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Iodine from brown algae in human nutrition, with an emphasis on bioaccessibility, bioavailability, chemistry, and effects of processing: A systematic review

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Abstract

Brown algae are becoming increasingly popular as a food source and dietary supplement in Europe and other Western countries. As they are highly rich in iodine, they represent a potential new dietary iodine source. Iodine deficiency has been re-emerging in Europe, and it is important to ensure adequate intake through one's diet. However, macroalgae, and especially brown algae, may contain very high amounts of iodine, and both iodine deficiency and excessive iodine may increase the risk of negative health effects. The iodine content of algae or foods containing algae is currently not regulated in the European Union. The aim of this paper is to review the literature to determine the chemical species of iodine in brown algae, the loss of iodine during processing, and the bioavailability and bioaccessibility of iodine. A systematic search of the literature was performed in April 2021, via the databases Web of Science and PubMed. The review includes studies of iodine in brown macroalgae in relation to bioavailability, bioaccessibility, processing and speciation. A meta-analysis was conducted in relation to the following topics: (i) the correlation between total iodine and iodide (I^-) content in brown algae; (ii) the correlation between the loss of iodine during processing and the I^- content; and (iii) the correlation between bioavailability and the I^- content. The bioavailability of iodine from brown algae was generally high, with in vivo bioavailability ranging from 31% to 90%. The in vitro bioavailability of iodine (2%–28%) was systematically lower than in vivo bioavailability (31%–90%), indicating an inadequate in vitro methodology. Processing may reduce the iodine content of brown algae, and a higher I^- content was positively correlated with increased iodine loss during processing. Although processing strategies may reduce the iodine content of brown algae significantly, the iodine content may still be high after processing. These findings may be used in food safety evaluations of brown algae as well as in the development of macroalgae-containing foods with iodine contents suitable for human consumption. Further research on processing techniques to reduce the iodine content in brown macroalgae are warranted.

KEYWORDS
Seaweed, Macroalgae, iodine, nutrition, bioavailability, speciation, processing

1 | INTRODUCTION

Seaweeds are a diverse group of marine plant-like organisms, also referred to as macroalgae, which are typically divided into three groups based on pigmentation: red (Rhodophyta), green (Chlorophyta), and brown algae (Phaeophyceae). Since seaweeds absorb carbon dioxide and nutrients from the surrounding ocean during growth without requiring fertilizers, they can be cultivated with an exceptionally low carbon footprint. In the last 10 years, European seaweed cultivation has increased, and in the northern part of Europe, brown algae currently dominate production, particularly sugar kelp (*Saccharina latissima*) and winged kelp (*Alaria esculenta*).

In accordance with sustainable development goals, support for vegetarian and vegan diets is on the rise, and seaweeds are emerging as a trendy food in Europe and the Western world. Often regarded as healthy and sustainable "superfoods," seaweeds are utilized to an increasing extent as ingredients in food items (Nova et al., 2020). Possibilities for seaweed inclusion in foods are vast since seaweeds contain many components that can enhance the functionality (e.g., texturizing agents) and taste (e.g., glutamic acid) of the food. Furthermore, seaweeds may contain many important nutrients, such as vitamins, minerals, fibers, and proteins (Holdt & Kraan, 2011; MacArtain et al., 2007; Mæhre et al., 2014; Nielsen et al., 2021). Brown algae are rich in minerals and fibers (especially water-soluble alginate), which are associated with positive health benefits (Brown et al., 2014). However, seaweeds are strong accumulators of iodine (Küpper et al., 2008, 2011; Leblanc et al., 2006) and heavy metals (Davis et al., 2003), and it is necessary to control the levels of these components in seaweeds used for human nutrition to prevent harmful effects for the consumers (European Commission, 2018). In this review, the focus will be on the iodine content of seaweeds and its relation to human health.

Iodine is an essential trace element that is required for the production of the hormones thyroxine and triiodothyronine (Zimmermann, 2009). These thyroid hormones are essential for normal growth and development and metabolic regulation (Brent, 2012). The recommended intake of iodine is 150 μg/day for adults (WHO & UNICEF, 2007), and the tolerable upper intake level set by the Scientific Committee on Food (SCF) is 600 μg/day (Scientific Committee on Food, 2002); thus, the window for the optimal consumption of iodine is narrow. Both low and high intakes of iodine may result in inadequate thyroid hormone production and negative health effects (Zimmermann, 2009).

Brown algae may contain high iodine concentrations, depending on the species (Biancarosa et al., 2018; Mæhre et al., 2014; Roleda et al., 2018), the part of the thallus (Kreissig et al., 2021; Küpper et al., 1998, 2013; Nitschke & Stengel, 2015; Verhaeghe et al., 2008), and growth conditions (Ar Gall et al., 2004; Roleda et al., 2018; Sharma et al., 2018). The loss of iodine during processing may be substantial (Hou et al., 1997; Nielsen et al., 2020) and is relevant when evaluating the iodine intake from macroalgae used as food. Furthermore, the chemical species of iodine may influence how readily iodine can be released or broken down during processing and digestion. Iodine may be found in several chemical forms or species, generally characterized as inorganic and organic forms. Iodide (I^-) is the most common inorganic form of iodine in brown algae (Küpper et al., 2008), but iodate (IO_3^-) is sometimes also identified (Hou et al., 1997). Iodine can also be organically bound to macromolecules in brown algae (Hou et al., 2000).

The concept of bioavailability is frequently relevant to discussions of the tolerable amounts of iodine from seaweeds. The bioavailability of iodine is defined as the proportion of iodine that is released from the ingested food, absorbed by the intestine, and brought into circulation. A related term, bioaccessibility, refers to the proportion of iodine that is released during digestion, without assessing further uptake into the body's circulation. Studies of bioavailability and bioaccessibility are necessary to understand how readily iodine from seaweeds is absorbed during digestion. Since some studies have yielded results indicating that the bioavailability of iodine from seaweeds is low (Romarís-Hortas et al., 2011), bioavailability has been used as an argument for allowing a higher daily consumption of iodine from seaweeds (Bak, 2019). However, contradictory results regarding bioavailability have been found in other studies (Aquaron et al., 2002), and an investigation into the various studies assessing the bioavailability of iodine from brown algae is needed to enhance our understanding of which results can and should be trusted during decision-making.

This paper will review the current literature regarding the chemical species of iodine in brown algae, the loss of iodine during processing and the bioavailability and bioaccessibility of iodine. Based on the reviewed results, tolerable amounts of processed brown algae will be calculated. The findings of this review are relevant for health authorities and food manufacturers in ensuring that the population consumes adequate but not excessive amounts of iodine. Furthermore, this information is important for decision-making regarding the food safety and labelling of seaweed foods, specifically foods containing brown algae.

