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...
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 319–24,26,27,29,30,36,43–53 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...
| Reference | Seaweed | Country     | Date harvested | Carbohydrate (g) | Percent RNI supplied by 5-g portion | Lipid (g) | Percent RNI supplied by 5-g portion | Protein (g) | Percent RNI supplied by 5-g portion | Fiber (g) | Percent RNI supplied by 5-g portion |
|-----------|---------|-------------|----------------|------------------|-------------------------------------|-----------|-------------------------------------|------------|-------------------------------------|-----------|-------------------------------------|
| Maehre et al (2014) | Alaria esculenta | Norway | May 2010 | 9.11 | 0.91 | 1.40 | 0.10 | – | – | – | – |
| Schiener et al (2015) | Alaria esculenta | Scotland | Mar 2011 – Jul 2011 | 11.04 | 1.10 | – | – | 72.10 | 1.39 | – | – |
| Tabarsa et al (2012) | Colpomenia sinuosa | Iran | Apr 2008 | 10.11 | 1.01 | 1.46 | 0.10 | – | – | 9.50 | 1.58 |
| El-Said & El-Sikaily (2013) | Colpomenia sinuosa | Egypt | Apr 2011 | 9.20 | 0.92 | 1.50 | 0.11 | 11.80 | 0.23 | – | – |
| Rohani-Ghadikolaei et al (2012) | Colpomenia sinuosa | Iran | – | 17.73 | 1.77 | 2.94 | 0.21 | – | – | 10.50 | 1.75 |
| Tabarsa et al (2012) | Dictyota dichotoma | Iran | Apr 2008 | 7.26 | 0.73 | 2.03 | 0.15 | 58.82 | 1.13 | – | – |
| Smith et al (2010) | Durvillaea antarctica | New Zealand | Apr 2004 | 11.06 | 1.16 | 4.30 | 0.31 | 58.40 | 1.12 | 56.40 | 9.40 |
| Ortiz et al (2006) | Durvillaea antarctica | Chile | Nov 2013 | 9.60 | 0.96 | 1.80 | 0.13 | 66.90 | 1.29 | – | – |
| Smith et al (2010) | Ecklonia radiata | New Zealand | Aug 2004 | 9.78 | 0.98 | 0.80 | 0.06 | 69.61 | 1.34 | – | – |
| Smith et al (2010) | Eisenia bicyclis | Japan | – | 9.71 | 0.97 | 5.23 | 0.37 | 17.59 | 0.34 | 11.15 | 1.86 |
| Paiva et al (2014) | Fucus spiralis | Portugal | Jan 2013 | 17.40 | 1.74 | 1.80 | 0.13 | – | – | 26.20 | 4.37 |
| Marsham et al (2007) | Fucus serratus | United Kingdom | – | 15.90 | 1.59 | 0.50 | 0.04 | – | – | 16.60 | 2.77 |
| Smith et al (2014) | Fucus vesiculosus | Norway | May 2010 | 6.11 | 0.61 | 3.08 | 0.22 | – | – | – | – |
| Sanchez-Machado et al (2004) | Himanthalia elongata | Spain | – | 5.46 | 0.55 | 0.97 | 0.07 | – | – | – | – |
| Sanchez-Machado et al (2004) | Himanthalia elongata | Spain | – | 10.95 | 1.10 | 0.93 | 0.07 | – | – | – | – |
| Misurcová et al (2010) | Hizikia fusiformis | Japan | – | – | – | – | – | – | 17.52 | 2.92 | – |
| Smith et al (2010) | Homosia banksii | New Zealand | Apr 2004 | 6.07 | 0.61 | 2.63 | 0.19 | 62.90 | 1.21 | – | – |
