Special Article

Risks and benefits of consuming edible seaweeds

Paul Cherry, Cathal O'Hara, Pamela J. Magee, Emeir M. McSorley, and Philip J. Allsopp

Recent interest in seaweeds as a source of macronutrients, micronutrients, and bioactive components has highlighted prospective applications within the functional food and nutraceutical industries, with impetus toward the alleviation of risk factors associated with noncommunicable diseases such as obesity, type 2 diabetes, and cardiovascular disease. This narrative review summarizes the nutritional composition of edible seaweeds; evaluates the evidence regarding the health benefits of whole seaweeds, extracted bioactive components, and seaweed-based food products in humans; and assesses the potential adverse effects of edible seaweeds, including those related to ingestion of excess iodine and arsenic. If the potential functional food and nutraceutical applications of seaweeds are to be realized, more evidence from human intervention studies is needed to evaluate the nutritional benefits of seaweeds and the efficacy of their purported bioactive components. Mechanistic evidence, in particular, is imperative to substantiate health claims.

INTRODUCTION

Edible seaweeds (macroalgae) have the potential to provide a rich and sustainable source of macronutrients and micronutrients to the human diet, particularly in regions where seaweed makes a significant contribution to regular meals, eg, in Japan, where approximately one-fifth of meals contain seaweed.[1–3] Inclusion of seaweeds in Western diets has traditionally been limited to artisanal practices and coastal communities but has gained wider consumer interest in recent years, courtesy of the health-food industry.[4] The recent surge of interest in seaweed is fueled by attention on the bioactive components of seaweed, which have potential applications in the lucrative functional food and nutraceutical industries, with impetus toward the alleviation of metabolic risk factors such as hyperglycemia, hypercholesterolemia, and hyperlipidemia.[5] The candidate bioactive components of interest to industry include isolated polysaccharides (eg, alginate, fucoidan), proteins (eg, phycobiliproteins), polyphenols (eg, phlorotannins), carotenoids (eg, fucoxanthin), and n-3 long-chain polyunsaturated fatty acids (eg, eicosapentaenoic acid). Scientific experiments and human studies to date have focused predominantly on brown seaweeds and derivatives, largely because of their commercial abundance and perceived sustainability.

Despite the nutritional attributes of red seaweeds such as *Porphyra* spp (also known as nori) and *Palmaria palmata* (dulse), which have a high protein content, relatively few investigations have focused on red seaweeds as a source of bioactive components. Current understanding of the health-promoting activities of red seaweeds derives from an abundance of in vitro studies and in vivo animal studies. There are only limited reports of green seaweeds contributing to

Affiliation: *P. Cherry*, *C. O'Hara*, *P.J. Magee*, *E.M. McSorley*, and *P.J. Allsopp* are with the Nutrition Innovation Centre for Food and Health, School of Biomedical Sciences, Ulster University, Coleraine, United Kingdom. *C. O'Hara* is with VOYA Products Limited, County Sligo, Ireland.

Correspondence: *P.J. Allsopp*, Nutrition Innovation Centre for Food and Health, School of Biomedical Sciences, Ulster University, Cromore Road, Coleraine, Co. Londonderry BT52 1SA, United Kingdom. Email: pj.allsopp@ulster.ac.uk.

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dietary intake of either essential nutrients or bioactive components, despite the potential for transient algal blooms to be exploited.[6]

Aquaculture is recognized as the most sustainable means of seaweed production and accounts for approximately 27.3 million tonnes (96%) of global seaweed production per annum, yet the growing demand for seaweed-based food ingredients calls for more established guidelines and regulations to ensure sustainability.[7] Future considerations for stakeholder management include resource ownership; best practices for cultivation; harvesting rights/licensing; certification/validation of origin; overexploitation; biomass regrowth; environmental impacts; and the development of a sustainable value chain within the agrifood sector.[2]

An abundance of commercially available seaweed products, including both whole seaweed and seaweed extracts, are marketed both directly and indirectly as value-added products for the promotion of health in the supplement market. The health claims associated with seaweed products are often based on insufficient (or completely absent) evidence from human intervention studies to substantiate such statements. Furthermore, there are considerable safety concerns related to potential adverse events associated with seaweed consumption, particularly in light of the variable and potentially dangerously high concentrations of iodine and heavy metals (including arsenic species) in certain seaweeds.[8,9] There is currently limited legislation to require food or supplement companies to disclose mineral, heavy metal, or iodine content of seaweed products or to provide guidance on a safe portion size of certain whole seaweeds in order to prevent excess intakes.[4] Ultimately, if seaweeds are to contribute to future global food security, either in their whole form or via extraction of their nutrients, the industry should develop a sustainable heavy metal/iodine monitoring program or, alternatively, identify novel processing technologies to ensure that unsafe components such as arsenic are minimized to safe levels, thus protecting the food chain.[2,10–14]

The health benefits of seaweed, beyond the provision of essential nutrients, have been supported by in vitro studies and some animal studies; however, many of these studies have inappropriate biomarkers to substantiate a claim and have not progressed to suitably designed human intervention trials to evaluate efficacy. The limited evidence that does exist makes some seaweed components attractive as functional food ingredients, but more human evidence (including mechanistic evidence) is needed to evaluate both the nutritional benefit conferred and the efficacy of purported bioactives and to determine any potential adverse effects. Through an evaluation of the nutritional composition of edible seaweeds, this review summarizes the available evidence and outlines the potential risks and health benefits of consuming whole seaweeds, extracted bioactive components, and seaweed-based food products in humans. Additionally, it identifies future opportunities for functional food and nutraceutical applications.

NUTRITIONAL COMPOSITION OF EDIBLE SEAWEEDS

A number of edible seaweeds are recognized as novel foods in Europe, although the nutritional composition of brown, red, and green seaweeds varies between species, season, and ecology of the harvesting location.[15] Therefore, there is a need to characterize the composition of seaweeds in relation to the influence of location and seasonality on seaweed content. Current efforts to catalog information on the variability of nutritional composition will facilitate the identification of optimal harvesting periods and/or locations for a given species. Such information would aid the functional food industry in targeting optimal conditions for isolating specific bioactive components.[16–18] Table 1,[17,19–32] Table 2,[19–22,26,27,29–31,33–42] and Table 3[19–24,26,27,29,30,36,43–53] present the macronutrient content of multiple brown, red, and green seaweeds, respectively, and consider a 5-g serving relative to reference nutrient intakes. To provide a basis for comparison, Tables S1 and S2 in the Supporting Information online present the same nutritional information for a selection of dried seaweed products commercially available throughout the United Kingdom and the Republic of Ireland.

Protein

The protein content of seaweed has gained considerable attention, given the emerging challenges to improve food security by identifying alternative and sustainable protein sources.[54] As outlined in Tables 1, 2, and 3, the protein content ranges from 5.02% to 19.66% in brown seaweeds; from 0.67% to 45.0% in red seaweeds; and from 3.42% to 29.80% in green seaweeds. A 5-g portion of dried brown, red, and green seaweed corresponds, respectively, to a maximum of 1.97%, 4.5%, and 2.98% of the Reference Nutrient Intake for protein. On a gram-for-gram basis, seaweeds have protein and amino acid contents comparable to those of beef; however, seaweeds are consumed in much smaller quantities.[55] It should also be noted that the protein content of seaweed is often derived from total nitrogen by using a conversion factor of 6.25 (Kjeldahl method), which likely produces an overestimate, given the nonprotein sources of nitrogen in seaweed. Hence, species-specific conversion factors ranging from 3.57 to 5.72 have been proposed for seaweed.[56] The amino acid composition of proteins