1.1 | Background

1.1.1 | Iodine deficiency and iodine excess

As for most nutrients, there is a U-shaped relationship between the intake of iodine and the risk of adverse health consequences (Laurberg et al., 2009), meaning that both too low intakes and excessively high intakes may lead to negative health impacts. The consequences of severe iodine deficiency are well-documented and may lead to impaired growth and development (Leung, 2017). Health consequences of mild-to-moderate iodine deficiency, on the other hand, lack thorough evidence (Eastman, 2017), but several observational studies have revealed neurocognitive impairment in children born to mothers who were mildly iodine-deficient during pregnancy (Abel et al., 2019; Bath et al., 2013; Hynes et al., 2013; Markhus et al., 2018; Zhou et al., 2019). In general, there have been more studies and reports on the health consequences of iodine deficiency as opposed to iodine excess. However, it has been established that excessive iodine intake may cause altered thyroid function and may lead to both hyperthyroidism and hypothyroidism (Bürgi, 2010). A systematic review and meta-analysis found an increased prevalence of thyroid dysfunction and goiter in both adults and children with iodine excess (Katagiri et al., 2017). The potential effects of iodine excess on growth and development is an area of limited research, but some studies have uncovered associations with lower Intelligence Quotient (IQ) scores or developmental status among children with excessive iodine status (Aakre et al., 2016; Liu et al., 2009; Ren & Zhong, 2014). Associations between iodine excess and impaired fetal growth have also been found (Chen et al., 2018). Furthermore, several epidemiological studies in different population groups have documented thyroid disorders in association with excessive iodine intake, specifically from dietary seaweed (Chung et al., 2009; Emder & Jack, 2011; Konno et al., 1994; Miyai et al., 2008; Suzuki et al., 1965). In studies from Japan, where frequent seaweed consumption is common, such as in coastal areas, a high prevalence of goiter and hypothyroidism have been discovered (Konno et al., 1994; Suzuki et al., 1965). Therefore, when incorporating macroalgae into the diet of the Western world, precautions must be taken to avoid excessive iodine intake from these foods.

2 | MATERIALS AND METHODS

The present systematic review was conducted based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement checklist.

2.1 | Data sources and search strategies

A systematic search of the literature was conducted on April 16, 2021, via two databases, Web of Science and PubMed, between 1990 and the current date. No language limitation was placed on the search. Keywords were as follows: “bioavailability” or “bioaccessibility” or “processing” or “boiling” or “cooking” or “speciation,” and “iodine” and “seaweed” or “alga’ or “kelp.” The literature search from the two databases generated a total of 182 hits. The potential articles from each database were identified, duplicates were removed (n = 68), and relevant articles were then scanned to confirm relevance. Six authors were contacted for more detailed information related to their articles. Furthermore, one report and seven articles were identified through other sources by manually searching reference lists and organizations with relevant work.

2.2 | Eligibility criteria

Studies were selected according to the following eligibility criteria: (i) studies published as an original article with full text; (ii) studies in which edible, brown algae were used as the raw material. Studies were excluded based on the following criteria: (i) the paper was secondary research, such as systematic reviews, review articles, author comments or conference abstracts; (ii) the article was not in the English language; (iii) brown algae were not used as the study material (but rather other groups of macroalgae, such as red or green macroalgae), or the brown algal species used was not used as food (such as species used for environmental monitoring or other non-food purposes); (iv) the article did not specify the species of brown algae used; (v) the topic of the article was not related to the keywords. For the literature on bioavailability, studies using mammal animal models were also included if they appeared in the search (n = 1), whereas studies concerning fish were excluded. Relevant reports and gray literature were also