| Maehre et al (2014) | Laminaria digitata | Norway | May 2010 | 5.31 | 0.53 | 0.99 | 0.07 | – | – | – | – |
| Schiener et al (2015) | Laminaria digitata | Scotland | Aug 2010 – Oct 2011 | 6.90 | 0.69 | – | – | 70.70 | 1.36 | – | – |
| Marsham et al (2007) | Laminaria digitata | United Kingdom | – | 15.90 | 1.59 | 0.50 | 0.04 | – | – | 16.60 | 2.77 |
| Maehre et al (2014) | Laminaria hyperborea | Norway | May 2010 | 5.02 | 0.50 | 1.28 | 0.09 | – | – | – | – |
| Schiener et al (2015) | Laminaria hyperborea | Scotland | Aug 2010 – Oct 2011 | 6.80 | 0.68 | – | – | 65.50 | 1.26 | – | – |
| Sanchez-Machado et al (2004) | Laminaria japonica | Japan | – | – | – | – | – | – | 10.45 | 1.74 | – |
| Smith et al (2010) | Laminaria ochroleuca | Spain | – | 7.49 | 0.75 | 0.92 | 0.07 | – | – | – | – |
| Tabarsa et al (2012) | Macrocystis spp | New Zealand | – | 11.02 | 1.10 | 1.56 | 0.11 | 44.54 | 0.86 | – | – |
| Padina pavonica | Japan | Apr 2008 | 11.83 | 1.18 | 1.79 | 0.13 | – | – | 11.00 | 1.83 |
| Maehre et al (2014) | Pelvetia canaliculata | Norway | May 2010 | 5.72 | 0.57 | 4.78 | 0.34 | – | – | – | – |
| Schiener et al (2015) | Saccharina latissima | Scotland | Aug 2010 – Oct 2011 | 7.10 | 0.71 | – | – | 63.10 | 1.21 | – | – |
| Sanchez-Machado et al (2004) | Saccorhiza polyphylla | Spain | – | 13.10 | 1.31 | 0.70 | 0.05 | – | – | – | – |
| Rodrigues et al (2015) | Sarcocirrus polycystum | Portugal | Apr 2012 | 14.44 | 1.44 | 1.10 | 0.08 | 45.60 | 0.88 | – | – |
| Rohani-Ghadikolaei et al (2012) | Sargassum ilicifolium | Iran | – | 8.90 | 0.89 | 2.00 | 0.14 | 32.90 | 0.63 | – | – |
| Matanjun et al (2009) | Sargassum polycystum | Borneo | – | 5.40 | 0.54 | 0.29 | 0.02 | 33.49 | 0.64 | 39.67 | 6.61 |
| Marinho-Soriano et al (2006) | 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) | Sargassum liniforme | Egypt | Apr 2011 | – | – | – | – | 8.59 | 0.17 | – | – |
| Rodrigues et al (2015) | Sargassum muticum | Portugal | Apr 2012 | 16.90 | 1.69 | 1.45 | 0.10 | 49.30 | 0.95 | – | – |
| Peng et al (2013) | Sargassum naazhouense | China | July 2011 | 11.20 | 1.12 | 1.06 | 0.08 | 47.43 | 0.91 | 4.83 | 0.81 |
| Smith et al (2010) | Undaria pinnatifida | New Zealand | – | 14.21 | 1.42 | 3.13 | 0.22 | 45.08 | 0.87 | – | – |
| Sanchez-Machado et al (2004) | Undaria pinnatifida | Spain | – | 18.00 | 1.80 | 1.05 | 0.08 | – | – | – | – |
| Smith et al (2010) | Undaria pinnatifida | New Zealand | Apr – Sep 2004 | 19.66 | 1.97 | 3.30 | 0.24 | 50.40 | 0.97 | – | – |
| Misurcová et al (2010) | Undaria pinnatifida | Japan | – | – | – | – | – | 9.03 | 1.51 | – | – |
| Misurcová et al (2010) | Undaria pinnatifida | Japan | – | – | – | – | – | 15.53 | 2.59 | – | – |