Table 1 **Macronutrient content of brown seaweeds**

Reference	Seaweed	Country	Date harvested	Protein (%)	Percent RNI supplied by 5-g portion	Lipid (%)	Percent RNI supplied by 5-g portion	Carbohydrate (%)	Percent RNI supplied by 5-g portion	Fiber (%)	Percent RNI supplied by 5-g portion
Maehre et al (2014)[19]	*Alaria esculenta*	Norway	May 2010	9.11	0.91	1.40	0.10	–	–	–	–
Schiener et al (2015)[17]	*Alaria esculenta*	Scotland	Mar 2011 – Jul 2011	11.04	1.10	–	–	72.10	1.39	–	–
Tabarsa et al (2012)[20]	*Colpomenia sinuosa*	Iran	Apr 2008	10.11	1.01	1.46	0.10	–	–	9.50	1.58
El-Said & El-Sikaily (2013)[21]	*Colpomenia sinuosa*	Egypt	Apr 2011	–	–	–	–	11.80	0.23	–	–
Rohani-Ghadikolaei et al (2012)[22]	*Colpomenia sinuosa*	Iran	–	9.20	0.92	1.50	0.11	32.10	0.62	–	–
Tabarsa et al (2012)[20]	*Dictyota dichotoma*	Iran	Apr 2008	17.73	1.77	2.94	0.21	–	–	10.50	1.75
Smith et al (2010)[23]	*Durvillaea antarctica*	New Zealand	Apr 2004	7.26	0.73	2.03	0.15	58.82	1.13	–	–
Ortiz et al (2006)[24]	*Durvillaea antarctica*	Chile	Nov 2013	10.40	1.04	0.80	0.06	70.90	1.36	71.40	11.90
Ortiz et al (2006)[24]	*Durvillaea antarctica*	Chile	Nov 2013	11.60	1.16	4.30	0.31	58.40	1.12	56.40	9.40
Smith et al (2010)[23]	*Ecklonia radiata*	New Zealand	Aug 2004	9.60	0.96	1.80	0.13	66.90	1.29	–	–
Smith et al (2010)[23]	*Ecklonia* spp	New Zealand	–	9.78	0.98	0.80	0.06	69.61	1.34	–	–
Mišurcová et al (2010)[25]	*Eisenia bicyclis*	Japan	–	–	–	–	–	–	–	11.15	1.86
Paiva et al (2014)[26]	*Fucus spiralis*	Portugal	Jan 2013	9.71	0.97	5.23	0.37	17.59	0.34	–	–
Marsham et al (2007)[27]	*Fucus serratus*	United Kingdom	–	17.40	1.74	1.80	0.13	–	–	26.20	4.37
Maehre et al (2014)[19]	*Fucus vesiculosus*	Norway	May 2010	6.11	0.61	3.08	0.22	–	–	–	–
Sanchez-Machado et al (2004)[28]	*Himanthalia elongata*	Spain	–	5.46	0.55	0.97	0.07	–	–	–	–
Sanchez-Machado et al (2004)[28]	*Himanthalia elongata*	Spain	–	10.95	1.10	0.93	0.07	–	–	–	–
Mišurcová et al (2010)[25]	*Hizikia fusiformis*	Japan	–	–	–	–	–	–	–	17.52	2.92
Smith et al (2010)[23]	*Hormosira banksii*	New Zealand	Apr 2004	6.07	0.61	2.63	0.19	62.90	1.21	–	–
Maehre et al (2014)[19]	*Laminaria digitata*	Norway	May 2010	5.31	0.53	0.99	0.07	–	–	–	
Schiener et al (2015)[17]	*Laminaria digitata*	Scotland	Aug 2010 – Oct 2011	6.90	0.69	–	–	70.70	1.36	–	–
Marsham et al (2007)[27]	*Laminaria digitata*	United Kingdom	–	15.90	1.59	0.50	0.04	–		16.60	2.77
Maehre et al (2014)[19]	*Laminaria hyperborea*	Norway	May 2010	5.02	0.50	1.28	0.09	–	–	–	–
Schiener et al (2015)[17]	*Laminaria hyperborea*	Scotland	Aug 2010 – Oct 2011	6.80	0.68	–	–	65.50	1.26	–	–
Mišurcová et al (2010)[25]	*Laminaria japonica*	Japan	–	–	–	–	–	–	–	10.45	1.74
Sanchez-Machado et al (2004)[28]	*Laminaria ochroleuca*	Spain	–	7.49	0.75	0.92	0.07	–	–	–	–
Smith et al (2010)[23]	*Macrocystis* spp	New Zealand	–	11.02	1.10	1.56	0.11	44.54	0.86	–	–
Tabarsa et al (2012)[20]	*Padina pavonica*	Iran	Apr 2008	11.83	1.18	1.79	0.13	–	–	11.00	1.83
Maehre et al (2014)[19]	*Pelvetia canaliculata*	Norway	May 2010	5.72	0.57	4.78	0.34	–	–	–	–
Schiener et al (2015)[17]	*Saccharina latissima*	Scotland	Aug 2010 – Oct 2011	7.10	0.71	–	–	63.10	1.21	–	–
Sanchez-Machado et al (2004)[28]	*Saccorhiza polyschides*	Spain	–	13.10	1.31	0.70	0.05	–	–	–	–
Rodrigues et al (2015)[29]	*Saccorhiza polyschides*	Portugal	Apr 2012	14.44	1.44	1.10	0.08	45.60	0.88	–	–
Rohani-Ghadikolaei et al (2012)[22]	*Sargassum ilicifolium*	Iran	–	8.90	0.89	2.00	0.14	32.90	0.63	–	–
Matanjun et al (2009)[30]	*Sargassum polycystum*	Borneo	–	5.40	0.54	0.29	0.02	33.49	0.64	39.67	6.61
Marinho-Soriano et al (2006)[31]	*Sargassum vulgare*	Brazil	Jul 2000 – Jun 2001	13.61	1.36	0.49	0.04	61.60	1.18	7.74	1.29
El-Said & El-Sikaily (2013)[21]	*Sargassum linifolium*	Egypt	Apr 2011	–	–	–	–	8.59	0.17	–	–
Rodrigues et al (2015)[29]	*Sargassum muticum*	Portugal	Apr 2012	16.90	1.69	1.45	0.10	49.30	0.95	–	–
Peng et al (2013)[32]	*Sargassum naozhouense*	China	Jul 2011	11.20	1.12	1.06	0.08	47.43	0.91	4.83	0.81
Smith et al (2010)[23]	*Undaria pinnatifida*	New Zealand	–	14.21	1.42	3.13	0.22	45.08	0.87	–	–
Sanchez-Machado et al (2004)[28]	*Undaria pinnatifida*	Spain	–	18.00	1.80	1.05	0.08	–	–	–	–
Smith et al (2010)[23]	*Undaria pinnatifida*	New Zealand	Apr – Sep 2004	19.66	1.97	3.30	0.24	50.40	0.97	–	–
Mišurcová et al (2010)[25]	*Undaria pinnatifida*	Japan	–	–	–	–	–	–	–	9.03	1.51
Mišurcová et al (2010)[25]	*Undaria pinnatifida*	Japan	–	–	–	–	–	–	–	15.53	2.59

Abbreviation: RNI, Reference Nutrient Intake.

Table 2 **Macronutrient content of red seaweeds**

Reference	Seaweed	Country	Date harvested	Protein (%)	Percent RNI supplied by 5-g portion	Lipid (%)	Percent RNI supplied by 5-g portion	Carbohydrate (%)	Percent RNI supplied by 5-g portion	Fiber (%)	Percent RNI supplied by 5-g portion
Parjikolaei et al (2016)[33]	*Ahnfeltia plicata*	Denmark	Sep 2011	31.10	3.11	1.10	0.08	59.10	1.14	–	–
Marsham et al (2007)[27]	*Ceramium* spp	United Kingdom	–	31.20	3.12	0.60	0.04	–	–	33.70	5.62
Parjikolaei et al (2016)[33]	*Chondrus crispus*	Denmark	Sep 2011	26.40	2.64	1.00	0.07	53.30	1.03	–	–
Marsham et al (2007)[27]	*Corallina officinalis*	United Kingdom	–	6.90	0.69	0.30	0.02	–	–	9.40	1.57
Parjikolaei et al (2016)[33]	*Delesseria sanguinea*	Denmark	Sep 2011	23.40	2.34	1.20	0.09	51.20	0.98	–	–
Parjikolaei et al (2016)[33]	*Dilsea carnosa*	Denmark	Sep 2011	21.50	2.15	1.20	0.09	53.00	1.02	–	–
Marsham et al (2007)[27]	*Dumontia contorta*	United Kingdom	–	31.70	3.17	0.12	0.01	–	–	34.30	5.72
Matanjun et al (2009)[30]	*Eucheuma cottonii*	Borneo	–	9.76	0.98	1.10	0.08	26.49	0.51	25.05	4.18
Parjikolaei et al (2016)[33]	*Furcellaria lumbricalis*	Denmark	Sep 2011	20.60	2.06	1.00	0.07	55.40	1.07	–	–
Paiva et al (2014)[26]	*Gelidium microdon*	Azores (Portugal)	Jan 2013	–	–	2.44	0.17	–	–	–	–
Marinho-Soriano et al (2006)[31]	*Gracilaria cervicornis*	Brazil	Jul 2000 – Jun 2001	19.70	1.97	0.43	0.03	63.10	1.21	5.65	0.94
El-Said & El-Sikaily (2013)[21]	*Gracilaria compressa*	Egypt	Apr 2011	–	–	–	–	11.62	0.22	–	–
Rohani-Ghadikolaei et al (2012)[22]	*Gracilaria corticata*	Iran	–	19.30	1.93	1.80	0.13	43.00	0.83	–	–
Sakthivel & Devi (2015)[34]	*Gracilaria edulis*	India	–	0.67	0.07	0.83	0.06	10.16	0.20	8.90	1.48
Francavilla et al (2013)[35]	*Gracilaria gracilis*	Italy	Jul 2011	31.00	3.10	1.98	0.14	27.50	0.53	–	–
Francavilla et al (2013)[35]	*Gracilaria gracilis*	Italy	Apr 2012	41.00	4.10	1.40	0.10	34.10	0.66	–	–
Francavilla et al (2013)[35]	*Gracilaria gracilis*	Italy	Oct 2011	41.00	4.10	1.38	0.10	24.80	0.48	–	–
Francavilla et al (2013)[35]	*Gracilaria gracilis*	Italy	Jan 2012	45.00	4.50	1.12	0.08	31.10	0.60	–	–
Rodrigues et al (2015)[29]	*Gracilaria gracilis*	Portugal	Apr 2012	20.20	2.02	0.60	0.04	46.60	0.90	–	–
Tabarsa et al (2012)[20]	*Gracilaria salicornia*	Iran	Apr 2008	9.58	0.96	2.00	0.14	–	–	10.40	1.73
Parjikolaei et al (2016)[33]	*Gracilaria vermiculophylla*	Denmark	Sep 2011	17.80	1.78	1.30	0.09	61.90	1.19	–	–
El-Said & El-Sikaily (2013)[21]	*Gracilaria verrucosa*	Egypt	Apr 2011	–	–	–	–	11.15	0.21	–	–
Rodrigues et al (2015)[29]	*Grateloupia turuturu*	Portugal	Apr 2012	22.50	2.25	2.20	0.16	43.20	0.83	–	–
Wong & Cheung (2000)[36]	*Hypnea charoides*	Hong Kong	Dec 1997	18.40	1.84	1.48	0.11	–	–	50.30	8.38
Wong & Cheung (2000)[36]	*Hypnea japonica*	Hong Kong	Dec 1997	19.00	1.90	1.42	0.10	–	–	53.20	8.87
Siddique (2013)[37]	*Hypnea musciformis*	Bangladesh	May 2005	18.64	1.86	1.27	0.09	20.60	0.40	37.92	6.32
El-Said & El-Sikaily (2013)[21]	*Hypnea musciformis*	Egypt	Apr 2011	–	–	–	–	11.17	0.21	–	–
Siddique (2013)[37]	*Hypnea pannosa*	Bangladesh	May 2005	16.31	1.63	1.56	0.11	22.89	0.44	40.59	6.77
Rohani-Ghadikolaei et al (2012)[22]	*Hypnea valentiae*	Iran	–	16.50	1.65	2.80	0.20	31.80	0.61	–	–
El-Said & El-Sikaily (2013)[21]	*Jania rubens*	Egypt	Apr 2011	–	–	–	–	12.96	0.25	–	–
Fayaz et al (2005)[38]	*Kappaphycus alvarezii*	India	–	16.24	1.62	0.74	0.05	27.40	0.53	29.40	4.90
Kumar et al (2015)[39]	*Kappaphycus alvarezii*	India	Sep 2004 – Apr 2006	19.25	1.93	0.64	0.05	–	–	14.52	2.42
Marsham et al (2007)[27]	*Mastocarpus stellatus*	United Kingdom	–	25.40	2.54	3.00	0.21	–	–	16.60	2.77
Gressler et al (2011)[40]	*Ochtodes secundiramea*	Brazil	–	10.10	1.01	3.54	0.25	45.07	0.87	–	–
Parjikolaei et al (2016)[33]	*Odonthalia dentata*	Denmark	Sep 2011	17.80	1.78	–	–	–	–	–	–
Paiva et al (2014)[26]	*Osmundea pinnatifida*	Portugal	Jan 2013	20.79	2.08	7.53	0.54	17.61	0.34	–	–