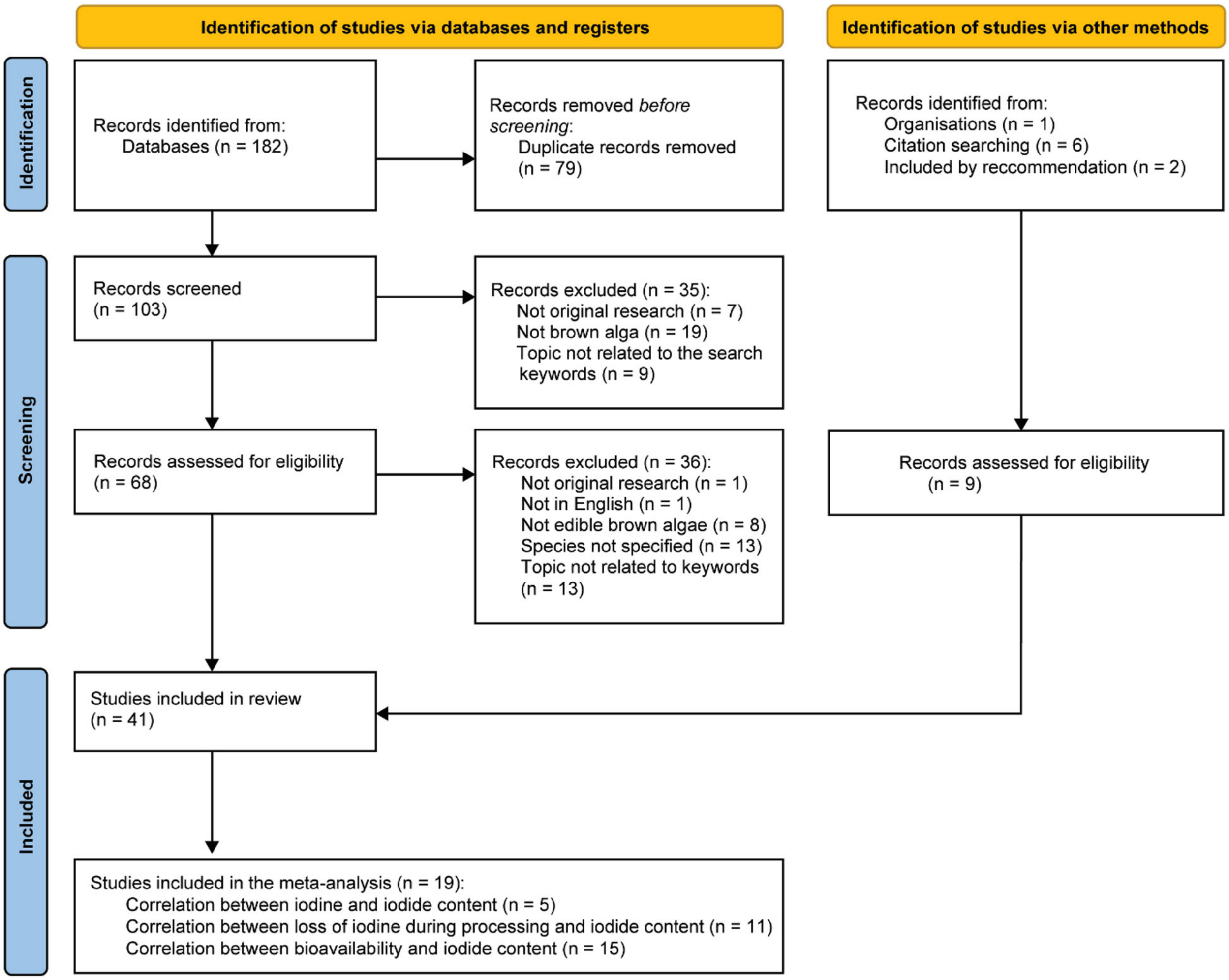

FIGURE 1 Flow chart of the selection of studies on chemical species of iodine in brown alga, loss of iodine during processing, and bioavailability and bioaccessibility of iodine in brown algae in the present systematic review and meta-analysis. Adjusted to the current study, based on the version by Page et al. (2021). For more information, visit: http://www.prisma-statement.org/

included if deemed eligible. When the brown algal species were characterized as "kombu" or "konbu" without reference to the species name, it was assumed that the species was *S. japonica*, and when characterized as "wakame," it was assumed that the species was *Undaria pinnatifida*. One hundred and eighty-two articles were identified from the databases; after removing duplicates (n = 79), 103 articles were screened, and 68 articles were assessed for eligibility by two of the authors (MJB, IA). There were 40 articles included in the review, along with one report (Figure 1).

2.3 | Meta-analyses

2.3.1 | Correlation between total iodine and I^- content in brown algae

For seven species, namely, *Laminaria hyperborea, L. digitata*, *L. ochroleuca*, *S. japonica*, *U. pinnatifida*, *Sargassum miyabei*, and *Himanthalia elongata*, I^- content was reported along with total iodine content in the eligible literature (Tables 1 and 2). In cases in which more than one study reported such data, the average I^- content and average total iodine content were extracted for the analysis to yield one set of data for each species. The data were plotted in Microsoft Excel to investigate any correlations, and an apparent exponential relationship was found. The y-intercept was set to 1. Five studies were used for this correlation analysis (Gamallo-Lorenzo et al., 2005; Hou et al., 1997; Lu et al., 2006; Romarís-Hortas et al., 2013; Shah et al., 2005).

2.3.2 | Correlation between the loss of iodine during processing and the I^- content

For three species, namely, *S. japonica*, *L. digitata*, and *S. miyabei*, data were available from the literature concerning both the loss of iodine during processing and the I^- con-

TABLE 1 Taxonomic relationship of food species of brown alga and their total iodine content

Order	Family	Genus	Species	Common name	Total iodine (μg/g dw[a])
Ectocarpales	Scytosiphonaceae	*Petalonia*	*binghamiae*	Habo-nori	81[1]
Fucales	Fucaceae	*Fucus*	*spiralis*	Spiral wrack	135[2]; 150 [3]; 190*[4]
			vesiculosis	Bladder wrack	226 [5]; 260 [3]; 276 [6]; 96-354 [7]; 570; 583*[4]; 732 [8]
		Ascophyllum	*nodosum*	Knotted wrack	482 [5]; 646 [6]; 670 [3]; 712[9]; 608-785*[4]; 265-871 [7]
		Pelvetica	*canaliculata*	Channel wrack	200 [3]; 248 [4]
	Sargassaceae	*Sargassum*	*miyabei*	-	273 [10]
			fusiforme	Hijiki	58–120 mg/kg fw [11]; 262 [12]; 436 [8]; 629 [6]
	Himanthaliaceae	*Himanthalia*	*elongata*	Sea spaghetti	59 [3]; 117 [13]; 116.6[14]; 135 [4]; 605 [15]
Laminariales (kelp)	Laminariaceae	*Laminaria*	*hyperborea*	Tangle	1734**[4]; 3170 [16]
			digitata	Oarweed	1997, 2984, 8165 [6]; 4834, 15505 [16]; 5762**[4]; 2300, 6300 [17]; 7080 [15]; 4000-9700** [18]; 10.000 [3], 2400-31.000 [19]
			ochroleuca	Kombu	2412 [15]; 6138 [13, 14]; 177–343 mg/kg fw [11]; 6545 [19]
		Saccharina	*japonica*	Kombu	241-4921 [20]; 2110 [8]; 2300 [21]; 2555 [22]; 3040 [10]; 4170 [23]; 4300 [18]
			latissima	Sugar kelp	238 [8]; 380, 420, 510, 1500, 1655, 2700, 3965 [22]; 2630 [24]; 3000, 3341**[4]; 778-3594** [7]; 560-3821 [7]; approx. 5000 [25]; 5900 [26]; ~4000 [27]; 4600 [3]; 4605 [28]; 4898, 6568 [29]
			longicruris	Atlantic Kombu	746 [6]; 764 [5]; 1054-1879** [7]
	Alariaceae	*Alaria*	*esculenta*	Winged kelp	95[30]; 110, 431 [6]; 213 [29]; 308 [3]; 431 [6]; 670 [31]; 495-1844** [7]
			marginata	Winged kelp	151 [8]
		Undaria	*pinnatifida*	Wakame	32, 41, 42, 115 [6]; 60, 102 [8]; 93.9-185.1 [20]; 163 [12]; 226 [23]; 306 [13, 14]; 177–343 mg/kg fw [11]; 326 [19]; 514 [15]
	Lessoniaceae	*Eisenia*	*bicyclis*	Arame	586 [6]; 600 [8]