Abbreviation: RNI, Reference Nutrient Intake.
| 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) | Ahnfeltia plicata | Denmark          | Sep 2011       | 31.10       | 3.11                                | 1.10      | 0.08                                | 59.10            | 1.14                               | –         | –                                 |
| Marsham et al (2007) | Ceramium spp     | United Kingdom   | –              | 31.20       | 3.12                                | 0.60      | 0.04                                | –                | –                                  | 33.70     | 5.62                              |
| Parjikolaei et al (2016) | Chondrus crispus | Denmark          | Sep 2011       | 26.40       | 2.64                                | 1.00      | 0.07                                | 53.30            | 1.03                               | –         | –                                 |
| Marsham et al (2007) | Coralina officinalis | United Kingdom | –              | 6.90        | 0.69                                | 0.30      | 0.02                                | –                | –                                  | 9.40      | 1.57                              |
| Parjikolaei et al (2016) | Delessera sanguinea | Denmark       | Sep 2011       | 23.40       | 2.34                                | 1.20      | 0.09                                | 51.20            | 1.09                               | –         | –                                 |
| Marsham et al (2007) | Dumontia cantorta | United Kingdom   | –              | 31.70       | 3.17                                | 0.12      | 0.01                                | –                | –                                  | 34.30     | 5.72                              |
| Matanjun et al (2009) | Eucheuma cottonii | United Kingdom   | –              | 9.76        | 0.98                                | 1.10      | 0.08                                | 26.49            | 0.51                               | –         | –                                 |
| Parjikolaei et al (2016) | Furcellaria lumbricalis | Denmark | Sep 2011       | 20.60       | 2.06                                | 1.00      | 0.07                                | 55.40            | 1.07                               | –         | –                                 |
| Paiva et al (2014) | 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) | Gracilaria compressa | Egypt        | Apr 2011       | –           | –                                  | –         | –                                  | 11.62            | 0.22                               | –         | –                                 |
| Rohani-Ghadikolaei et al (2012) | Gracilaria corticata | India         | –              | 19.30       | 1.93                                | 1.80      | 0.13                                | 43.00            | 0.83                               | –         | –                                 |
| Sathivel & Devi (2015) | Gracilaria edulis | India           | –              | 0.67        | 0.07                                | 0.83      | 0.06                                | 10.16            | 0.20                               | 8.90      | 1.48                              |
| Francavilla et al (2013) | Gracilaria gracilis | Italy        | Jul 2011       | 31.00       | 3.10                                | 1.98      | 0.14                                | 27.50            | 0.53                               | –         | –                                 |
| Francavilla et al (2013) | Gracilaria gracilis | Italy        | Apr 2012       | 41.00       | 4.10                                | 1.40      | 0.10                                | 34.10            | 0.66                               | –         | –                                 |
| Francavilla et al (2013) | Gracilaria gracilis | Italy        | Oct 2011       | 41.00       | 4.10                                | 1.38      | 0.10                                | 24.80            | 0.48                               | –         | –                                 |
| Francavilla et al (2013) | Gracilaria gracilis | Italy        | Jan 2012       | 45.00       | 4.50                                | 1.12      | 0.08                                | 31.10            | 0.60                               | –         | –                                 |
| Rodrigues et al (2015) | Gracilaria gracilis | Portugal    | Apr 2012       | 20.20       | 2.02                                | 0.60      | 0.04                                | 46.60            | 0.90                               | –         | –                                 |
| Tabarsa et al (2012) | Gracilaria salicornia | Iran          | Apr 2008       | 9.58        | 0.96                                | 2.00      | 0.14                                | –                | –                                  | –         | –                                 |
| Parjikolaei et al (2016) | Gracilaria vermiculophylla | Denmark | Sep 2011       | 17.80       | 1.78                                | 1.30      | 0.09                                | 61.90            | 1.19                               | –         | –                                 |
| El-Said & El-Sikaily (2013) | Gracilaria verucosa | Egypt      | Apr 2011       | –           | –                                  | –         | –                                  | 11.15            | 0.21                               | –         | –                                 |
| Rodrigues et al (2015) | Grateloupia turuturu | Portugal    | Apr 2012       | 22.50       | 2.25                                | 2.20      | 0.16                                | 43.20            | 0.83                               | –         | –                                 |
| Wong & Cheung (2000) | Hypnea charoides | Hong Kong       | Dec 1997       | 18.40       | 1.84                                | 1.48      | 0.11                                | –                | –                                  | 50.30     | 8.38                              |
| Wong & Cheung (2000) | Hypnea japonica | Hong Kong       | Dec 1997       | 19.00       | 1.90                                | 1.42      | 0.10                                | –                | –                                  | 53.20     | 8.87                              |
| Siddique (2013) | 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) | Hypnea pinnosa | Egypt          | Apr 2011       | –           | –                                  | –         | –                                  | 11.17            | 0.21                               | –         | –                                 |
| Siddique (2013) | Hypnea pinnosa | Bangladesh   | May 2005       | 16.31       | 1.63                                | 1.56      | 0.11                                | 22.89            | 0.44                               | 40.59     | 6.77                              |
| Rohani-Ghadikolaei et al (2012) | Hypnea valentiae | India         | –              | 16.50       | 1.65                                | 2.80      | 0.20                                | 31.80            | 0.61                               | –         | –                                 |
| El-Said & El-Sikaily (2013) | Jania rubens | Egypt          | Apr 2011       | –           | –                                  | –         | –                                  | 12.96            | 0.25                               | –         | –                                 |
| Fayaz et al (2005) | Kappaphycus alvarezi | India       | –              | 16.24       | 1.62                                | 0.74      | 0.05                                | 27.40            | 0.53                               | 29.40     | 4.90                              |
| Kumar et al (2015) | Kappaphycus alvarezi | India       | Sep 2004 – Apr 2006 | 19.25 | 1.93                                | 0.64      | 0.05                                | –                | –                                  | 14.52     | 2.42                              |
| Marsham et al (2007) | Mastocarpus stellatus | United Kingdom | –              | 25.40       | 2.54                                | 3.00      | 0.21                                | –                | –                                  | 16.60     | 2.77                              |
| Gressier et al (2011) | Ochotoda secundiramea | Brazil       | –              | 10.50       | 1.01                                | 3.54      | 0.25                                | 45.07            | 0.87                               | –         | –                                 |
| Paiva et al (2016) | Odonthalia dentata | Denmark       | Sep 2011       | 17.80       | 1.78                                | 1.28      | –                                   | –                | –                                  | –         | –                                 |
| Paiva et al (2014) | Osmundea pinnatifida | Portugal    | Jan 2013       | 20.79       | 2.08                                | 7.53      | 0.54                                | 17.61            | 0.34                               | –         | –                                 |