(continued)

Table 2 **Continued**

Reference	Seaweed	Country	Date harvested	Protein (%)	Percent RNI supplied by 5-g portion	Lipid (%)	Percent RNI supplied by 5-g portion	Carbohydrate (%)	Percent RNI supplied by 5-g portion	Fiber (%)	Percent RNI supplied by 5-g portion
Rodrigues et al (2015)[29]	*Osmundea pinnatifida*	Portugal	Apr 2012	23.80	2.38	0.90	0.06	32.40	0.62	–	–
Marsham et al (2007)[27]	*Osmundea pinnatifida*	United Kingdom	–	27.30	2.73	4.30	0.31	–	–	25.60	4.27
Maehre et al (2014)[19]	*Palmaria palmata*	Norway	Jun 2012	12.26	1.23	1.36	0.10	–	–	–	–
Parjikolaei et al (2016)[33]	*Palmaria palmata*	Denmark	Sep 2011	14.90	1.49	1.20	0.09	71.00	1.37	–	–
Mišurcová et al (2010)[25]	*Palmaria palmata*	United States	–	–	–	–	–	–	–	5.05	0.84
Sanchez-Machado et al (2004)[28]	*Palmaria* spp	Spain	–	13.87	1.39	1.80	0.13	–	–	–	–
Parjikolaei et al (2016)[33]	*Phycodrys rubens*	Denmark	Sep 2011	28.80	2.88	1.30	0.09	40.20	0.77	–	–
Gressler et al (2011)[40]	*Plocamium brasiliense*	Brazil	–	15.72	1.57	3.63	0.26	52.03	1.00	–	–
Marsham et al (2007)[27]	*Polysiphonia* spp	United Kingdom	–	31.80	3.18	0.05	0.00	–	–	52.80	8.80
Cian et al (2014)[41]	*Porphyra columbina*	Argentina	Aug – Oct 2010	24.61	2.46	0.25	0.02	–	–	48.02	8.00
Sanchez-Machado et al (2004)[28]	*Porphyra* spp	Spain	–	24.11	2.41	1.03	0.07	–	–	–	–
Paiva et al (2014)[26]	*Porphyra* spp	Portugal	Jan 2007	24.82	2.48	8.88	0.63	25.37	0.49	–	–
Smith et al (2010)[23]	*Porphyra* spp	New Zealand	–	26.36	2.64	3.03	0.22	43.99	0.85	–	–
Smith et al (2010)[23]	*Porphyra* spp	New Zealand	May – Oct 2004	32.71	3.27	2.00	0.14	45.40	0.87	–	–
Marsham et al (2007)[27]	*Porphyra* spp	United Kingdom	–	44.00	4.40	0.70	0.05	–	–	33.50	5.58
Cofrades et al (2010)[42]	*Porphyra umbilicalis*	Spain	–	39.00	3.90	–	–	–	–	–	–
El-Said & El-Sikaily (2013)[21]	*Pterocladia capillacea*	Egypt	Apr 2011	–	–	–	–	9.64	0.19	–	–
El-Said & El-Sikaily (2013)[21]	*Pterocladia capillacea*	Egypt	Apr 2011	–	–	–	–	11.20	0.22	–	–
El-Said & El-Sikaily (2013)[21]	*Pterocladia capillacea*	Egypt	Apr 2011	–	–	–	–	7.89	0.15	–	–
El-Said & El-Sikaily (2013)[21]	*Pterocladia capillacea*	Egypt	Apr 2011	–	–	–	–	8.06	0.16	–	–
Paiva et al (2014)[26]	*Pterocladia capillacea*	Azores (Portugal)	Jan 2013	–	–	4.32	0.31	–	–	–	–
Maehre et al (2014)[19]	*Vertebrata lanosa*	Norway	June 2012	11.56	1.16	1.55	0.11	–	–	–	–

Abbreviation: RNI, Reference Nutrient Intake.

Table 3 **Macronutrient content of green seaweeds**

Reference	Seaweed	Country	Date harvested	Protein (%)	Percent RNI supplied by 5-g portion	Lipid (%)	Percent RNI supplied by 5-g portion	Carbohydrate (%)	Percent RNI supplied by 5-g portion	Fiber (%)	Percent RNI supplied by 5-g portion
Nguyen et al (2011)[43]	*Caulerpa lentillifera*	Taiwan	–	9.26	0.93	1.57	0.11	64.00	1.23	2.97	0.50
Matanjun et al (2009)[30]	*Caulerpa lentillifera*	Borneo	–	10.41	1.04	1.11	0.08	38.66	0.74	32.99	5.50
Ratana-Arporn & Chirapart (2006)[44]	*Caulerpa lentillifera*	Thailand	March	12.49	1.25	0.86	0.06	59.27	1.14	3.17	0.53
Mandlik et al (2014)[45]	*Caulerpa racemosa*	India	–	–	–	–	–	10.02	0.19	–	–
Kokilam & Vasuki (2013)[46]	*Caulerpa taxifolia*	India	–	12.44	1.24	0.32	0.02	23.86	0.46	–	–
Maehre et al (2014)[19]	*Cladophora rupestris*	Norway	May 2010	3.42	0.34	0.76	0.05	–	–	–	–
Marsham et al (2007)[27]	*Cladophora rupestris*	United Kingdom	–	29.80	2.98	1.00	0.07	–	–	45.70	7.62
Rodrigues et al (2015)[29]	*Codium tomentosum*	Portugal	April 2012	18.80	1.88	3.60	0.26	32.80	0.63	–	–
El-Said & El-Sikaily (2013)[21]	*Codium tomentosum*	Egypt	April 2011	–	–	–	–	11.15	0.21	–	–
Aguilera-Morales et al (2005)[47]	*Enteromorpha* spp	Mexico	Winter 1997	9.45	0.95	2.24	0.16	–	–	–	–
Aguilera-Morales et al (2005)[47]	*Enteromorpha* spp	Mexico	Winter 1998	14.10	1.41	2.27	0.16	–	–	–	–
Pirian et al (2016)[48]	*Ulva californica*	Iran	March 2015	15.20	1.52	3.75	0.27	–	–	–	–
Pirian et al (2016)[48]	*Ulva californica*	Iran	February 2015	15.76	1.58	3.45	0.25	–	–	–	–
Pirian et al (2016)[48]	*Ulva compressa*	Iran	February 2015	18.12	1.81	1.03	0.07	–	–	–	–
Pirian et al (2016)[48]	*Ulva compressa*	Iran	March 2015	18.64	1.86	0.90	0.06	–	–	–	–
Paiva et al (2016)[49]	*Ulva compressa*	Azores (Portugal)	April 2013	–	–	1.67	0.12	–	–	–	–
Pirian et al (2016)[48]	*Ulva fasciata*	Iran	March 2015	14.06	1.41	0.56	0.04	–	–	–	–
Pirian et al (2016)[48]	*Ulva fasciata*	Iran	February 2015	14.69	1.47	0.47	0.03	–	–	–	–
Pirian et al (2016)[48]	*Ulva flexuosa*	Iran	March 2015	10.55	1.06	2.82	0.20	–	–	–	–
Pirian et al (2016)[48]	*Ulva flexuosa*	Iran	March 2015	11.23	1.12	2.34	0.17	–	–	–	–
Escobido et al (2016)[50]	*Ulva intestinalis*	Philippines	January – April 2016	5.57	0.56	0.43	0.03	37.28	0.72	–	–
Rohani-Ghadikolaei et al (2012)[22]	*Ulva intestinalis*	Iran	–	10.50	1.05	2.90	0.21	35.50	0.68	–	–
Maehre et al (2014)[19]	*Ulva intestinalis*	Norway	May 2010	11.33	1.13	1.62	0.12	–	–	–	–
El-Said & El-Sikaily (2013)[21]	*Ulva intestinalis*	Egypt	April 2011	–	–	–	–	8.72	0.17	–	–
Wong & Cheung (2000)[36]	*Ulva lactuca*	Hong Kong	December 1997	7.06	0.71	1.64	0.12	–	–	55.40	9.23
Yaich et al (2011)[51]	*Ulva lactuca*	Tunisia	July 2007	8.46	0.85	7.87	0.56	–	–	54.90	9.15
Maehre et al (2014)[19]	*Ulva lactuca*	Norway	June 2012	8.65	0.87	2.00	0.14	–	–	–	–
Tabarsa et al (2012)[20]	*Ulva lactuca*	Iran	April 2008	10.69	1.07	0.99	0.07	–	–	5.60	0.93
Pirian et al (2016)[48]	*Ulva lactuca*	Iran	February 2015	20.85	2.09	0.85	0.06	–	–	–	–
Pirian et al (2016)[48]	*Ulva lactuca*	Iran	March 2015	21.55	2.16	0.75	0.05	–	–	–	–
Bikker et al (2016)[52]	*Ulva lactuca*	Ireland	May 2015	26.30	2.63	2.11	0.15	24.00	0.46	–	–
Ortiz et al (2006)[24]	*Ulva lactuca*	Chile	November 2013	27.20	2.72	0.30	0.02	61.50	1.18	60.50	10.08
Marsham et al (2007)[27]	*Ulva lactuca*	United Kingdom	–	29.00	2.90	0.50	0.04	–	–	32.90	5.48
El-Said & El-Sikaily (2013)[21]	*Ulva lactuca*	Egypt	April 2011	–	–	–	–	11.15	0.21	–	–
El-Said & El-Sikaily (2013)[21]	*Ulva lactuca*	Egypt	April 2011	–	–	–	–	10.95	0.21	–	–
El-Said & El-Sikaily (2013)[21]	*Ulva lactuca*	Egypt	April 2011	–	–	–	–	11.54	0.22	–	–
El-Said & El-Sikaily (2013)[21]	*Ulva lactuca*	Egypt	April 2011	–	–	–	–	11.28	0.22	–	–

(continued)