Note: Algaebase (Guiry & Guiry, 2021) was consulted for taxonomic relations.
Abbreviation: Fw, fresh weight.
[a]Unless otherwise stated;
[*]Middle portion;
[**] blade.
Source: [1] Afonso et al. (2021); [2] Francisco et al. (2018); [3] Biancarosa et al. (2018); [4] Nitschke and Stengel (2015); [5] Phaneuf et al. (1999); [6] Teas et al. (2004); [7] Kreissig et al. (2021); [8] van Netten et al. (2000); [9] Combet et al. (2014); [10] Hou et al. (1997); [11] Domínguez-González et al. (2017); [12] Dawczynski et al. (2007); [13] Romarís-Hortas et al. (2012); [14] Romarís-Hortas et al. (2011); [15] Gamallo-Lorenzo et al. (2005); [16] Lu et al. (2006); [17] Küpper et al. (2013); [18] Küpper et al. (1998); [19] Ar Gall et al. (2004); [20] Ownsworth et al. (2019); [21] Romarís-Hortas, Bermejo-Barrera, and Moreda-Piñeiro (2013); [22] Yeh et al. (2014); [23] Miyai et al. (2008); [24] Lüning and Mortensen (2015); [25] Shah et al. (2005); [26] Bruhn et al. (2019); [27] Granby et al. (2020); [28] Stévant, Indergård et al. (2018); [29] Duinker et al. (2020); [30] Nielsen et al. (2020); [31] Stévant, Marfaing et al. (2018); [32] Teas et al. (2007); [33] Nitschke and Stengel (2016).

TABLE 2 Iodine species in edible brown alga (μg/g dw)

Species	Water soluble iodine	Iodide	Iodate	Organic bound	Bound to Protein	Pig-ment	Poly-phenol
Fucus vesiculosis	n.a.	108 [1]	n.a.	n.a.	n.a.	n.a.	n.a.
Alaria nodosum	n.a.	275 [1] (~40%)	n.a.	n.a.	n.a.	n.a.	n.a.
Saccharina miyabei	41% [2]; 40 [3]	27% [2]	1.8% [2]	71% [2];70% [3]	66% [3]	1.6% [3]	3.1% [3]
Himanthalia elongata	n.a.	90%, that is, 546 [4]	n.a.	n.a.	n.a.	n.a.	n.a.
Laminaria hyperborea	n.a.	98% [5]	n.a.	n.a.	n.a.	n.a.	n.a.
L. digitata	n.a.	98% [5]; 3134 [1]	n.a.	n.a.	n.a.	n.a.	n.a.
L. ochroleuca	n.a.	95%, that is, 2305 [4]; 105%, that is, 6646 [6]	n.a.	n.a.	MIT and DIT detected [7]; MIT: 0.27%, that is, 17, DIT: 0.005%, that is, 0.3 [6]	n.a.	n.a.
Saccharina japonica	99% [2]	88% [2]; 94%, that is, 3940 [8]; 5260 [9]	1.4% [2]	10% [2]	Mono-iodo-tyrosine (MIT) and di-iodo-tyrosine (DIT) n.d. [8]	n.a.	n.a.
S. latissima	n.a.	574 [1]	n.a.	n.a.	n.a.	n.a.	n.a.
A. esculenta	n.a.	111, 151 [1]	n.a.	n.a.	n.a.	n.a.	n.a.
Undaria pinnatifida	n.a.	62%, that is, 140 [8]; 14 [9]; 231 [10]; 79%, that is, 194 [6]; 91%, that is, 469 [4]	1.8%, that is, 4.16 [8]	n.a.	MIT: 0.3 and DIT: 7.4 [10]; MIT and DIT detected [7, 8, 11]; MIT: 4%, that is, 10, DIT: 0.05%, that is, 0.1 [6]	n.a.	n.a.

Abbreviations: n.a., not available; n.d., not detected.
Source: [1] Martinelango, Tian, and Dasgupta (2006); [2] Hou et al. (1997); [3] Hou, Yan, and Chai (2000); [4] Gamallo-Lorenzo et al. (2005); [5] Lu et al. (2006); [6] Romarís-Hortas, Bermejo-Barrera, and Moreda-Piñeiro (2013); [7] Romarís-Hortas et al. (2012); [8] Shah et al. (2005); [9] Yang et al. (2014); [10] Cao et al. (2016); [11] Romarís-Hortas, Bermejo-Barrera, and Moreda (2012).

tent. Data concerning the loss of iodine content during processing was also available for *S. latissima* and *A. esculenta*, and due to their close genetic relationship with *S. japonica* and *U. pinnatifida*, respectively, data for the I^- content for the latter species were applied for the former. Algaebase (Guiry & Guiry, 2021) was consulted to determine taxonomic relations. During the calculations, the average I^- content was used when more than one value was found in the literature search. The largest (maximum) reported loss (in %) was applied for the total iodine loss during processing. In total, eight studies were used for the analysis as indicated in Table 2 (I^-, all data presented as % of total iodine were used) and Table 3 (the maximum reported loss was used).

2.3.3 | Correlation between bioavailability and I^- content

For *L. hyperborea* and *S. japonica*, data for both in vivo bioavailability and I^- content (%) were available. For *A. nodosum*, the I^- content found in a separate study, which did not measure the total iodine content was used (Martinelango et al., 2006), and the total iodine content was estimated based on the average of the minimum and maximum iodine content as found in six studies yielding similar results (Table 1; Biancarosa et al., 2018; Combet et al., 2014; Kreissig et al., 2021; Nitschke & Stengel, 2015; Phaneuf et al., 1999; Teas et al., 2007). An in vivo bioavailability result was also available for *A. esculenta* (Teas et al., 2007) and *S. latissima* (Duinker et al., 2020). For these species, the I^- content was also available but not as a percentage of total iodine. In addition, the total iodine content varied from 95 to 1844 and 238 to 6568 μg/g dry weight (dw) for these species (Table 1); therefore, it was not possible to approximate the total iodine content used in the experiment in which the I^- content was measured. Therefore, the I^- content (%) was assumed to resemble the genetically similar *U. pinnatifida* and *S. japonica*, which have highly similar total iodine content relative to the former species (Table 1). Since the I^- content of *L. ochroleuca* and *U. pinnatifida* was available (Gamallo-Lorenzo et al.,