(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                                | –         | –                                  |
| Miurcová 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)60                        | 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                           | Porphyrina columbia | Argentina       | Aug –          | 24.61       | 2.46                                | 0.25      | 0.02                                | –                | –                                   | 48.02     | 8.00                               |
| Sanchez-Machado et al (2004)28                 | Porphyrina spp    | Spain           | –              | 24.11       | 2.41                                | 1.03      | 0.07                                | –                | –                                   | –         | –                                  |
| Paiva et al (2014)16                           | Porphyrina spp    | Portugal        | Jan 2007       | 24.82       | 2.48                                | 8.88      | 0.63                                | 25.37            | 0.49                                | –         | –                                  |
| Smith et al (2010)23                           | Porphyrina spp    | New Zealand     | –              | 26.36       | 2.64                                | 3.03      | 0.22                                | 43.99            | 0.85                                | –         | –                                  |
| Smith et al (2010)23                           | Porphyrina spp    | New Zealand     | May –          | 32.71       | 3.27                                | 2.00      | 0.14                                | 45.40            | 0.87                                | –         | –                                  |
| Marsham et al (2007)27                         | Porphyrina spp    | United Kingdom  | –              | 44.00       | 4.40                                | 0.70      | 0.05                                | –                | 33.50                               | 5.58      |                                    |
| Cofrades et al (2010)12                        | Porphyrina umbilicalis | Spain       | –              | 39.00       | 3.90                                | –         | –                                   | –                | –                                   | –         | –                                  |
| El-Said & El-Sikaily (2013)21                   | Pterocladi capillacea | Egypt       | Apr 2011       | –           | –                                   | –         | 9.64                                | 0.19             | –                                   | –         | –                                  |
| El-Said & El-Sikaily (2013)21                   | Pterocladi capillacea | Egypt       | Apr 2011       | –           | –                                   | –         | 11.20                               | 0.22             | –                                   | –         | –                                  |
| El-Said & El-Sikaily (2013)21                   | Pterocladi capillacea | Egypt       | Apr 2011       | –           | –                                   | –         | 7.89                                | 0.15             | –                                   | –         | –                                  |
| El-Said & El-Sikaily (2013)21                   | Pterocladi capillacea | Egypt       | Apr 2011       | –           | –                                   | –         | 8.06                                | 0.16             | –                                   | –         | –                                  |
| Paiva et al (2014)26                           | Pterocladi 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)            | Caulerpa lentillifera | Taiwan        | –              | 9.26        | 0.93                                | 1.57      | 0.11                                | 64.00            | 1.23                               | 2.97      | 0.50                               |
| Matanjun et al (2009)          | Caulerpa lentillifera | Borneo        | –              | 10.41       | 1.04                                | 1.11      | 0.08                                | 38.66            | 0.74                               | 32.99     | 5.50                               |
| Ratana-Arporn & Chirapart      | Caulerpa lentillifera | Thailand      | March          | 12.49       | 1.25                                | 0.86      | 0.06                                | 59.27            | 1.14                               | 3.17      | 0.53                               |
| Mandlik et al (2014)           | Caulerpa racemosa    | India         | –              | –           | –                                   | –         | –                                   | –                | –                                 | –         | –                                  |
| Kokilam & Vasuki (2013)        | Caulerpa taxifolia   | India         | –              | 12.44       | 1.24                                | 0.32      | 0.02                                | 23.86            | 0.46                               | –         | –                                  |
| Maehre et al (2014)            | Cladophora rupestris | Norway        | May 2010       | 3.42        | 0.34                                | 0.76      | 0.05                                | –                | –                                 | –         | –                                  |
| Rodrigues et al (2015)         | Codium tomentosum    | Portugal      | April 2012     | 18.80       | 1.88                                | 3.60      | 0.26                                | 32.80            | 0.63                               | –         | –                                  |
| El-Said & El-Sikaily (2013)    | Codium tomentosum    | Egypt         | April 2011     | –           | –                                   | –         | –                                   | –                | –                                 | –         | –                                  |