Table 3 **Continued**

Reference	Seaweed	Country	Date harvested	Protein (%)	Percent RNI supplied by 5-g portion	Lipid (%)	Percent RNI supplied by 5-g portion	Carbohydrate (%)	Percent RNI supplied by 5-g portion	Fiber (%)	Percent RNI supplied by 5-g portion
El-Said & El-Sikaily (2013)[21]	*Ulva lactuca*	Egypt	April 2011	–	–	–	–	11.41	0.22	–	–
El-Said & El-Sikaily (2013)[21]	*Ulva lactuca*	Egypt	April 2011	–	–	–	–	11.15	0.21	–	–
El-Said & El-Sikaily (2013)[21]	*Ulva lactuca*	Egypt	April 2011	–	–	–	–	10.16	0.20	–	–
Rohani-Ghadikolaei et al (2012)[22]	*Ulva lactuca*	Iran	–	17.10	1.71	3.60	0.26	59.10	1.14	–	–
Pirian et al (2016)[48]	*Ulva linza*	Iran	March 2015	10.16	1.02	3.70	0.26	–	–	–	–
Pirian et al (2016)[48]	*Ulva linza*	Iran	March 2015	10.45	1.05	3.30	0.24	–	–	–	–
Pirian et al (2016)[48]	*Ulva prolifera*	Iran	February 2015	19.87	1.99	6.06	0.43	–	–	–	–
Pirian et al (2016)[48]	*Ulva prolifera*	Iran	March 2015	20.30	2.03	6.06	0.43	–	–	–	–
Ratana-Arporn & Chirapart (2006)[44]	*Ulva reticulata*	Thailand	May	21.06	2.11	0.75	0.05	55.77	1.07	4.84	0.81
Taboada et al (2010)[53]	*Ulva rigida*	Spain	–	17.80	1.78	0.90	0.06	42.60	0.82	11.90	1.98
Paiva et al (2014)[26]	*Ulva rigida*	Azores (Portugal)	April 2013	–	–	1.02	0.07	–	–	–	–
Smith et al (2010)[23]	*Ulva stenophylla*	New Zealand	April 2004	20.43	2.04	1.24	0.09	55.60	1.07	–	–

Abbreviation: RNI, Reference Nutrient Intake.

is critical to determining the value of proteins to the human diet, particularly in achieving an adequate intake of essential amino acids. However, the digestibility of seaweed protein within the gastrointestinal tract will significantly affect the nutritional value of the protein, with protein–polysaccharide interactions reducing digestion efficiency considerably.

An overview of the amino acid contents of several brown, red, and green seaweeds is presented in Tables S3, S4, and S5 in the Supporting Information online. Seaweeds are a source of lysine,[58,59] an essential amino acid often present in limited quantities in terrestrial plant protein sources such as corn, maize, soy, rice, and wheat.[57] An 8-g portion of *Palmaria palmata* contains up to 21.9% of the recommended daily intake of cysteine, yet the total protein content of *Palmaria palmata* varies seasonally.[58] For example, protein content was reported as 21.9% in winter/spring and as 11.9% in summer/autumn, with essential amino acids constituting 26% to 50% of the protein.[60] Thus, exploiting seaweeds as nonanimal protein sources may be possible through harvesting plans that optimize protein and amino acid contents.

The digestibility of protein in species of edible seaweeds, estimated by in vitro methods, is reported as follows: *Fucus vesiculosus*, 14.7%; *Laminaria digitata*, 16.9%; *Undaria pinnatifida*, 28.0%; *Chondrus crispus*, 45.0%; *Porphyra tenera*, 69.4%[61]; *Palmaria palmata*, 56.0%[60]; and *Porphyra columbina*, 74.3%.[41] The digestibility of protein from *Undaria pinnatifida* and *Porphyra tenera* in rodents is reported as 86.1% and 86.2%, respectively, while the digestibility of *Undaria pinnatifida* protein in humans is reported as 70.0%, which is similar to the digestibility of protein from terranean plants.[62,63] Although data on in vivo digestibility suggest that seaweed protein is bioaccessible, protein–polysaccharide interactions within the seaweed matrix could prevent the formation of enzyme–substrate complexes and hinder proteolysis of seaweed proteins. Indeed, enzymatic treatment with xylanase and cellulase polysaccharidases improved *Palmaria palmata* protein bioaccessibility 1.7-fold and 3-fold, respectively.[65] This may favor the use of seaweed protein extracts to provide the maximal protein and amino acid content, with possible food, feed, supplement, and nutraceutical applications.[63,64] Methods for extracting protein from brown, red, and green seaweeds are described comprehensively elsewhere; for example, the use of proteolytic and saccharolytic enzymes such as Celluclast or Shearzyme are reported to improve both protein extraction yield and endogenous digestion.[66–69]

Up to now, the bioactivities reported in the literature pertained to peptides extracted from red seaweeds such as *Palmaria palmata* and *Porphyra* spp and from

brown seaweeds such as *Undaria pinnatifida* and were associated with antihypertensive, antioxidant, and antidiabetic effects.[70] Among the effects reported are cardioprotective effects such as reduced blood pressure via inhibition of angiotensin-converting enzyme,[71–74] antidiabetic activity via inhibition of dipeptidyl-peptidase 4,[77] and promotion of iron absorption.[76] The potential application of seaweed peptides, which have antioxidant properties,[75] as food preservatives has also been suggested.[72] Therefore, protein extracts from seaweeds hold promise as a protein source, providing their bioactivity is validated in humans.

It is estimated that 56 million metric tonnes of algae will be required per annum as an alternative protein source by 2054, which will represent 5.94% of global protein demand.[78] Given the variability of both the content and the bioavailability of protein from whole seaweeds, protein extracts may contribute substantially to nonanimal protein sources in the future.

Dietary fiber

Many populations are failing to meet daily requirements for dietary fiber intake.[79,80] The potential functional properties of dietary fiber are associated with the viscous and water-binding properties of fiber within the gastrointestinal tract.[82] As a result, fiber has been suggested to promote satiety and weight loss; delay gastric emptying to improve glycemic control; enhance stool bulking to reduce gut transit time and increase defecation frequency; and enhance bile acid excretion, resulting in reduced low-density lipoprotein cholesterol (LDL-C) in blood.[81–83] Dietary fiber components are also suggested to improve health via their fermentation by the colonic microbiota, which can favorably alter gut microbial composition and enhance the production of health-associated volatile fatty acids such as acetate, propionate, and butyrate. The fiber-induced alterations to the microbiota composition and the associated metabolites produced are increasingly associated with the promotion of gastrointestinal, cardiometabolic, immune, bone, and mental health.[84]

Owing to the range of proposed beneficial health effects associated with consumption of dietary fiber, there is increasing interest from the food industry in identifying sustainable, alternative sources of dietary fiber.[81,83] Seaweed, with its high fiber content, is a promising candidate. However, the contribution of whole seaweed to the currently recommended intake of dietary fiber, ie, 25 g/d, is limited, with a 5-g serving of brown, red, or green seaweed contributing up to 14.28%, 10.64%, or 12.10% of dietary fiber intake, respectively (Tables 1, 2, and 3).[79] This has led to increasing interest in the industrially applicable extraction and isolation of individual fiber components from seaweed. Seaweeds contain a diverse range of fiber components. Brown seaweeds contain alginate,[85] laminarin,[86] and fucoidan polysaccharides[89]; red seaweeds contain agar, carrageenan, porphyran, and xylan[88,90]; and green seaweeds contain ulvan, xylan, and cellulose.[87]

While some seaweed-derived fibers (alginate, carrageenan, and agar) have been used for decades for their emulsifying, stabilizing, and thickening characteristics to improve the sensory properties of food, there is limited interest in their application as functional dietary fibers. The existing widespread use of these seaweed-derived fibers in the food industry ensures they are safe for human consumption, according to the European Food Safety Authority (EFSA) and the US Food and Drug Administration. Thus, alginate isolated from brown seaweeds, long used by the food industry, is a leading candidate for application in the functional food market.[91–93] Fucoidan was recently classified by the EFSA as a novel food,[94] making it an another candidate for an emerging functional food ingredient, while suggestions that low-molecular-weight carrageenan components (< 50 kDa) may negatively impact health (on the basis of proinflammatory properties) have tempered interest in the potential use of carrageenan as a functional ingredient.[95] Other seaweed fibers, such as xylan, laminarin, and ulvan, have not received official EFSA approval, and thus more research is needed to ascertain whether these carbohydrates are safe for human consumption. Once these seaweed-derived fiber components have been deemed safe, they will likely be marketed as nutritional ingredients, provided the associated health claims are substantiated.

The majority of research on the health benefits of seaweed-derived dietary fiber components in humans has focused on potential antiobesogenic effects, including improved satiation, delayed nutrient absorption, and delayed gastric emptying, but the effects of whole seaweeds containing alginate appear to be limited.[85,96,97] Several placebo-controlled intervention trials in humans have shown alginate consumption to significantly impact appetite and food intake. An acute study by Peters et al[98] showed that an alginate drink enhanced self-reported satiety and reduced the feeling of hunger in a dose-dependent manner when compared with placebo. Another parallel study in overweight men showed that consumption of an *Ascophyllum nodosum*–enriched (4%) bread reduced energy intake by 109 kcal and 506 kcal at 4 hours and 24 hours post consumption, respectively, compared with an isocaloric placebo.[99] Similar results were reported when consumption of a preload alginate drink reduced energy intake by 44 kcal following an ad libitum lunch.[100] A crossover study reported that daily energy intake was reduced by

135 kcal when participants consumed alginate (1.5 g/100 mL) prior to meals,[101] but no significant effect of a preload alginate drink on measures of energy intake or concentration of satiety hormones in overweight/obese individuals was reported elsewhere.[102] Alginate appears to affect appetite and food intake, yet research is needed to the characterize the action of alginates by examining both the relationship between structure and function (particularly molecular weight and the ratio of guluronate to mannuronate) and the role of the gelling capacity of alginate. Research into the mechanism of action of alginate is required, given that alginate does not seem to affect gastric emptying.[100,102] The formulation of alginate food products organoleptically acceptable to the consumer is another consideration for industry. Longer-term studies are required to demonstrate the effects of alginate on appetite control and weight management.

There is also considerable interest in the effect of alginate on glycemic control, particularly its impact on postprandial glucose absorption. A review of the evidence by the EFSA concluded that sodium alginate failed to reduce postprandial glycemic responses without a disproportionate increase in postprandial insulinemic responses, and thus a health claim was rejected.[83,103] Other fibers, such as beta glucan, have received favorable EFSA opinions for their ability to reduce postprandial glucose absorption by slowing the rate of gastric emptying.[83] The effect of alginate on glucose metabolism, particularly the postprandial insulinemic response, needs to be further investigated.