TABLE 3 Processing of brown alga and its effect on the iodine content

Species	Origin	Initial state	Processing	Iodine (µg/g dw) Initial	Final	Iodine red. (%, dw)	Reference
F. vesiculosis	Maine	Fresh, chopped	Washing, once	108*	61*	44*	[1]
A. nodosum	Maine	Fresh, chopped	Washing, once	275*	182*	34*	[1]
S. miyabei	China	Frozen, defrozen, cut, and grinded	Soaking thrice (3 h and 2 × 30 min)	273	162	41	[2]
L. digitata	Scotland	Washed and dried	Rehydration 30 min (r.t.)	2400	245	90	[3]
			Blanching 10–20 s	2400	1143	52	[3]
			Rehydration 30 min (r.t.) and bringing to boil	2400	333	86	[3]
		Dried (not washed)	Rehydration 30 min (r.t.)	6341	157	98	[3]
			Blanching 10–20 s	6341	1127	82	[3]
			Rehydration 30 min (r.t.) and bringing to boil	6341	179	97	[3]
S. japonica	Japan	Purchased	Rehydration 30 min (r.t.)	4360	909	79	[3]
			Blanching 10–20 s	4360	3946	10	[3]
			Rehydration 30 min (r.t.) and bringing to boil	4360	182	96	[3]
	China	Frozen, defrozen, cut, and grinded	Soaking once (3 h)	3040	468	85	[2]
			Soaking twice (3 h and 30 min)	3040	55	98	[2]
			Soaking thrice (3 h and 2 × 30 min)	3040	25	99	[2]
S. latissima	Faroe Islands	Frozen, cut, refrozen	Boiling 15 min	2630	1620	38	[4]
			Boiling 15 min and fermenting (37°C, 48 h)	2630	902	66	[4]
	Norway	Fresh**	Drying (40°C)	5900	5700	3	[5]
			Drying (70°C)	5900	4900	17	[5]
			Freeze-drying	5900	3000	49	[5]
	France	Fresh, < 2 h post-harvest	Soaking in tap water (32°C) w/ air bubbling (1–22 h)	6568	~1000	85	[6]
			Soaking in tap water (16°C) w/ air bubbling	4898	n.a.	NSR	[6]
			Soaking in seawater (18°C) w/ air bubbling	4898	n.a.	NSR	[6]
	Norway	Fresh, whole thallus	Soaking/blanching–300 s (30°C)	4605	1014	78	[7]
			Blanching–300 s (45°C)	4605	388	92	[7]
			Blanching–300 s (60°C)	4605	321	93	[7]
			Blanching–120 s (80°C)	4605	293	94	[7]
	Germany	Sun dried	Boiling–2 min	380	~130	~67	[8]
			Boiling–10 min	380	~90	~77	[8]
A. esculenta	Ireland	Fresh	Washing w/stirring	670	603	10	[9]
			Washing w/stirring and airdrying (23°C)	670	n.a.	NSR	[9]

(Continues)

TABLE 3 (Continued)

Species	Origin	Initial state	Processing	Iodine (μg/g dw) Initial	Final	Iodine red. (%, dw)	Reference
			Washing w/stirring and oven drying (60°C)	670	n.a.	NSR	[9]
			Washing w/stirring and freeze dried	670	n.a.	NSR	[9]
			Rehydration (1 h)	599	228	62	[9]
			Rehydration (avg. 1–24 h) and boiling	599	165	73	[9]

Abbreviations: n.a., not available; NSR, no significant loss.

*I^- was analyzed;

**Compared with fresh seaweed dried at 25°C.

Source: [1] Martinelango and Dasgupta (2006); [2] Hou et al. (1997); [3] Ownsworth et al. (2019); [4] Bruhn et al. (2019); [5] Stévant, Indergård et al. (2018); [6] Stévant, Marfaing et al. (2018); [7] Nielsen et al. (2020); [8] Lüning and Mortensen (2015); [9] Nitschke and Stengel (2016).

2005; Romarís-Hortas et al., 2013; Shah et al., 2005), and the bioaccessibility results for these species were highly similar to in vivo bioavailability results assessing similar species (will be discussed in Section 3.2), these were also included. Data for *L. digitata* were not included since not all of the urine was collected via the methodology used, and the remaining portion of the urine was not compensated for (Table S2; Lu et al., 2006). This result is therefore artificially low. In the case of more than one value of I^- content, the value to be used for the correlation was calculated as the average of the reported maximum and the minimum values from the eligible literature, whereas the maximum value reported was used for the bioavailability. The data were plotted in Microsoft Excel to investigate any correlations, and an apparent linear relationship was identified. Fifteen studies were used for this correlation analysis, of which 11 were used for iodine and I^- results (Biancarosa et al., 2018; Combet et al., 2014; Gamallo-Lorenzo et al., 2005; Hou et al., 1997; Lu et al., 2006; Martinelango et al., 2006; Nitschke & Stengel, 2015; Phaneuf et al., 1999; Romarís-Hortas et al., 2013; Shah et al., 2005; Teas et al., 2007), and seven were used for bioavailability and bioaccessibility results (Andersen et al., 2019; Combet et al., 2014; Domínguez-González et al., 2017; Duinker et al., 2020; Miyai et al., 2008; Teas et al., 2007).

2.4 | Tolerable amount of iodine in processed brown algae

Based on the results found for bioavailability (in vivo) and residual iodine in brown algae after processing, the residual bioavailable fraction was calculated. In the calculation, it was assumed that the bioavailability (%) remained the same regardless of processing. In cases in which more than one in vivo bioavailability result was found, the highest bioavailability result was selected since a lower bioavailability may be expressed in persons with insufficient iodine status initially (see Section 5.1.2). The result was used to calculate the amount of algae (g dry weight) needed to achieve an intake of 150 and 600-μg iodine. These amounts equal the population reference intake and tolerable upper intake of iodine for a general adult person according to European regulations (EFSA Panel on Dietetic Products and Nutrition and Allergies (NDA), 2014). Eleven studies were used for this meta-analysis, of which four studies reported bioavailability results (Duinker et al., 2020; Lu et al., 2006; Miyai et al., 2008; Teas et al., 2007), and seven studies reported iodine loss during processing (Table 3; Bruhn et al., 2019; Lüning & Mortensen, 2015; Nielsen et al., 2020; Nitschke & Stengel, 2016; Ownsworth et al., 2019; Stévant, Indergård, et al., 2018; Stévant, Marfaing, et al., 2018).

3 | RESULTS AND DISCUSSION

3.1 | Results

We included a total of 41 studies in this review, comprising a large number of species of brown macroalgae. The studies included were conducted in the United States, China, the United Kingdom, Japan, Denmark, Norway, France, Germany, Ireland, Greenland, Portugal, Faroe Islands, Spain, Canada, South Korea, and Taiwan. Regarding the total iodine content of edible brown macroalgae, we included 33 studies describing this topic in one or several species of edible brown macroalgae (Table 1). Eleven studies assessing different species of iodine in edible brown macroalgae were included (Table 2). On the topic of processing and its effect on iodine contents, we included nine studies (Table 3). Details regarding the methodology applied in the reviewed studies are presented in Table S1.