| Aguilera-Morales et al (2005)  | Enteromorpha spp     | Mexico        | Winter 1997    | 9.45        | 0.95                                | 2.24      | 0.16                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva compressa       | Iran          | March 2015     | 15.20       | 1.52                                | 3.75      | 0.27                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva californica     | Iran          | February 2015  | 15.76       | 1.58                                | 3.45      | 0.25                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva compressa       | Iran          | February 2015  | 18.12       | 1.81                                | 1.03      | 0.07                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva fascicata       | Iran          | March 2015     | 18.64       | 1.86                                | 0.90      | 0.06                                | –                | –                                 | –         | –                                  |
| Paiva et al (2016)             | Ulva compressa       | Azores (Portugal) | April 2013       | –           | –                                   | –         | –                                   | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva californica     | Iran          | March 2015     | 14.06       | 1.41                                | 0.56      | 0.04                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva fascicata       | Iran          | February 2015  | 14.69       | 1.47                                | 0.47      | 0.03                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva flexuosa        | Iran          | March 2015     | 10.55       | 1.06                                | 2.82      | 0.20                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva flexuosa        | Iran          | March 2015     | 11.23       | 1.12                                | 2.34      | 0.17                                | –                | –                                 | –         | –                                  |
| Escobido et al (2016)          | Ulva intestinalis    | Philippines   | January – April 2016 | 5.57       | 0.56                                | 0.43      | 0.03                                | 37.28            | 0.72                               | –         | –                                  |
| Rohani-Ghadikolaei et al (2012)| Ulva intestinalis    | Iran          | –              | 10.50       | 1.05                                | 2.90      | 0.21                                | 35.50            | 0.68                               | –         | –                                  |
| Maehre et al (2014)            | Ulva intestinalis    | Norway        | May 2010       | 11.33       | 1.13                                | 1.62      | 0.12                                | –                | –                                 | –         | –                                  |
| El-Said & El-Sikaily (2013)    | Ulva intestinalis    | Egypt         | April 2011     | –           | –                                   | –         | –                                   | –                | –                                 | –         | –                                  |
| Wong & Cheung (2000)           | Ulva lactuca         | Hong Kong     | December 1997  | 7.06        | 0.71                                | 1.64      | 0.12                                | –                | –                                 | 55.40     | 9.23                               |
| Yaich et al (2011)             | Ulva lactuca         | Tunisia       | July 2007      | 8.46        | 0.85                                | 7.87      | 0.56                                | –                | –                                 | 54.90     | 9.15                               |
| Maehre et al (2014)            | Ulva lactuca         | Norway        | June 2012      | 8.65        | 0.87                                | 2.00      | 0.14                                | –                | –                                 | –         | –                                  |
| Tabarsa et al (2012)           | Ulva lactuca         | Iran          | April 2008     | 10.69       | 1.07                                | 0.99      | 0.07                                | –                | –                                 | 5.60      | 0.93                               |
| Pirian et al (2016)            | Ulva lactuca         | Iran          | February 2015  | 20.85       | 2.09                                | 0.85      | 0.06                                | –                | –                                 | –         | –                                  |
| Pirian et al (2016)            | Ulva lactuca         | Iran          | March 2015     | 21.55       | 2.16                                | 0.75      | 0.05                                | –                | –                                 | –         | –                                  |
| Bikker et al (2016)            | Ulva lactuca         | Ireland       | May 2015       | 26.30       | 2.63                                | 2.11      | 0.15                                | 24.00            | 0.46                               | –         | –                                  |
| Ortiz et al (2006)             | 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)           | Ulva lactuca         | United Kingdom | –              | 29.00       | 2.90                                | 0.50      | 0.04                                | –                | –                                 | 32.90     | 5.48                               |
| El-Said & El-Sikaily (2013)    | Ulva lactuca         | Egypt         | April 2011     | –           | –                                   | –         | –                                   | 11.15            | 0.21                               | –         | –                                  |
| El-Said & El-Sikaily (2013)    | Ulva lactuca         | Egypt         | April 2011     | –           | –                                   | –         | –                                   | 10.95            | 0.21                               | –         | –                                  |
| El-Said & El-Sikaily (2013)    | Ulva lactuca         | Egypt         | April 2011     | –           | –                                   | –         | –                                   | 11.54            | 0.22                               | –         | –                                  |
| El-Said & El-Sikaily (2013)    | Ulva lactuca         | Egypt         | April 2011     | –           | –                                   | –         | –                                   | 11.28            | 0.22                               | –         | –                                  |