The recent designation of fucoidan as Generally Recognized as Safe (GRAS) by the US Food and Drug Administration[104] and as a novel food by the European Union,[94] along with accumulating in vitro and in vivo evidence of fucoidan's potential antiobesogenic effects,[105] make fucoidan an attractive ingredient for the functional food industry.[106] Nevertheless, only 1 human study has investigated the antiobesogenic effects of seaweed-derived fucoidan. A randomized, double-blind, parallel, placebo-controlled trial in an overweight/obese cohort showed that participants who consumed fucoidan (500 mg/d) for 3 months had significantly reduced diastolic blood pressure and LDL-C compared with those who received placebo.[107] No changes in weight, waist circumference, body mass index (BMI), adiposity, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol (HDL-C), blood glucose, or blood triglycerides were observed; however, blood insulin and homeostasis model assessment of insulin resistance (HOMA-IR) were increased in the fucoidan group compared with baseline values, but not compared with the placebo group. The authors suggested that fucoidan consumption downregulated expression of the transcription factor peroxisome proliferator-activated receptor-γ (PPARγ) to suppress adipocyte differentiation and insulin signaling.

Conversely, evidence from animal models of obesity and diabetes suggests that low-molecular-weight fucoidan could ameliorate dyslipidemia and improve insulin sensitivity through the activation of insulin signaling pathways in adipocytes and hepatocytes.[105,108–111] Further evidence from human intervention trials is required to understand how dietary fucoidan may modulate host glucose and lipid metabolism to exert antiobesogenic and antidiabetic effects. This may also require an understanding of how the molecular weight of fucoidan affects bioactivity.

Fucoidan is also reported to have anticoagulant properties, serving as a catalyst for antithrombin-mediated and heparin cofactor II–mediated inhibition of thrombin.[112–114] Oral administration of *Undaria pinnatifida* extract (9 g/d) with 75% fucoidan (molecular weight $\approx$ 713 kDa) for 12 days increased activated partial thromboplastin time, decreased thrombin time, and increased antithrombin-III compared with placebo, although the authors concluded the improvements were small and the impact of oral delivery may be limited.[112] Another study investigated oral administration of fucoidan (extracted from *Laminaria japonica*, molecular weight $\approx$ 300 kDa) at a dosage of 400 mg/d for 5 weeks and reported a significant reduction in thrombus lysis time, although a fucoidan-specific monoclonal antibody enzyme-linked immunosorbent assay failed to detect fucoidan in the blood of study participants.[115] This suggests fucoidan may not be bioavailable in humans, although in vitro and in vivo experiments have demonstrated fucoidan to be absorbed through the small intestine.[116] The anticoagulant properties of fucoidan are gaining the attention of the pharmaceutical industry, but the use of fucoidan as a food ingredient will require much more human evidence to verify safe and efficacious doses, particularly in individuals receiving anticoagulant therapy.

There is also a wealth of evidence to support an anticancer function of fucoidan, but the majority of evidence is from in vitro or animal studies and is reviewed elsewhere.[117] A recent clinical trial in colon cancer patients investigated the effect of an oral fucoidan supplement (4 g twice daily) administered in conjunction with chemotherapy.[118] Patients who received fucoidan had a significantly better disease control rate compared with placebo control patients but showed no change in overall response rate, progression-free survival, overall survival, adverse effects, or quality of life. While the effect on disease control rate is a notable benefit, the role of fucoidan in cancer treatment remains unknown. Advertisement of cancer treatments is prohibited in the

United Kingdom,[119] although legislation regarding advertisement of cancer prevention is less clear.[120] Furthermore, marketing fucoidan as a food ingredient with cancer-preventive effects is extremely difficult to substantiate and may prove very difficult within the existing regulatory environment.

There is increasing interest in the potential prebiotic effect of seaweed-derived fiber, which can modulate the composition and metabolism of the colonic microbiota, as well as growing interest in the effect of fiber fermentation on human health. Several in vitro fecal batch culture studies have demonstrated the fermentability of seaweed fiber components, noting increased production of short-chain fatty acids and modulation of gut microbial communities.[121–125] Modulation of the gut microbiota and production of short-chain fatty acids have been observed in animal studies employing a seaweed fiber–containing diet.[86,126] However, thus far, the only health benefit associated with the prebiotic effects of seaweed fibers is the slowing of weight gain in animals on a high-fat diet.[127] There is a lack of human intervention trials investigating the fermentability of seaweed fiber components and their potential to affect health outcomes.[84]

Fat

The fat content of seaweed tends to be low relative to total dry weight. Percent fat content is highest in winter and lowest in summer, and fatty acid composition varies by season.[16,40,128] For example, both the lipid concentration and the polyunsaturated fatty acid (PUFA) content of *Saccharina latissima* grown in integrated multitrophic aquaculture were highest in March and November, yet lowest in January.[129] Moreover, seaweed-derived lipids are highly digestible. For example, up to 98% of the fat content of *Undaria pinnatifida* (1.5% dry weight) is digestible in adults.[128]

Tables 1, 2, and 3 present the total fat content of several brown, red, and green seaweeds, respectively, while Tables S6, S7, and S8 in the Supporting Information online present a breakdown of the lipid content. Total lipid content ranges from 0.29% in *Sargassum polycystum*[30] to 8.88% in *Porphyra* spp.[26] *Porphyra* spp have the lowest saturated fatty acid (SFA) content (17.4% of total fatty acids), whereas *Plocamium brasiliense* has the highest (74% of total fatty acids).[40] Monounsaturated fatty acid content relative to total fatty acid content ranged from 3.3% in *Ochtodes secundiramea* to 47.1% in *Fucus vesiculosus*.[19] The PUFA content of total fatty acids ranges from 6.7% in *Ulva lactuca*[51] to 69.1% in *Undaria pinnatifida*.[28] *Undaria pinnatifida* also has the highest PUFA:SFA ratio (3.39). As shown in Table S7 in the Supporting Information online, *Palmaria* spp had the lowest ratio of n-6 to n-3 fatty acids,[19,28] whereas *Gracilaria gracilis* had the highest.[35]

Dietary reference values have not been established for PUFAs collectively, but an intake of 4% of total energy is recommended for n-6 linoleic acid.[130] Foods with a greater ratio of PUFAs to SFAs may be favorable for maintaining blood LDL-C within normal concentrations,[83] although more human intervention studies are needed to confirm the efficacy of PUFAs in managing dyslipidemia and attenuating low-grade inflammation.[131]

Evidence of bioactivity specific to seaweed lipids is limited, although male KK-Ay mice treated with 1% *Undaria pinnatifida* lipid showed a significant reduction in body weight after 4 weeks when compared with controls, while total weight of white adipose tissue was reduced in mice who consumed both the *Undaria pinnatifida* lipid and n-3 PUFA-rich scallop phospholipids.[132] Other anti-inflammatory activities of seaweed lipids include the inhibition of lipopolysaccharide-induced inflammation in human THP-1 macrophages by lipids derived from the red seaweeds *Porphyra dioica*, *Palmaria palmata*, and *Chondrus crispus*.[133] Lipids extracted from *Gracilaria* spp also inhibited lipopolysaccharide-induced nitric oxide production in murine RAW 264.7 macrophage cells and decreased the viability of human T-47D breast cancer cells and of 5637 human bladder cancer cells.[134] Lastly, a C18 fatty acid extracted from *Ulva lactuca* was reported to exert an anticancer effect via activation of the Nrf2-ARE pathway to promote scavenging of reactive oxygen species.[135]

Given that consumption of whole seaweed, which has a low lipid content, is unlikely to contribute significantly to dietary fat intake, macroalgae may offer a sustainable sources of extractable PUFAs that can be further investigated for their anti-inflammatory effects on obesity and obesity-associated comorbidities. These extractable PUFAs may have prospective applications as dietary supplements or nutraceutical products.

Polyphenols

Polyphenols are highly complex, structural components of the cell wall. They are often bound to cell wall polysaccharides, protecting against oxidative damage.[136] Brown seaweeds contain diverse flavonoid and phlorotannin polyphenols that vary in structure, molecular weight, and level of isomerization.[137,138]

The purported bioactivities of seaweed polyphenols include potential anticancer[141] and antioxidant activities.[140,142,143] Inhibition of digestive enzymes, which

may prevent lipid absorption and help maintain glucose homeostasis, has also been suggested.[138,139]

The bioavailability of polyphenolic compounds in food varies greatly but is known to be low.[144] Information about the bioavailability of seaweed-derived polyphenolic compounds is limited, but a recent human intervention trial that investigated the bioavailability of polyphenols extracted from *Ascophyllum nodosum* provided initial indications of interpersonal variation in polyphenol uptake. Polyphenols detected in serum ranged from 0.011 to 7.757 μg/mL, while the total concentration of urinary phlorotannin and its metabolites ranged from 0.15 to 33.52 μg/mL.[145] The authors concluded, on basis of the absorption rate (6–24 hours), that the gut microbiota–mediated metabolism of the polyphenols could be a major contributor to the apparent interpersonal variation in polyphenol absorption. Consequently, more human studies are needed to investigate the bioavailability of polyphenols from ingested whole seaweeds, as there is potential for seaweed-derived fermentable fibers and polyphenols to exert synergistic effects on the gut microbiota and the host. Additional fundamental research to determine the extent to which the gut microbiota's metabolism of phlorotannins impacts the reported health benefits is also warranted.

There is considerable evidence from animal studies to support a role for an effect of seaweed polyphenols on glucose and lipid digestion and metabolism, giving rise to suggestions that these polyphenols may have potential in preventing diabetes and obesity-associated complications. Diabetic rats fed an ethanol extract (150 and 300 mg/kg) or a water extract (300 mg/kg) from *Sargassum polycystum* showed significant reductions in blood glucose, glycated hemoglobin, total cholesterol, blood triglycerides, and plasma atherogenic index.[146,147] Polyphenols from both *Ecklonia stolonifera*[149] and *Ascophyllum nodosum*[148] have been shown to favorably alter glucose and insulin metabolism in diabetic mouse models, while *Ecklonia cava* polyphenols significantly reduced serum and liver triglycerides and total cholesterol in a diabetic mouse model.[150] Another study showed that a *Gelidium amansii* phenolic-rich extract reduced blood glucose and serum insulin and protected against the adverse effects of diet-induced obesity in mice via decreased blood triglycerides and total cholesterol.[151] The mechanism of action is unknown, but current evidence supports a role in the inhibition of digestive enzymes, including α-amylase, α-glucosidase, and lipase.[97,148,152,153]

There is limited evidence that seaweed polyphenols may exert antiobesogenic effects or may play a role in maintaining glucose homeostasis in healthy humans. For example, consumption of 500 mg of seaweed extract containing at least 10% polyphenols did not improve the postprandial glucose concentration after a 50-g carbohydrate load (bread) compared with placebo, but it did lower the plasma insulin incremental area under the curve in healthy adults (n = 23).[154] Elsewhere, neither a 500-mg nor a 2000-mg dose of *Fucus vesiculosus* polyphenol-rich extract reduced postprandial glucose or insulin responses beyond that of the cellulose placebo after a 50-g carbohydrate load (white bread) in healthy adults (n = 38).[155]