3.1.1 | Total iodine and chemical species of iodine in brown algae

Brown algae are typically rich sources of iodine, but the iodine contents of the species consumed as food vary immensely (approx. 30–31,000-μg iodine/g dw; Table 1). In relation to the order Laminariales (the kelps), 31 different studies described the iodine content of different species and were used in this review. Two main genera used for food purposes are part of this family, namely, *Laminaria* and *Saccharina*. The food species of interest in the *Laminaria* genus have iodine contents ranging from around 1700 to 31,000 μg/g dw, whereas the food species of interest in the *Saccharina* genus range from around 200 to 7000 μg/g dw (Table 1). Two other families belonging to the kelps are also of interest as food, namely, Alariaceae, with species *A. esculenta* and *U. pinnatifida*, and Lessoniaceae, with species *Eisenia bicyclis*. These species contain less iodine than the other kelps, with reported values typically ranging between 30 and 700 μg/g dw, although up to 1844 μg/g dw has been reported for *A. esculenta*. Other brown macroalgae food species of interest belong to the Fucales order. Sixteen studies were included in this review, which describes the iodine content of species in this order, wherein the iodine content ranges from 60 to 800 μg/g dw. One relevant species of the Ectocarpales was also identified, which has a low iodine content (81 μg/g dw; Afonso et al., 2021; Table 1).

For the description of iodine species in edible brown macroalgae, 11 studies were identified and included. Species in the Laminariaceae family contain most of the iodine in the form of I^- (Table 2). *Laminaria hyperborea* and *L. digitata* were found to contain 98% of the iodine as I^- (Lu et al., 2006). *Saccharina japonica* (kombu) was found to contain 88% to 94% of the iodine as I^- (Shah et al., 2005). No other chemical species of iodine was found in the species of algae in these studies. *Laminaria ochroleuca* has been found to contain 95% to 105% of its iodine in the form of I^- (Gamallo-Lorenzo et al., 2005; Romarís-Hortas et al., 2013). One study analyzed the amount of I^- in *S. latissima* (574 μg/g dw), but the total amount of iodine in the sample was not analyzed in the study (Martinelango et al., 2006). Since the reported total iodine contents of *S. latissima* vary so greatly (approx. 200–7000 μg/g dw), it is not possible to estimate what percentage of I^- *S. latissima* contains based on this information.

Another form of inorganic iodine found in brown algae is IO_3^-. In *U. pinnatifida*, 1.8% of the iodine was IO_3^-, while 62%–91% was I^- (Gamallo-Lorenzo et al., 2005; Romarís-Hortas et al., 2013; Shah et al., 2005). Minor amounts of IO_3^- were also found in *S. miyabei* (previously *S. kjellanianum*; 1.8%) and *S. japonica* (1.4%; Hou et al., 1997). In the remaining species, IO_3^- was either not analyzed or not detected.

Iodine in brown algae can also be associated with macromolecules, referred to as organic iodine. In *S. miyabei*, 66% of the total iodine was found to be associated with proteins, 3.1% with polyphenols, and 1.6% with pigments (Hou et al., 2000). Protein-associated iodine was also found in *U. pinnatifida* (Shah et al., 2005). This finding was confirmed by reducing the molecular weight of the iodated macromolecules with enzymatic digestion using protein-specific enzymes: proteases (Shah et al., 2005). The iodine was found to be bound with tyrosine, ultimately revealing mono-iodo-tyrosine (MIT) and di-iodo-tyrosine (DIT) upon enzymatic digestion. MIT and DIT were also successfully extracted from *U. pinnatifida* using solid-phase dispersion (Cao et al., 2016). After the simulated gastric digestion (involving proteases) of *L. ochroleuca*, MIT and DIT were found in the dialysate (Romarís-Hortas, Bermejo-Barrera, & Moreda-Piñeiro, 2012; Romarís-Hortas, Bermejo-Barrera, Moreda-Piñeiro, & Moreda-Piñeiro, 2012).

Correlation between total iodine and I^- content in brown algae

Upon plotting the amount of iodine relative to its fraction as I^- in brown algae, there appears to be a clear correlation between total iodine and the amount of iodine present as I^- (Figure 2a). In the algae with high amounts of iodine (> 3000 μg/g dw), much of this is in the form of I^- (> 90%), whereas in the algae with low iodine contents (< 400 μg/g dw), the fraction of iodine in the form of I^- is lower. An intermediate result was found for *H. elongata*, which was reported to have a relatively low iodine content (600 μg/g dw) but a high I^- content (90%). It is uncertain whether the correlation will have any predictive power since the variability is great, and it should be confirmed, refined, or rejected when further data are gathered.

3.1.2 | Iodine loss during processing

For the description of iodine loss during processing in edible brown macroalgae, nine studies were identified and included in the review. The loss of iodine during processing depends on the iodine species in the seaweed and its properties, including solubility and evaporation temperature, as well as the processing conditions used, such as time, temperature, solvent, solvent purity, and solvent-to-substrate ratio. It also requires that the iodine can be extracted from the matrix during the processing conditions, meaning that it is not “trapped” within the complex fiber structure of the alga. The loss of iodine from