(continued)
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, an essential amino acid often present in limited quantities in terrestrial plant protein sources such as corn, maize, soy, rice, and wheat. 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. 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. 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%; *Palmaria palmata*, 56.0%; and *Porphyra columbina*, 74.3%. 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 terrestrial plants. 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. 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. 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.

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 anti-diabetic effects. Among the effects reported are cardioprotective effects such as reduced blood pressure via inhibition of angiotensin-converting enzyme, anti-diabetic activity via inhibition of dipeptidyl-peptidase 4, and promotion of iron absorption. The potential application of seaweed peptides, which have antioxidant properties, as food preservatives has also been suggested. 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. 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. The potential functional properties of dietary fiber are associated with the viscous and water-binding properties of fiber within the gastrointestinal tract. 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. 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.

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. 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). 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, laminarin, and fucoidan polysaccharides; red seaweeds contain agar, carrageenan, porphyran, and xylan; and green seaweeds contain ulvan, xylan, and cellulose.

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. Fucoidan was recently classified by the EFSA as a novel food, 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. 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. 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. 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 Asophyllum 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. Similar results were reported when consumption of a preload alginate drink reduced energy intake by 44 kcal following an ad libitum lunch. A crossover study reported that daily energy intake was reduced by...
rejected. Other fibers, such as beta glucan, have re-

cidence by the EFSA concluded that sodium alginate

duced fucoidan (500 mg/d) for 3 months had

reports, and thus a health claim was failed to reduce postprandial glycemic responses with-

d the role of the gelling capacity of alginate. Research into the mech-

again 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 demon-

weight/obese cohort showed that participants who con-


tal thromboplastin time, decreased thrombin time, and increased antithrombin-III compared with placebo, al-

sity 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 understand-

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 disproportion rate of gastric emptying.83 The effect of alginate on glucose metabolism, particularly the postprandial insuline-