In Korean adults with increased cholesterol, however, a significant reduction in total cholesterol, LDL-C, and C-reactive protein was observed compared with baseline values following treatment with *Ecklonia cava* polyphenol extract at a dosage of 400 mg/d for 12 weeks.[156] Potential mechanisms of action may be associated with the inhibition of adipogenesis, as the phlorotannin dieckol has been shown to downregulate AMP-activated protein kinase (AMPK) signaling in 3T3-L1 preadipocytes.[157]

A recent meta-analysis concluded that polyphenol-rich marine extracts could reduce fasting blood glucose, total cholesterol, and LDL-C in humans, but the few interventions conducted in humans have reported inconsistent findings for the effect of seaweed polyphenols on other biomarkers associated with risk of type 2 diabetes and cardiovascular disease, including postprandial blood glucose, fasting insulin, HDL-C, and triglycerides.[158]

With *Ecklonia cava* phlorotannins deemed safe for use as food supplements in the European Union,[159] further evidence in healthy and at-risk human populations is required to ascertain the bioactivities of seaweed polyphenols.[155] Efforts to optimize polyphenol extraction procedures will be crucial for maximizing the potential of seaweed polyphenols as food ingredients.[160–162]

Fucoxanthin

Carotenoids are a group of tetrapenoid compounds in seaweeds that contribute to photosynthesis. Their antioxidant properties facilitate protection from UV damage. In seaweeds, the main carotenoid with potential application in the food industry is fucoxanthin, extracted from brown seaweeds.[163,164] Evidence suggests that fucoxanthin, through its antioxidant activity, may have potential as a food preservative to prevent lipid peroxidation in meat.[165]

Previous research on fucoxanthin has focused on its potential as a functional food ingredient to reduce the risk of diabetes and obesity, although the evidence is derived predominantly from in vitro and animal studies. Fucoxanthin is thought to exert its effects by inhibiting the digestive enzymes α-amylase and

α-glucosidase, which in turn affects lipid metabolism by modulating leptin and adiponectin, resulting in downregulation of lipogenesis and upregulation lipolysis.[166,167] In several in vivo animal studies, fucoxanthin supplementation was shown to reduce blood glucose, plasma insulin, body weight gain, and accumulation of lipid in the liver; to decrease insulin resistance; and to improve the plasma lipid profile.[168,169] Results of studies investigating the impact of fucoxanthin on cholesterol metabolism in mice have differed. Beppu et al[170] reported increased serum HDL-C, non-HDL-C, and total cholesterol, while Jeon et al[108] reported decreased serum cholesterol and increased fecal cholesterol following fucoxanthin diets.

The antiobesogenic effects of fucoxanthin have been reported in a human intervention trial in which consumption of fucoxanthin over 4 weeks significantly decreased BMI, body weight, and visceral fat area in mildly obese adults (BMI, 25–30 kg/m^2), with no adverse events reported.[171] However, mixed tocopherol and kelp extract components (the composition of which was undefined) were included in each capsule. Abidov et al[172] found evidence to support a role for a proprietary product containing brown seaweed fucoxanthin, n-3 fatty acids, and punicic acid to exert antiobesogenic effects. Premenopausal woman with nonalcoholic fatty liver disease and premenopausal women with normal liver fat who consumed the fucoxanthin product over 16 weeks showed a significant reduction in body weight, by 5.5 kg and 5 kg, respectively, compared with the placebo group. Furthermore, statistically significant improvements in liver fat content, systolic and diastolic blood pressure, and C-reactive protein were observed in both cohorts that consumed the fucoxanthin product, but not in the placebo group, while significantly reduced waist circumference and serum triglycerides were observed only in the intervention group with nonalcoholic fatty liver disease. Interpretation of the role of fucoxanthin in this study is confounded by the additional components (omega-3 fatty acids, punicic acids derived from pomegranate seed oil) present in the treatment, and thus further study is needed to verify the effects of fucoxanthin alone.

More research in healthy human participants is needed to determine whether fucoxanthin plays a role in altering lipid metabolism or in reducing the risk of obesity. Other carotenoids present in red seaweeds, such as lutein, β-carotene, and zeaxanthin, as well as carotenoids present in green seaweeds, such as lutein, β-carotene, echinenone, violaxanthin, and neoxanthin, warrant investigation for their potential antiobesogenic, antidiabetic, or antioxidant bioactivities.[33,48,173–175]

As with polyphenols, cost-effective and scalable extraction protocols must be developed to produce quantities of fucoxanthin sufficient to assess bioactive efficacy and mechanisms of action in clinical trials and to assess prospective applications as food ingredients or in supplements.

Micronutrients

Several studies indicate that seaweed consumption contributes to dietary mineral intake,[1,176] and a higher intake of foods containing seaweed has been associated with sufficient calcium intake to prevent osteoporosis in Korean postmenopausal women.[177] In contrast, 1 report indicates no meaningful contribution to dietary intakes of sodium, potassium, magnesium, phosphorus, calcium, iron, manganese, zinc, selenium, or copper when considering a daily portion of 5 g (dry weight) of 17 brown seaweed and 17 red seaweed food products sourced from China, Japan, and South Korea.[178] This suggests wide differences in mineral content between sources, as shown by the data presented in Tables S9, S10, and S11 in the Supporting Information online.

Seaweed may be an important source of iron, as *Sargassum* spp are reported to contain 156.9 mg of iron per 100 g of dry weight, and the addition of this seaweed to both wheat- and maize-based bread increased the proportion of absorbed iron.[179] Elsewhere, *Sargassum* spp improved iron absorption from a rice meal, with the iron content of the *Sargassum* spp used ranging from 81 to 290 mg/100 g of dry weight over 12 months (highest iron content in July, and lowest content in January).[180]

Seaweeds are also considered a rich source of magnesium, but the bioaccessibility of magnesium varies between seaweeds. The magnesium content of *Ulva pertusa*, *Laminaria japonica*, and *Gloiopeltis furcata* is 10.47 mg/kg (41.8% bioaccessible), 6.55 mg/kg (60.8% bioaccessible), and 8.18 mg/kg (72.5% bioaccessible), respectively, under simulated gastrointestinal conditions.[181] A subsequent mouse study found that magnesium from *Laminaria japonica* was absorbed most efficiently, which indicates that magnesium intake from seaweed will vary between sources.

Vitamins

Multivitamin supplements are commonly used in the general population to achieve recommended daily intakes, but seaweeds may represent an abundant source of both fat- and water-soluble vitamins, as outlined in Tables S12, S13, and S14 in the Supporting Information online. For example, the vitamin A content (retinol equivalents of carotenoid content, determined by high-performance liquid chromatography) of a 5-g portion of dried seaweed varies from 14.5 μg (2% of

Reference Nutrient Intake [RNI]) in *Ulva rigida*[53] to 70.5 μg in *Fucus spiralis* (10% of RNI).[26] The vitamin C content varies from 0.41 mg (1% of RNI) in *Ascophyllum nodosum* to 9.24 mg (23% of RNI) in *Undaria pinnatifida*.[1] Reported folate (vitamin B_9) content varies from 7.5 μg (3.75% of RNI) in *Ulva* spp[1] to 5400 μg (2700% of RNI) in *Ulva rigida*.[53] Both seasonal and geographical variations may explain such wide variation within the same genus.

Only 1 study to date has analyzed the vitamin D_3 content of seaweeds, reporting amounts of 0.83 mg/100 g of dry weight in *Fucus spiralis* and 1.05 mg/100 g of dry weight in *Porphyra* spp.[26] This equates to 41.5 μg (415% of RNI) and 63.5 μg (635% of RNI) in a 5-g dried portion of *Fucus spiralis* and *Porphyra* spp, respectively.[182] Further characterization studies are required to corroborate these findings, which suggest seaweed is a valuable dietary source of vitamin D.

Seaweed is one of the few nonanimal sources of vitamin B_{12}. *Enteromorpha* spp and *Porphyra* spp are reported to contain 63.58 μg and from 32.26[183] to 133.8 μg[184] per 100 g of dry weight, respectively. This equates to 3.18 μg (212% of RNI) and from 1.6 μg (107% of RNI) to 6.69 μg (446% of RNI) in a 5-g dried portion of *Enteromorpha* spp and *Porphyra* spp, respectively. Other studies reporting the vitamin B_{12} content of seaweeds do not specify whether the vitamin B_{12} is present in the active form that can be absorbed and utilized in humans. Seaweeds containing active vitamin B_{12} may be useful for individuals following a vegan diet, who are at risk of vitamin B_{12} deficiency.[185] For example, the authors of a cohort study in children following a vegan diet for 4 to 10 years attributed healthy vitamin B_{12} status to nori consumption (*Porphyra* spp).[186] Other seaweeds examined in this study, such as hijiki, wakame, and kombu, are understood to contain limited amounts of vitamin B_{12} or to contain vitamin B_{12} analogs that, because of structural differences, do not have vitamin B_{12} activity in humans.[187] It has also been reported that the drying of *Porphyra* spp inactivates vitamin B_{12}; therefore, processing methods may impact vitamin bioavailability.[188]

In summary, seaweeds are a source of both fat- and water-soluble vitamins. Seaweed consumption may improve vitamin status; however, characterization of the vitamin content of seaweed is required to improve the development of seaweed supplements, as vitamin content varies with seaweed species, time of harvesting, and geographical location. Moreover, only a limited number of studies in humans, with few participants, have investigated the bioavailability and activity of vitamins obtained from seaweeds.

