.17±0.02	0.15±0.08	0.75±0.01	33.6±0.2
		Ise wild arame (dried tender algae)	29±1	0.185±0.005	0.18±0.01	0.67±0.03	42±3
		Arame (dried edible algae)	30.0±0.1	0.15±0.06	0.19±0.02	0.74±0.02	38±3
	Undaria pinnatifida	Wakame (dried edible algae)	32±1	0.15±0.10	<LOD	1.5±0.1	12±1
		Wakame (dried edible algae)	42±2	0.26±0.03	<LOD	0.13±0.03	23±3
		Japanese wakame (dried tender algae)	34.6±0.3	0.18±0.05	<LOD	1.9±0.1	14±1
	Laminaria japonica	Japanese kombu (dried tender algae)	47±1	0.297±0.001	<LOD	0.15±0.02	30±5
		Kombu (dried algae)	53±1	0.254±0.005	<LOD	0.30±0.02	37±4
	Saccharina latissima	Irish coast	49.5				
	Fucus vesiculosus	Alga fucus	50.0±0.3	0.34±0.04	0.51±0.04	0.55±0.01	36±6
		Irish coast	31.2±8.42				
	Hizikia fusiformis	Iziki	128±5	88±6	0.63±0.08	1.45±0.14	35±3
		Hijiki	141±6	85±6	0.89±0.15	1.46±0.02	25.9±0.2
		Japanese hijiki (dried tender Japanese algae)	115±12	83±5	0.53±0.06	1.0±0.1	30.32±0.03

Seaweed put on market and Irish seaweed from nature. Free after Almela et al. (2002) and Durcan et al. (2010)

Three subsamples were analysed for each typ of macroalgae. Values are expressed as mean ± SD. Results of As, Pb and Cd are expressed in milligrams per kilogram dry weight. Results for Hg are expressed in micrograms per kilogram dry weight. Pb=0.05 mg/kg dry weight

LOD limit of detection

and similar to the US. In other countries, functional foods tend to be seen as medicines, and in Germany, for example, legislators have tried to push them into the pharmaceutical regulatory system. Scandinavia is traditionally very reserved towards industry involvement and wants safeguards against possible abuse (Korver et al. 2008). Nevertheless, the regulation was adopted as Regulation (EC) No. 1924/2006 of the European Parliament and of the Council on Nutrition and Health Claims made on foods by the end of 2006. This Regulation lays down harmonised rules for the use of nutrition and health claims and contributes to a high level of consumer protection. It ensures that any claim made on a food label in the EU is clear, accurate and substantiated, enabling consumers to make informed and meaningful choices. The Regulation also aims to ensure fair competition and promote and protect innovation in the area of food. Regulation EC No. 1924/2006 on nutrition and health claims made on foods came into force on 19 January 2007 and has been applied from 1 July 2007.

Health claims

A "health claim" means any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health. The nutrition and health claims Regulation 1924/2006 does what the name says and is something that innovative food industries and those carrying out research and development should be aware of because it has a major bearing on the marketability of a potential food or ingredient. A 'positive list' of well-established claims should be elaborated within 3 years of the Regulation entering into force. This list should describe the role of a nutrient or of another substance in growth, development and the normal functions of the body, which are based on generally accepted scientific data and well understood by the average consumer. As an example, the claim that calcium plays an important role in the strengthening of teeth and bones would be permitted. For more novel claims, scientific evaluation and premarketing approval will be required. Implied health claims will not be allowed, for

Table 20 Seaweed authorised for human consumption in France (free after Burtin 2003)

Phyllum	Seaweed species
Brown seaweed	*Ascophyllum nodosum*
	Fucus serratus
	Fucus vesiculosus
	Himanthalia elongata
	Undaria pinnatifida
Red seaweed	*Porphyra umbilicalis*
	Palmaria palmata
	Chondrus crispus
	Gracilaria verrucosa
Green seaweed	*Enteromorpha* spp.
	Ulva spp.

example claims which make reference to general non-specific benefits of the nutrient or food for overall good health. Claims will not be permitted that make reference to the advice of doctors, other health professionals, their professional associations or charities, or suggest that health could be affected by not consuming the food (EAS 2009).