The recent designation of fucoidan as Generally Recognized as Safe (GRAS) by the US Food and Drug Administration104 and as a novel food by the European Union,104 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 over-

weight/obese cohort showed that participants who con-

sumed 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 in-

dex (BMI), adiposity, systolic blood pressure, total cho-

lesterol, 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 obe-

sity 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 understand-

there is also a wealth of evidence to support an antican-
United Kingdom, although legislation regarding advertisement of cancer prevention is less clear. 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 and antioxidant activities. 140,142,143 Inhibition of digestive enzymes, which
may prevent lipid absorption and help maintain glucose homeostasis, has also been suggested.\textsuperscript{138,139}

The bioavailability of polyphenolic compounds in food varies greatly but is known to be low.\textsuperscript{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 \textit{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.\textsuperscript{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 \textit{Sargassum polycystum} showed significant reductions in blood glucose, glycated hemoglobin, total cholesterol, blood triglycerides, and plasma atherogenic index.\textsuperscript{146,147} Polyphenols from both \textit{Ecklonia stolonifera}\textsuperscript{149} and \textit{Ascophyllum nodosum}\textsuperscript{148} have been shown to favorably alter glucose and insulin metabolism in diabetic mouse models, while \textit{Ecklonia cava} polyphenols significantly reduced serum and liver triglycerides and total cholesterol in a diabetic mouse model.\textsuperscript{150} Another study showed that a \textit{Gelidi um 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.\textsuperscript{151} The mechanism of action is unknown, but current evidence supports a role in the inhibition of digestive enzymes, including \(\alpha\)-amylase, \(\alpha\)-glucosidase, and lipase.\textsuperscript{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).\textsuperscript{154} Elsewhere, neither a 500-mg nor a 2000-mg dose of \textit{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).\textsuperscript{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 \textit{Ecklonia cava} polyphenol extract at a dosage of 400 mg/d for 12 weeks.\textsuperscript{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.\textsuperscript{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.\textsuperscript{158}

With \textit{Ecklonia cava} phlorotannins deemed safe for use as food supplements in the European Union,\textsuperscript{159} further evidence in healthy and at-risk human populations is required to ascertain the bioactivities of seaweed polyphenols.\textsuperscript{155} Efforts to optimize polyphenol extraction procedures will be crucial for maximizing the potential of seaweed polyphenols as food ingredients.\textsuperscript{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.\textsuperscript{163,164} Evidence suggests that fucoxanthin, through its antioxidant activity, may have potential as a food preservative to prevent lipid peroxidation in meat.\textsuperscript{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 \(\alpha\)-amylase and
\(\alpha\)-glucosidase, which in turn affects lipid metabolism by modulating leptin and adiponectin, resulting in down-regulation of lipogenesis and upregulation lipolysis. 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. Results of studies investigating the impact of fucoxanthin on cholesterol metabolism in mice have differed. Beppu et al reported increased serum HDL-C, non-HDL-C, and total cholesterol, while Jeon et al 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. However, mixed tocopherol and kelp extract components (the composition of which was undefined) were included in each capsule. Abidov et al 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, \(\beta\)-carotene, and zeaxanthin, as well as carotenoids present in green seaweeds, such as lutein, \(\beta\)-carotene, echinenone, violaxanthin, and neoxanthin, warrant investigation for their potential antiobesogenic, antidiabetic, or antioxidant bioactivities.

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, and a higher intake of foods containing seaweed has been associated with sufficient calcium intake to prevent osteoporosis in Korean postmenopausal women. In contrast, a 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. 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. 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).