Salt

According to the assessment of dietary sodium in the UK National Diet and Nutrition Survey, adults aged 19 to 64 years consume, on average, 7.8 g, 8.0 g, and 8.6 g of salt per day in Scotland, England, and Northern Ireland, respectively, intakes that far exceed the RNIs for salt (6 g/d) and sodium (1.6 g/d).[189] Of the dried seaweed products shown in Tables S1 and S2 in the Supporting Information online, *Laminaria digitata* and *Palmaria palmata* have a ratio of sodium to potassium that may be favorable for their application as condiments to replace salt (1.03 and 0.84, respectively).[29] However, small portion sizes of seaweed may be required to prevent excessive salt intake, given that a 5-g portion of *Laminaria digitata* can provide up to 0.35 g of salt and 0.26 g of sodium, while *Palmaria palmata* may provide up to 0.27 g of salt and 0.15 g of sodium. These amounts exceed salt and sodium quantities in an equivalent amount of bacon (0.144 g of salt and 0.0575 g of sodium), which is considered a high-salt food.[190]

Iodine

Iodine is a trace element required for the synthesis and function of triiodothyronine (T3) and thyroxine (T4) thyroid hormones. In Japan, where approximately 20 different types of seaweed are consumed, the majority being wakame (*Undaria* spp), kombu (*Laminaria* spp), and nori (*Porphyra* spp), iodine intake varies from 0.1 to 20 mg/d (average intake, 1–3 mg/d), which can exceed the upper tolerable limits of 600 μg/d (EFSA) and 1100 μg/d (World Health Organization).[191–193]

The epidemiological evidence detailing the risks and benefits of iodine intake from seaweeds remains inconclusive. Seaweed consumption was associated with increased risk of papillary carcinoma of the thyroid in Japanese postmenopausal women but not premenopausal women.[194] However, another study found no association between seaweed consumption and total thyroid cancer risk or papillary carcinoma in premenopausal or postmenopausal women.[195] Iodine-induced hypothyroidism is reported in iodine-sufficient, kelp-consuming populations of Japan,[196] yet iodine-induced hyperthyroidism is also reported in individuals who consume kelp.[197,198] The use of seaweed supplements is not recommended for pregnant women, owing to the variability and excessive iodine content of seaweeds, with kelp-based products being of particular concern.[199,200] Synergy between iodine supplementation and exposure to heavy metals in seaweed, such as mercury, may also impair thyroid function through the reduction of total T3.[201]

The iodine content of the seaweeds shown in Tables S9, S10, and S11 in the Supporting Information online ranges from 0.06 mg/100 g of dry weight (*Ulva lactuca*) to 624.5 mg/100 g of dry weight (*Laminaria digitata*), but many characterization studies do not quantify iodine. Desideri et al[176] found that 3.3 g of *Laminaria digitata* would provide 4017% of the tolerable daily intake for iodine and suggested that habitual intake of seaweed with an iodine content exceeding 45 mg/kg of dry weight could impair thyroid function. Given that *Laminaria* spp are widely abundant, currently used as food ingredients, and have such a high iodine content, characterization of iodine in *Laminaria*-containing products is warranted. In contrast, a 5-g portion of *Porphyra tenera* is reported to provide only 80 µg of iodine.[202]

Static in vitro digestion studies have reported the bioavailability of iodine in seaweed as follows: *Laminaria* spp (17%–28%), *Sargassum fusiforme* (12%), *Palmaria palmata* (10%), *Undaria pinnatifida* (2%–12%), *Himanthalia elongata* (4%), *Porphyra* spp (5%), *Ulva rigida* (2%), and cooked *Himanthalia elongata* and *Sacchoriza polyschides* (below the limit of detection).[203,204] Boiling has been shown to reduce the iodine content of *Alaria esculenta* (from 670 µg/g to 165 µg/g), *Palmaria palmata* (97 µg/g to 66 µg/g), and *Ulva intestinalis* (92 µg/g to 79 µg/g), information that may be beneficial for industry to provide to consumers.[204]

In humans, urinary excretion of iodine following *Ascophyllum nodosum* ingestion was reported as only 33% (excretion of potassium iodide control = 59%).[205] The reduced iodine bioavailability was attributed to reduced release of iodine from the seaweed food matrix (ie, iodine bound to proteins, polysaccharides, polyphenols, and pigments). In a Caco-2 and HT29-MTX coculture, iodine uptake following in vitro digestion was only 4% to 6% (hijiki), 2% to 4% (kombu), and 4% to 7% (wakame),[203] which also suggests limited liberation of iodine species, limited solubility of iodine, or limited absorption of iodine.[206–208]

Urinary excretion of iodine from *Gracilaria verrucosa* and *Laminaria hyperborea* was reported as 101% and 90%, respectively, in an iodine-sufficient population, yet as 85% and 61.5% in an iodine-deficient population.[209] Reduced urinary iodine excretion in the deficient cohort was attributed to increased iodine storage in the thyroid[210]; thus, seaweed consumption may improve iodine status in those at risk of iodine deficiency, as demonstrated in vegan populations.[211,212]

Iodine absorption from *Laminaria japonica* is estimated as 57% to 71%, although serum thyroid-stimulating hormone (TSH) was significantly increased above the normal limits in 4 of 6 participants who consumed 15 g of *Laminaria japonica* daily for 7 to 10 days, in 4 of 14 who consumed 30 g/d for 7 to 10 days, and in 1 of 3 who consumed 15 g/d for 55 to 87 days.[213] These findings corroborate previous evidence that kelp supplementation increased serum TSH over 4 weeks.[214] Urinary iodide excretion increased 30-fold and 44-fold from baseline (in subgroups that received 15 g and 30 g, respectively), but returned to baseline 7 to 40 days after seaweed consumption ceased. Furthermore, iodine intake was improved without compromising thyroid function when 500 mg *of Ascophyllum nodosum* containing 356 µg of iodine was given to healthy women for 14 days.[215] Urinary iodine concentrations increased significantly, reflecting sufficient intake and subsequent renal excretion. Plasma concentrations of T3, T4, free T3, and free T4 were unchanged between pre- and post-intervention, while serum TSH increased significantly, albeit within the normal range.

Some have suggested that future human intervention studies should quantify the iodine content of a seaweed food ingredient or supplement during product development, so that urinary iodine concentrations could be measured as a biomarker of iodine intake and bioavailability at time points throughout interventions.[216,217]

Strategies to prevent excessive iodine intake from seaweed food products include the disclosure of iodine content and the provision of cooking instructions on product labeling. Disclosure of iodine content on food labeling was reported for only 22 of 224 seaweed-containing food products on sale in the United Kingdom, while estimated content was provided for 40 products.[4] Some 26 products had the potential to provide iodine in excess of the tolerable upper intake level of 600 µg/d when serving suggestions were applied, but for the remaining 162, this was unknown. Guidance about an individual's iodine status and how seaweed consumption may benefit the individual could also ensure consumer safety.

The myriad variations in iodine concentration between seaweed species, season, and harvest location present challenges to the food industry, since there is limited and conflicting information about how individual seaweeds may impact iodine status and thyroid health.

Heavy metals

One concern about seaweed consumption is exposure to heavy metals such as arsenic, aluminum, cadmium, lead, rubidium, silicon, strontium, and tin.[176] The contamination of seaweeds with heavy metals depends on habitat or ecology, which has led to inconsistency in research findings. Seaweeds growing in areas of contamination, often caused by industry or poor sewage

systems, accumulate heavy metals from the surrounding water and rocks, but at levels that pose little risk to human health.[218] However, exposure to contaminants is increased in perennial seaweeds, the regular consumption of which may lead to risk of heavy metal toxicity in humans.[219,220] Levels of arsenic, mercury, lead, and cadmium in 426 Korean dried seaweed products ranged from 0.2% to 6.7% of provisional tolerable weekly intakes when 8.5 g of seaweed was consumed per day.[176,218,221] In 1 study, the authors called for continuous monitoring of heavy metals in seaweed-based food products, owing to differences between species in the bioabsorption of metals.[221] An example of these between-species differences is evident in *Laminaria* spp. At an intake of 3.3 to 12.5 g/d, *Laminaria digitata* contains 24 to 90 µg of cadmium,[176] which corresponds to 40% to 150% of the tolerable daily intake, while *Laminaria japonica* contains 0.45 to 0.80 mg/kg, which exceeds the maximum limits for seaweed products according to legislation in France (0.5 mg/kg of dry weight) and Australia/New Zealand (0.2 mg/kg of dry weight), but not in China (1.0 mg/kg).[225] Tables S15, S16, and S17 in the Supporting Information online provide details of the heavy metal content of several brown, red, and green seaweeds, respectively, although information about the toxicokinetics of heavy metals ingested from seaweeds is too limited to make conclusions about potential health risks.

In a cross-sectional study of heavy metal concentrations in 3404 healthy Korean adults, urinary arsenic concentrations were significantly increased in both the second and third tertiles of seaweed consumption.[226] Arsenic species were not determined in this study, but blood mercury was significantly higher in the highest consumers of seaweed versus the lowest consumers. Preliminary research shows that increased water temperatures can increase mercury absorption by fish, and the same biosorption of mercury may occur in seaweed.[227] Considering global warming, trends in the heavy metal content of seaweed should also be monitored; likewise, the presence of rare earth elements, recently identified in northwest Mediterranean seaweeds, should be watched.[228] The placental transfer of heavy metals from mother to fetus can cause neurological, developmental, and endocrine disorders in infants.[230,231] Ultimately, the extraction of bioactive or nutritional components from seaweeds may mitigate ingestion of excessive heavy metals, which can be mutagenic and carcinogenic to humans.[229]

Arsenic

A major consideration for the exploitation of seaweeds as health foods or functional food ingredients is the need to speciate and quantify the levels of arsenic present in seaweed products. Arsenic species may be categorized as toxic (inorganic arsenic, which are class I carcinogens), nontoxic (arsenobetaine), or potentially toxic (fat-soluble arsenic, arsenosugars, and other organoarsenicals).[232] The health risks associated with inorganic hydrogen arsenate species are related to DNA damage, which predisposes cells to carcinogenesis. Consumption of inorganic arsenic has been shown to increase the incidence of lung, bladder, skin, and kidney cancers and has also been linked to skin lesions, cardiovascular disease, neurological effects, and diabetes.[233–235]

Most arsenic species in seaweeds are arsenosugars, typically ligated to glycerol, sulfonate, or phosphonate. Arsenosugars resist degradation in the stomach and, upon entering the lower gastrointestinal tract, are metabolized to at least 12 different metabolites, including dimethylarsinate, methylarsinate, and dimethylarsinoylethanol, but the toxicity of these metabolites is unknown.[232,236–238]

Speciation and concentration of arsenic in brown seaweeds (*Ascophyllum nodosum*, *Laminaria digitata*, *Fucus vesiculosus*, *Fucus spiralis*, *Alaria esculenta*, and *Saccharina latissima*),[239,240] red seaweeds (*Porphyra umbilicalus*, *Chondrus crispus*, *Gracilaria vermiculophylla*, and *Palmaria palmata*), and green seaweeds (*Ulva prolifera* and *Ulva lactuca*)[240] revealed that total arsenic content ranged from 4.1 to 111.0 µg/g, with the majority of arsenic present as arsenosugars (inorganic arsenic content was < 1.0 µg/g). The exception was *Laminaria digitata*, which contained inorganic arsenic at levels of 2.8 to 20.0 µg/g (USA)[240] and 2.2 to 87.0 µg/g (Ireland).[239] These levels represent a large proportion of the total arsenic content of *Laminaria digitata*, reported to range from 36.0 to 131.0 µg/g of dry weight.[176,239,240] In contrast, *Laminaria japonica* sourced from China contained inorganic arsenics at a concentration of 0.16 to 0.58 mg/kg, which is below maximum limits set by China (1.0 mg/kg of dry weight),[225] France (3.0 mg/kg of dry weight),[241] and Australia/New Zealand (1.0 mg/kg of dry weight). [242] Such variation in inorganic arsenic contents may warrant regular testing for inorganic arsenic content in *Laminaria* spp food products.