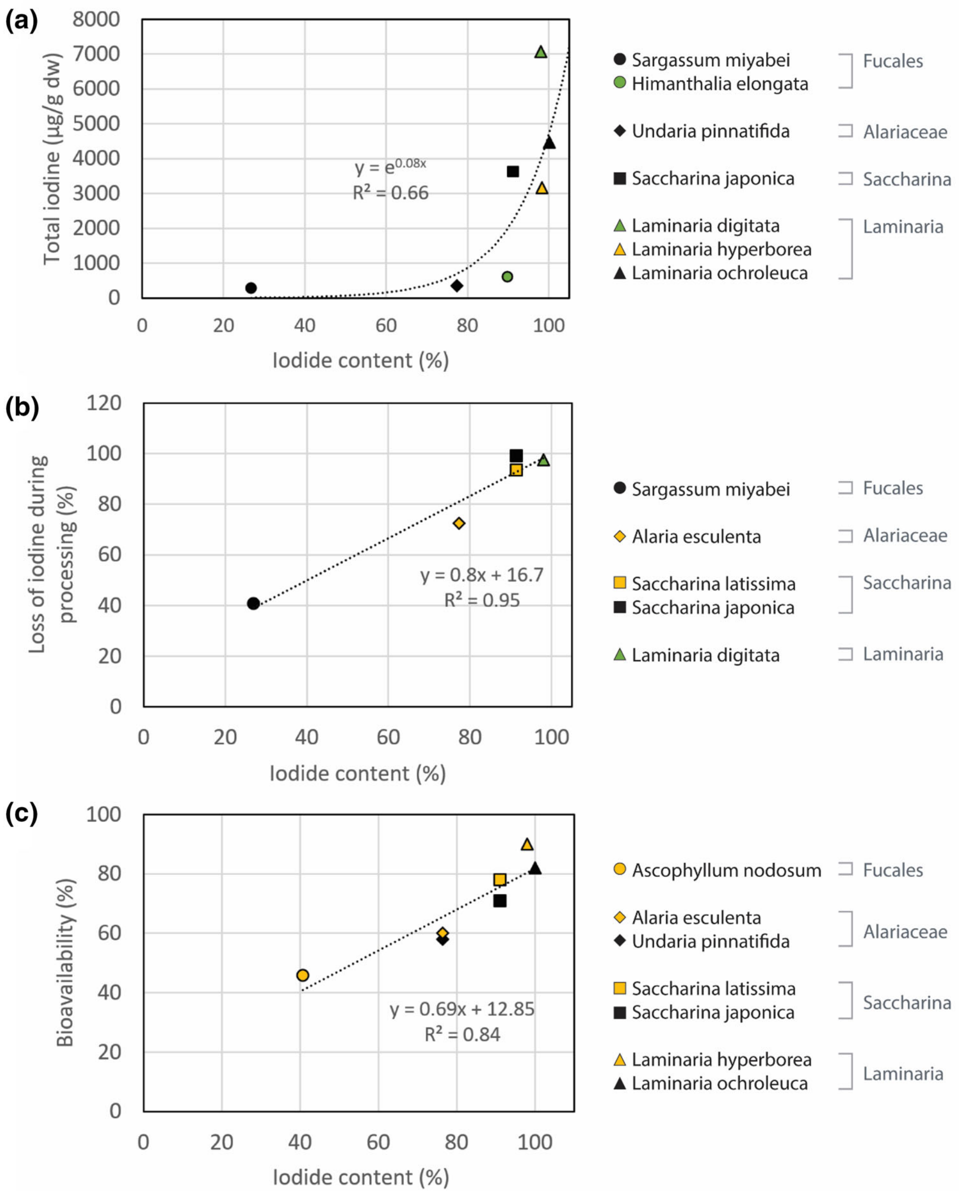

FIGURE 2 Results from correlation analyses. (a) Correlation between total iodine and iodide content (I^-; as % of total iodine) in brown alga. (b) Correlation between total iodine and I^- (as % of total iodine) in brown alga. (c) Correlation between the fraction of iodine present as I^- (average result) and the in vivo bioavailability (maximum result)

brown algae has been reported after several types of processing, including washing, blanching, boiling, soaking, drying, and fermentation (Table 3).

Iodine may be removed by processing in water even at low temperatures, including washing, soaking, and rehydration of dried algae. After washing fresh pieces of *A. esculenta* for 10 min in deionized water (1.5–2 g dw/100 ml), approximately 10% of the iodine was removed, reducing the iodine content from 670 to 603 μg/g dw, although a significant loss was not achieved (Nitschke & Stengel, 2016). Washing also reduced the content of I^- in fresh *A. nodosum* and *Fucus vesiculosis* by 34% and 44%, leaving 182 and 61 μg/g dw I^- in the algae, respectively (Martinelango et al., 2006). Soaking fresh sugar kelp in either tap water or seawater for up to 22 h did not have a significant effect on the iodine content when the water was 16 to 18°C (Stévant, Marfaing, et al., 2018). This might be attributed to the kelp still being alive and thus being able to withstand the diffusion of iodine into the surrounding water. Soaking fresh *S. latissima* in 30–32°C (≥5 min, tap water) resulted in a significant loss of iodine of around 78% to 85%, and the final iodine content was ~1000 μg/g dw (Nielsen et al., 2020; Stévant, Marfaing, et al., 2018). The rehydration of dried kelp at room temperature (30 min) reduced the iodine content by 90% to 98% in the case of *L. digitata* and 79% in the case of *S. japonica* (Ownsworth et al., 2019). *Alaria esculenta*, rehydrated for 1 h, lost 62% of its iodine, achieving an iodine content of 228 μg/g dw (Nitschke & Stengel, 2016). Longer soaking times (12 and 24 h) did not result in further iodine losses.

Processing in warm water is also frequently used to reduce the iodine content in brown algae, including blanching and boiling. Blanching treatments using brief time intervals (2–5 min) and higher temperatures (45–80°C) reduced the iodine content of fresh, whole-thallus samples of *S. latissima* by 92% to 94% to around 300 to 400 μg/g dw (Nielsen et al., 2020). Blanching dried (not rehydrated) kelp for 10 to 20 s reduced the iodine content by 52% to 82% in the case of *L. digitata*, and 10% in the case of *S. japonica* (Ownsworth et al., 2019). In a study in which frozen-thawed *S. latissima* was boiled, 38% of the iodine content was lost, yielding a final iodine content of 1620 μg/g dw (Bruhn et al., 2019). Boiling sundried *S. latissima* (containing 308 μg/g iodine initially) for 2 min yielded a loss of around 2/3 of the iodine, and around 77% was lost after 10 min (Lüning & Mortensen, 2015). Bringing soaked seaweed to a boil in the same water as that used for rehydration yielded an additional loss of iodine for *S. japonica* (−96% total), but not in the case of *L. digitata* (Ownsworth et al., 2019). The final content of iodine after rehydration and boiling was 182 μg/g dw for *S. japonica* and 179 to 333 μg/g dw for *L. digitata* (Ownsworth et al., 2019). In the case of *A. esculenta*, boiling after washing, drying, and rehydration further reduced the iodine content from 228 μg/g dw (after rehydration) to 165 μg/g dw (after boiling), thus achieving a further loss of 28% (Nitschke & Stengel, 2016).

A loss of iodine content during drying has been reported in some but not all the studies examined during this review process. Drying in the air (23°C) in an oven (60°C) and freeze-drying washed pieces of *A. esculenta* resulted in no significant loss in the iodine content (Nitschke & Stengel, 2016). In contrast, freeze-drying *S. latissima* resulted in a significantly lower quantified value of iodine (−49%), compared to drying at 25°C (Stévant, Indergård, et al., 2018). However, the authors noted that this result should be interpreted with caution since the resulting iodine content (3000 μg/g dw) was still in the range found for cultivated, fresh *S. latissima* in other studies. More recently, a 25% loss of iodine from *S. latissima* was reported after air drying using a mushroom dryer (Duinker et al., 2020).