Proactive companies seeking to keep ahead of the competition will be assisted by a European Commission decision to fast track health claims based on newly developed science and a decision to give exclusive use for 5 years of claims requiring proprietary data protection (EAS 2009). Article 13.5 allows data protection, which means that competitors must have similar data of their own to submit in order to make the same claim. The decision to allow these claims to be submitted in February 2008 rather than waiting until the final cutoff in 2010 will boost industry competitiveness on the European Union food market. Claims which are not based on proprietary data, but which are currently in use, should already be scientifically justified. This makes it difficult to say the

Table 21 Quality criteria applied to edible seaweed sold in France (Burtin 2003), regulations in the USA (Mabeau and Fleurence 1993) and for dietary supplements in EU (EU 2008)

Toxic minerals	Limit (mg kg^{-1} dry matter, ppm)		
	France	USA	EU regulation
Inorganic arsenic	<3.0	<3.0	No regulation
Lead	<5.0	<10	<3.0
Cadmium	<0.5		<3.0
Tin	<5.0		
Mercury	<0.1		<0.1
Iodine	<0.5	<5,000	
Heavy metals		<40	

claim is based on newly developed scientific evidence. Such claims should be introduced into the Article 13 list before the deadline of 31 January 2009. If they are not, then the companies would either have to withdraw their claim when the claims list is established in 2010 or in the intervening time submit an application to have it approved under the Article 13.5 procedure (EAS 2009).

If a company makes a nutrition or health claim about a product, it *must* comply with Regulation 1924/2006 on nutrition and health claims made on foods. Permitted nutrition claims are listed in the Annex to the legislation. A list of approved health claims and conditions for their use should have been published by the European Commission by 31 January 2010 at the latest, but it has not yet been released. Health claims not on this list will not be permitted.

It is the food business operator's responsibility to comply with this Regulation. Claims that are not compliant will not be permitted.

Novel food authorisation in the EU

A novel food is any food or ingredient that does not have a significant history of consumption in the EU prior to 15 May 1997 (European Commission 1997). This legislation is currently being revised, but will be in place for another year or so yet. To introduce a novel food or ingredient to the EU market, prior authorisation is required through this Regulation, which includes a safety assessment carried out by a Member State and possibly also by the European Food Safety Authority. Final authorisation is completed by a voting process (Comitology) by Member States.

Authorisation to market a novel food in Europe, which includes manufacturing processes, requires a rigorous assessment of toxicological, nutritional, compositional and other relevant data by the competent authorities of EU Member States. A new food does not qualify as a 'novel' food and may be placed on the market within the EU after notification to the European Commission if it is proven to be substantially equivalent to one already on the market. However, a food or food manufacturing process is considered 'novel' if it has not been available within the EU (at least one Member State) to a significant degree prior to 15 May 1997 (Novel Food Regulation EC 258/97; European Commission 2007). The authorisation process is a multi-step procedure with defined time limits coordinated by the European Commission (DG SANCO) and involves the applicant and EU Member States with their expert advisory personnel (O'Mahony 2009, personal communication). This process is outlined in Fig. 1.