Another recent study reported that the content of inorganic arsenic was negligible in 23 seaweed food products except for hijiki (19.83 µg/g), agar (0.06 µg/g), and nori (0.03 µg/g).[235] Total arsenic concentrations in seaweed products were as follows, in descending order: hijiki (83.7 µg/g), kombu (51.2 µg/g), kelp seasoning (43.5 µg/g), arame (41.6 µg/g), wakame (34.7 µg/g), dried red seaweed (35.2 µg/g), nori (19.4 µg/g), dulse (12.1 µg/g), agar (0.23 µg/g), and kelp noodles (0.08 µg/g).

The amount of inorganic arsenic in 112 edible seaweed products sold in Spain was also within safe limits, with the exception of hijiki, in which the level of inorganic arsenic ranged from 41.6 to 117.0 μg/g.[243]

Inclusion of 3% hijiki powder has caused arsenic poisoning in rats,[249] and the risk of hijiki to public health has led to current recommendations against the consumption of hijiki in Asia,[244] Australia,[246] Europe,[245,247,248] and the United States.[246] Seaweeds such as arame, wakame, kombu, and nori, however, are suggested as safe to eat because they contain inorganic arsenic at a concentration of less than 0.3 μg/g, which is encouraging for potential food ingredient applications.[250]

The amounts of potentially bioaccessible arsenite, arsenate, methylarsonate, and dimethylarsinate following the in vitro digestion of *Laminaria japonica*, *Undaria pinnatifida*, *Hizikia fusiformis*, *Porphyra yezoensis*, and *Enteromorpha prolifera* were low enough to indicate no hazard of inorganic arsenic to human health.[251] However, cooking of *Porphyra* spp and *Hizikia fusiforme* by baking and boiling, respectively, has been shown to increase inorganic arsenic species,[252] while soaking, cooking, boiling, and washing/soaking of other seaweeds reduced total arsenic by up to 58.8%, 91.5%, 50%, and 60%, respectively.[253]

Wei et al[254] investigated the bioavailability of arsenic from *Porphyra* spp, reporting that total urinary arsenic peaked (average, 92.5 ng/mL) after 20 to 30 hours, resulting in a 20-fold increase in DMA before returning to normal levels after 80 hours. Another study showed that 2 arsenic metabolites, DMA and 2-dimethylarsinoyl ethanol (DMAE), were detected in the urine of 5 volunteers who consumed 20 to 25 g of *Laminaria* spp (total arsenic, 43.2 μg/g): the peak ratio of arsenic to creatinine was 228, 158, 141, 72, and 70 ng/mL, and levels normalized after 80 hours.[236]

Consumption of 10 g of nori, kombu, or wakame per day for 3 days, followed by a 3-day washout period between seaweeds, resulted in increased levels of the arsenosugars DMA, thio-dimethylarsenoacetic acid (DMAA), and thio-DMAE in 24-hour urine samples obtained during the 3 days of seaweed consumption. The extent of these increases varied between seaweeds and individuals.[235] Toxic thio-DMA was present only at trace levels, and the authors identified thio-DMAE and thio-DMAA as unique arsenosugar metabolites that could potentially be used as urinary biomarkers for dietary intake of arsenic from seaweeds.

The arsenosugars present in seaweed resist cooking and in vitro digestion processes and have been suggested to be absorbed, in part, into the hepatic portal system intact.[255] Human studies have shown considerable differences in the rate of excretion of arsenosugars, ranging from 4% to 95%.[256] The high variability associated with arsenosugar metabolism may be attributable to between-individual differences in endogenous digestion, gut microbiota composition and activity, passage across the intestinal barrier, or transformation in the liver.[256] Thus, there is a need to characterize the metabolic fate of arsenosugars in order to clarify the safety associated with arsenosugar-rich seafoods.[257]

While regulatory bodies have attempted to provide guidance about arsenic intake, there is a need for clearer regulation and guidance regarding the permissible arsenic content of foods. For example, the UK Food Standards Agency has advised against consuming *Sargassum fusiforme* (hijiki) because of significant food safety concerns over high levels of inorganic arsenic.[248] To reduce health risks, regular environmental assessment and analysis of the arsenic species present in seaweed-containing food products may be required to ascertain the exposure to and the potential toxicity of heavy metals.[221,242] Indirect exposure to arsenic could also be a concern if arsenic accumulates in the food chain following the use of seaweed either as feed for livestock[258] or as fertilizer.[259] The majority of edible seaweeds have been reported to contain heavy metals in safe amounts. As with iodine, it has been suggested that food regulation should ensure the disclosure of heavy metal contents on food labeling and establish legal limits for the content of inorganic arsenic in seaweed.[260] Cooking methods and food processing procedures may help reduce the amount of heavy metal present in edible seaweeds, but regulatory bodies and industry both face challenges. For regulatory bodies, the greatest challenge in developing safe limits is the interindividual differences in biotransformation, metabolism, and excretion of arsenic, while for industry, the greatest challenge is the high within-species variability of arsenic levels in seaweed and the potential costs of regularly monitoring product(s).

HEALTH IMPACT OF HABITUAL INTAKE OF WHOLE SEAWEEDS

While this review highlights the lack of human intervention trials investigating the potential risks and benefits of consuming seaweed components, some observational evidence does exist. Epidemiological evidence indicates that seaweed-containing diets are inversely associated with all-cause mortality and cardiovascular disease mortality in Japanese adults.[261] On the other hand, Korean men with metabolic syndrome are reported to consume significantly more seaweed than those without metabolic syndrome, although no mechanistic insight has been published.[262]

Consumption of *Porphyra* spp was inversely associated with breast cancer risk in premenopausal women but not in postmenopausal women, and no association was found between *Undaria pinnatifida* consumption and breast cancer risk.[265] A study by Michikawa et al[194] identified a positive association between seaweed consumption and the risk of thyroid cancer (especially papillary carcinoma) in postmenopausal women, while Wang et al[195] did not find an association between seaweed intake and thyroid cancer incidence in either premenopausal or postmenopausal women. Case-controlled studies by Hoshiyama et al[266,267] implicated an inverse relationship between seaweed consumption and stomach and colon cancer; nevertheless, interpretation warrants caution in light of the low sample power of the studies.

An inverse association was also reported between *Undaria pinnatifida*, *Sargassum fusiforme*, and *Porphyra* spp intake and prevalence of allergic rhinitis in pregnant Japanese women (n = 1002).[268] The study did not measure iodine intake or iodine status, which would have contributed to the knowledge of iodine intake from seaweeds during pregnancy, since current recommendations in Australia and New Zealand limit brown seaweed intake to 1 portion per week in pregnant women.[269] There are also concerns about the potential for seaweed to contribute to foodborne infections, as noted by reports of norovirus contamination of *Enteromorpha* spp[270] and the presence of polycavernoside A toxin in *Gracilaria edulis*.[271,272]

Current Asian populations are reported to consume less seaweed than previous generations, shifting toward a high-energy, low-fiber Westernized diet that promotes the development of metabolic syndrome and has increased the number of iodine-deficient individuals in Japan.[273,274] One recent intervention study in a European population concluded that *Palmaria palmata* consumption could improve iodine status in adults, as serum TSH was significantly increased (within the normal clinical range) following *Palmaria palmata* intake of 5 g/d for 28 days.[275] The authors of this study highlighted the need to characterize seaweed composition when undertaking human interventions to help ascertain which components of seaweed affect health, immune function, and disease risk. While the evidence from observational studies reviewed here may indicate potential benefits, the outcomes must be viewed with considerable caution. Randomized controlled trials with suitable biomarkers, as well as supportive in vitro and in vivo animal studies, are warranted to verify previous observations and eludicate the mechanisms of action of edible seaweeds in humans.

CONCLUSION

Edible seaweeds are a rich and sustainable source of macronutrients (particularly dietary fiber) and micronutrients, but if seaweeds are to contribute to future global food security, legislative measures to ensure monitoring and labeling of food products are needed to safeguard against excessive intakes of salt, iodine, and heavy metals.

While heavy metal concentrations in edible seaweeds are generally below toxic levels, bioaccumulation of arsenic is a risk, and more studies of heavy metal toxicokinetics are needed. A trade-off between iodine and/or heavy metal ingestion and the amount of whole seaweed needed to obtain meaningful amounts of PUFAs, protein, or dietary fiber may limit the recommended portion size. Therefore, the extraction of individual components from the complex seaweed matrix is a legitimate strategy to create added-value products, particularly since novel bioactive components extracted from seaweeds are increasingly studied as potential agents to combat noncommunicable diseases.

Looking ahead, more human intervention studies with defined health-related endpoints are needed to establish how chronic consumption of whole seaweeds and their extracted bioactive components affects human health. Mechanisms of action must also be elucidated to substantiate any future health claims associated with seaweed consumption and to support applications within the food and nutraceutical industries.

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Supporting Information

The following Supporting Information is available through the online version of this article at the publisher's website.

Table S1 **Nutritional information for a selection of seaweed products sold throughout the United Kingdom and the Republic of Ireland**

Table S2 **Nutritional information for a selection of seaweed products sold throughout the United Kingdom and the Republic of Ireland**

Table S3 **Amino acid content of brown seaweeds**

Table S4 **Amino acid content of red seaweeds**

Table S5 **Amino acid content of green seaweeds**

Table S6 **Lipid content of brown seaweeds**

Table S7 **Lipid content of red seaweeds**

Table S8 **Lipid content of green seaweeds**

Table S9 **Essential minerals present in brown seaweeds**

Table S10 **Essential minerals present in red seaweeds**

Table S11 **Essential minerals present in green seaweeds**

Table S12 **Vitamin content of brown seaweeds**

Table S13 **Vitamin content of red seaweeds**

Table S14 **Vitamin content of green seaweeds**

Table S15 **Heavy metal content of brown seaweeds**

Table S16 **Heavy metal content of red seaweeds**

Table S17 **Heavy metal content of green seaweeds**

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