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. 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 \(\mu\)g (2% of
Reference Nutrient Intake [RNI]) in Ulva rigida 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 B9) content varies from 7.5 μg (3.75% of RNI) in Ulva spp1 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 D3 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 B12. Enteromorpha spp and Porphyra spp are reported to contain 63.58 μg and from 32.26 to 133.8 μg 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 B12 content of seaweeds do not specify whether the vitamin B12 is present in the active form that can be absorbed and utilized in humans. Seaweeds containing active vitamin B12 may be useful for individuals following a vegan diet, who are at risk of vitamin B12 deficiency.185 For example, the authors of a cohort study in children following a vegan diet for 4 to 10 years attributed healthy vitamin B12 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 B12 or to contain vitamin B12 analogs that, because of structural differences, do not have vitamin B12 activity in humans.187 It has also been reported that the drying of Porphyra spp inactivates vitamin B12; 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 (0.14 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.\textsuperscript{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.\textsuperscript{202}

Static in vitro digestion studies have reported the bioavailability of iodine in seaweed as follows: Laminaria spp (17%–28%), Sargassum fusiforme (12%), Palmario 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).\textsuperscript{203,204} Boiling has been shown to reduce the iodine content of Alaria esculenta (from 670 µg/g to 165 µg/g), Palmario 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.\textsuperscript{204}

In humans, urinary excretion of iodide following Ascophyllum nodosum ingestion was reported as only 33% (excretion of potassium iodide control = 59%).\textsuperscript{205} The reduced iodine bioavailability was attributed to reduced release of iodine from the seaweed food matrix (ie, iodine bound to proteins, polysaccharides, polypeptides, 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),\textsuperscript{203} which also suggests limited liberation of iodine species, limited solubility of iodine, or limited absorption of iodine.\textsuperscript{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.\textsuperscript{209} Reduced urinary iodine excretion in the deficient cohort was attributed to increased iodine storage in the thyroid\textsuperscript{210}; thus, seaweed consumption may improve iodine status in those at risk of iodine deficiency, as demonstrated in vegan populations.\textsuperscript{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.\textsuperscript{213} These findings corroborate previous evidence that kelp supplementation increased serum TSH over 4 weeks.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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. However, exposure to contaminants is increased in perennial seaweeds, the regular consumption of which may lead to risk of heavy metal toxicity in humans. 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. 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. 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, 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). 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 seafood consumption. Arsenic species were not determined in this study, but blood mercury was significantly higher in the highest consumers of seafood 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. 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. The placental transfer of heavy metals from mother to fetus can cause neurological, developmental, and endocrine disorders in infants. 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.

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 organoarsenic). 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.

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 dimethylarsinol-ethanol, but the toxicity of these metabolites is unknown. Speciation and concentration of arsenic in brown seaweeds (Ascophyllum nodosum, Laminaria digitata, Fucus vesiculosus, Fucus spiralis, Alaria esculenta, and Saccharina latissima), red seaweeds (Porphyra umbilicalus, Chondrus crispus, Gracilaria vermiculophylla, and Palmaria palmata), and green seaweeds (Ulva prolifera and Ulva lactuca) 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) and 2.2 to 87.0 μg/g (Ireland). 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. 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), France (3.0 mg/kg of dry weight), and Australia/New Zealand (1.0 mg/kg of dry weight). 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). 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.\textsuperscript{243} Inclusion of 3% hijiki powder has caused arsenic poisoning in rats,\textsuperscript{249} and the risk of hijiki to public health has led to current recommendations against the consumption of hijiki in Asia,\textsuperscript{244} Australia,\textsuperscript{246} Europe,\textsuperscript{245,247,248} and the United States.\textsuperscript{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.\textsuperscript{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.\textsuperscript{251} However, cooking of Porphyra spp and Hizikia fusiforme by baking and boiling, respectively, has been shown to increase inorganic arsenic species,\textsuperscript{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.\textsuperscript{253} Wei et al\textsuperscript{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-dimethylarsinoacetic acid (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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{255} Human studies have shown considerable differences in the rate of excretion of arsenosugars, ranging from 4% to 95%.\textsuperscript{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.\textsuperscript{256} Thus, there is a need to characterize the metabolic fate of arsenosugars in order to clarify the safety associated with arsenosugar-rich seafoods.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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\textsuperscript{258} or as fertilizer.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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. A study by Michikawa et al identified a positive association between seaweed consumption and the risk of thyroid cancer (especially papillary carcinoma) in postmenopausal women, while Wang et al 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 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). 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. There are also concerns about the potential for seaweed to contribute to foodborne infections, as noted by reports of norovirus contamination of *Enteromorpha* spp and the presence of polycavernoside A toxin in *Gracilaria edulis*.

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. 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. 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 elucidate 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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