The FSAI became the competent authority for novel foods, taking over from the Department of Health and Children on 1 January 2001. The FSAI is a consumer-oriented, science-based independent body and draws on the
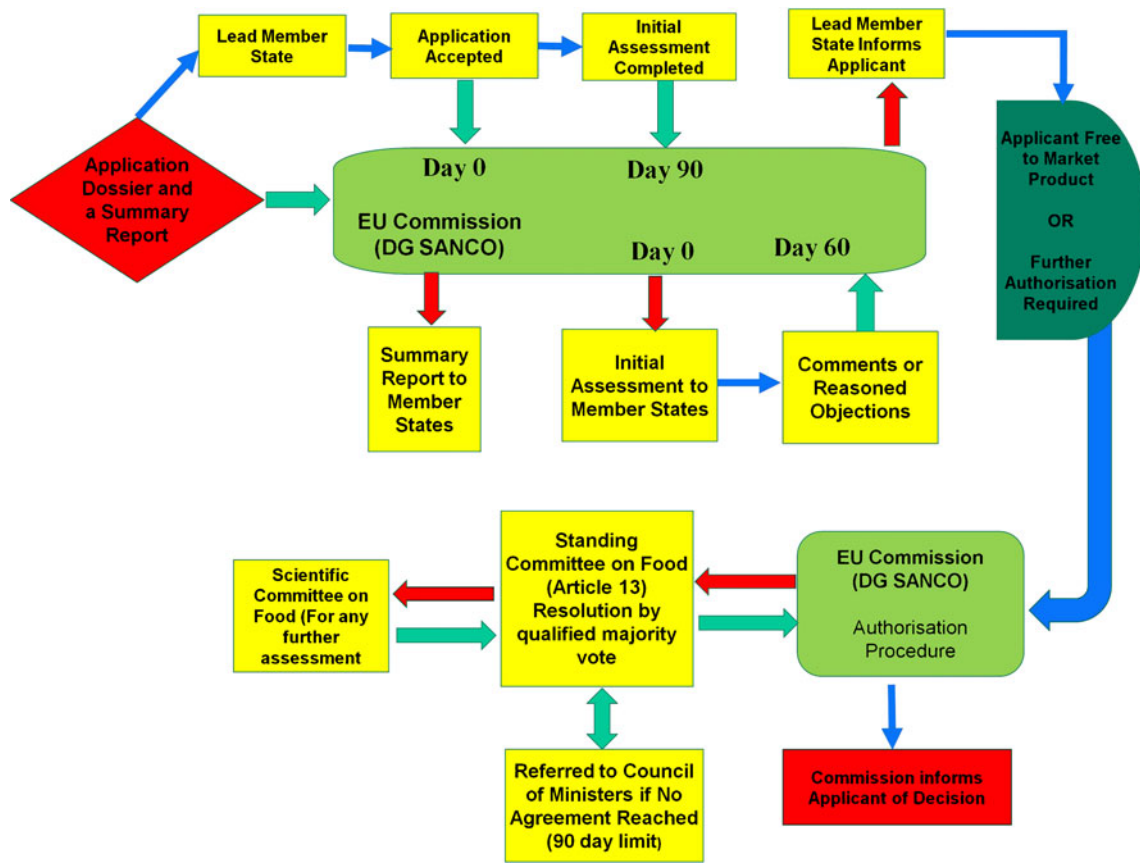
Fig. 1 Procedure for authorisation of novel food within EU (FSAI 2010)

expertise of scientists throughout the country for advice. The FSAI is responsible for the premarketing safety assessment of any novel food to be marketed in Ireland and Europe (Fig. 2). Whilst Ireland has not yet had any direct applications, it has reviewed and provided comments with the help of its scientific advisers on novel food assessments by other Member States. The FSAI is also responsible for ensuring compliance with novel food regulations in Ireland, including appropriate labelling laws. The FSAI handles all aspects of novel foods, including application assessments, regular surveys of the marketplace, and dissemination of information on procedures and legislation (FSAI 2010).

Fig. 2 Management of novel foods (FSAI 2010)
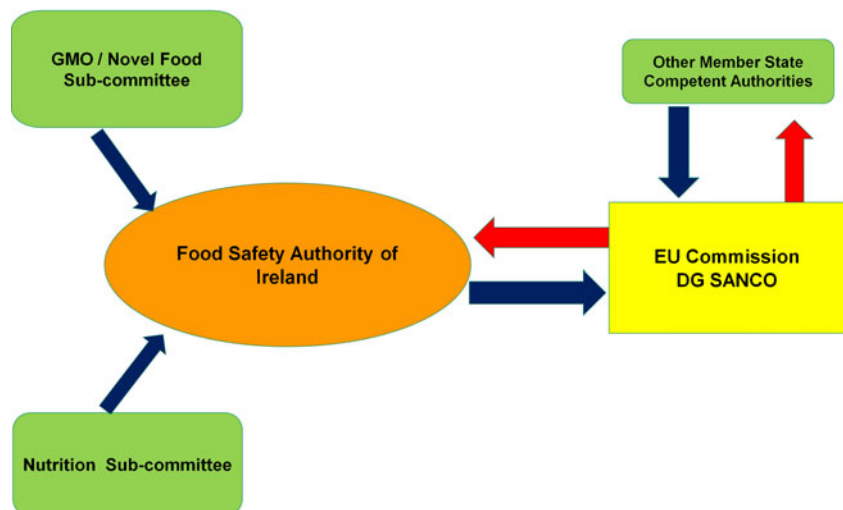
One to two novel food applications are assessed on average each month by EU Member States, whilst a number of others are simply notified to the Commission as being substantially equivalent. To have a novel food marketed within the EU, a company must prepare a dossier detailing prescribed safety-related scientific data and present it to a lead Member State along with an assessment fee that varies between Member States. An initial assessment of the data is carried out by the 'lead' Member State that presents a report to the Commission, which in turn provides it for other Member States. The summary report and initial assessment are then critically reviewed by Member States before a decision is made. A positive decision means that the applicant is free to market the product within the EU. Reasoned objections, or a request for further assessment, lead to the application being referred to the Standing Committee on Food who may seek advice from the Scientific Committee on Food before making its own decision through a qualified majority vote. It is referred to the Council of Ministers who may decide to accept or reject a Commission proposal by qualified majority if the Standing Committee on Food fails to reach a decision. The Commission will be free to implement its proposal as it stands if the Council of Ministers fails to successfully address the issue within 90 days.

Novel foods containing, or derived from, genetically modified organisms (GMOs) have attracted much attention in recent years. This notoriety has subsided despite the de facto moratorium that has been in place on such foods, resulting in numerous foods derived from GMOs (GM food) being stranded in the authorisation process. In the meantime, other non-GM novel food applications are being assessed and, whilst most are eventually authorised, a small number have been rejected. However, the FSAI anticipates this to be an active area for the foreseeable future with the expected evolution of current and pending EU novel food regulations and the increasing numbers of foods and food processes seeking a marketplace within the EU. The constant vigilance and heightened awareness of the EU and its Member States on the issue of novel foods can be justified by consumer concerns about the food supply and in light of serious food scares of the recent past (O'Mahony 2009, personal communication). Legislation has appeared in piecemeal fashion over the years as and when required. What usually happens is that consolidated legislation is developed which simplifies matters into one or a few documents, but advances in food production and processing are still growing, so consolidation is still a long way.

The FSAI has interaction with the IMB. Unlike most food legislation, medicine legislation is not as harmonised in the EU. Therefore, interpretation can vary between Member States, whilst there is common EU medicinal legislation. What this means is that what one Member State considers a medicine, another may not. When the IMB considers an ingredient medicinal, they have the prerogative to bring it under medicines control, though not a written rule. A claim that a food can bring about the treatment or cure of a disease automatically brings the product under medicine legislation. The nutrition and health claim legislation will only affect the marketing of a product and not its legal status as long as medicinal claims are not made.

Food supplements (certain vitamins and minerals) are covered by Directive 2002/46, and to be able to use these ingredients in dietary supplements, they must be listed in the annex to this legislation. To introduce new vitamins and minerals into supplements would firstly require a safety assessment and authorisation under the Novel Food Regulation 258/97. Those supplements containing non-vitamin or mineral ingredients (herbal supplements) would fall under novel food legislation (Novel Food Regulation 258/97).

The Food Fortification Regulation 1925/2006 sets out standards of purity and other conditions for the addition of vitamins, minerals and certain other substances to foods (fortification). Only vitamins and minerals (and their formulations) listed in the Annex may be added to foods, and to add a new one would require authorisation through novel food legislation (1925/2006).

Summary and conclusion

This review summarises the potential of bioactive molecules in species that could be of interest for utilisation for health and functional food applications. The compounds of interest need to be identified before making choices of which species to exploit because one species may be high in one compound, but low in another.

Most of the polysaccharides stimulate human health, for example by the creation of a better intestinal environment or because of their antiviral, anti-tumour and hypocholesterolemic and hypolipidemic properties. As an example, fucans are in large concentrations in large brown seaweed species. These are easy to isolate and have numerous health benefits, which give them the potential to serve as a valuable bioactive ingredient in natural health foods. The choice of species to exploit the content of bioactive compounds relies on the aim and property of the polysaccharide. Proteins, peptides and amino acids from seaweed have shown positive bioactive effects in the treatment of diabetes, cancer, and AIDS and the prevention of vascular diseases. The amino acid profile of some seaweed species is similar to that of animal foods. Extracts of valuable amino acids for feed supplement could be of potential because essential amino acids cannot be replaced by other compounds. The essential amino acids need to be present in the right quantities in order to make proteins. The genera *Ulva*,

Laminaria, *Saccharina*, *Sargassum* and *Chondrus* have some of the best profiles for the amino acids needed in fish feed. Seaweed lipids have high percentages of the omega-3 fatty acids and have been tested positive as immune stimulants, whilst the fucosterol content decreases the concentration of cholesterol in animal and humans. In addition to this, other general effects of PUFAs include anti-arteriosclerosis, anti-hypertension, anti-inflammation and immunoregulation. The pigments have shown bioactivity effect towards, e.g. cancer, obesity, decreasing blood glucose and as an antioxidant. *Fucus*, *Ascophyllum* and *Sargassum* are some of the best sources of phenols for antioxidant purposes. The phlorotannins show bioactive effects such as antioxidant activity, radiation protection, antibiotics, anti-diabetes, etc. Phlorotannins would be potential candidates for the development of natural antioxidants for further industrial applications such as functional foods, cosmetics and pharmaceuticals.

Powder and extracts of seaweed have shown bioactive effects such as antioxidant, peroxidation of fatty acids, antibacterial, anti-fungical and anti-inflammatory. Almost all genera of seaweed have shown effects. Effects on animals when seaweeds are used as ingredients in food have been interesting, including higher milk yield in cattle, increased growth rate of lambs, increased iodine concentration in tissues and change in intestinal bacterial communities of pigs, and accumulation of triglycerides in sea bream. In several of the experiments, growth performances are increased or at least there are no negative effects. Seaweed species are potentially good candidates as feed supplements, with beneficial effects on health or the desired properties of the animal and product.

However, seaweed not only accumulates the desired minerals and trace metals but also accumulates undesirable metals and heavy metals from the surrounding environment. This can be exploited, and seaweed can be used as a biofilter. Kainic acid and high inorganic arsenic are toxic and accumulated in species such as *P. palmata* and *Sargassum* sp., respectively.

This review finishes with rules and regulations in respect to heavy metals in seaweed for human consumption and other EU regulations on food supplements and health claims. There are different views in respect to seaweed as food. For example, edible seaweed species have been approved as a human food product in France and are recognised by the EU. Legislative aspects are compared with the current situations in the US, Japan and some other major players in the functional food markets.

Clearly, it is not easy to market a bioactive component derived from seaweed because one has to adhere to the current legislation, which is continuously changing and not very transparent. Other licences are required to source material for processing and extraction and to deal with waste issues that might arise from extraction. In order to market seaweed and/or bioactive compounds derived from seaweed as novel or functional food and make health claims, one needs proven scientific evidence and an extensive scientific dossier needs to be submitted to the EU. This is often an expensive exercise.

Legislation is complicated and will become even more complicated with time, according to experts at food safety authorities. The high cost of scientific dossier (if a new activity or compound is discovered) makes it difficult to further develop seaweed as a functional food ingredient. Nevertheless, seaweed as a whole food product, or bioactive compounds extracted from seaweed, show a tremendous potential for human health and should be further developed and exploited.

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