Only one study reported a change in iodine content during fermentation. Boiling for 15 min, followed by lactic acid fermentation in the same water (tap water), reduced the iodine content of sugar kelp by 66% to a final concentration of 902 μg/g dw (Bruhn et al., 2019). The fermentation step accounted for 28% of the loss. Frying has also been reported to reduce the iodine content of *S. latissimi* by 50% on average (Duinker et al., 2020).

Correlation between loss of iodine during processing and I^- content

Iodine is readily lost during processing involving water, and there is a clear correlation between the species' I^- content and its maximum loss of iodine during processing (Figure 2b). However, more research is needed on this topic since these data were only available for a few species.

3.1.3 | Iodine bioaccessibility and bioavailability

Of the studies identified in the review process, seven studies measured in vivo bioavailability, three measured in vitro bioaccessibility, and three measured in vitro bioavailability (Figure 3). The in vivo bioavailability studies yielded results ranging from 31% to 90%. In the in vitro bioaccessibility studies, results between 48% and 82% were found. In vitro bioavailability studies reported results ranging from 2% to 28%, with higher results for dialysis (2%–28%) relative to cell cultures (2%–7%).

For the in vivo bioavailability studies, there are some trends regarding species-specific differences in iodine bioavailability from brown algae. Generally, species in the genus *Laminaria* have high bioavailability (61.5%–90%). *Saccharina* species have overlapping bioavailability with *Laminaria* species but in the lower range (57% to 71% in humans; Miyai et al., 2008; 73%–78% in rats; Duinker et al., 2020). *Alaria*, with 60% bioavailability (Teas et al., 2007), represents the Alariaceae family, in the lower end of the *Laminaria* and *Saccharina* range of bioavailability. Considering in vivo bioavailability studies performed using human intervention studies, *A. nodosum* is the species with the lowest in vivo bioavailability, with 31% to 46% (Andersen et al., 2019; Combet et al., 2014). In addition to the trends indicated above, the overlap in values between the different taxonomic genera and families should be noted. It is also clear from the data that not only species and methodology, but also other factors influence the results, particularly the iodine status of the participants (Aquaron et al., 2002; Combet et al., 2014).

Correlation between bioavailability and I^- content

A linear relationship was found between the I^- content of macroalgae and the in vivo bioavailability (Figure 2c). The in vivo bioavailability of iodine from species containing 88% to 98% I^- ranged from 57% to 90%, whereas the in vivo bioavailability of iodine from species containing less iodine was lower, ranging from 31% to 60%.

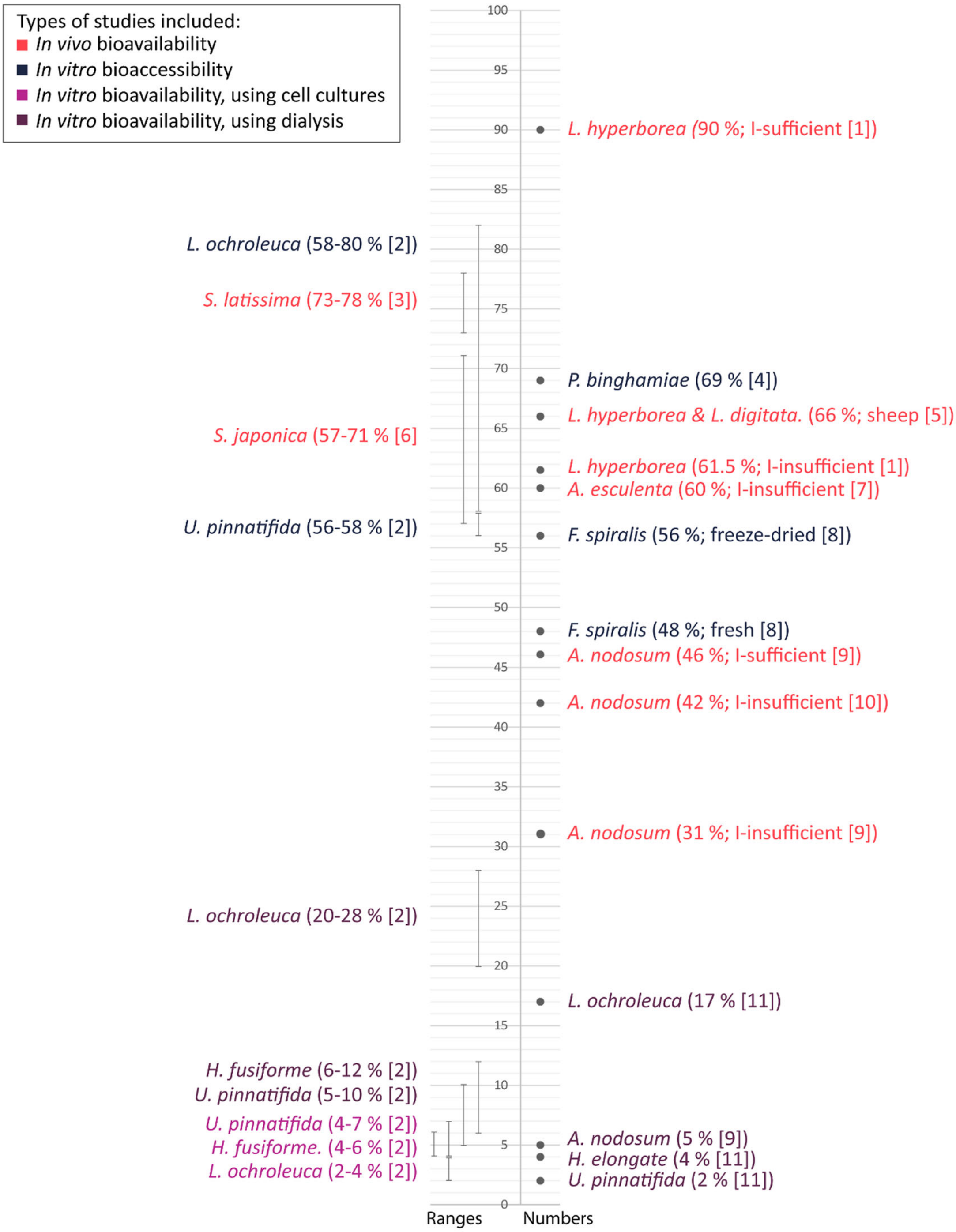

FIGURE 3 Literature review of data found for in vitro bioaccessibility, in vitro and in vivo bioavailability of iodine from brown alga. In cases where the results are presented as numbers, these are given to the right, whereas ranges are given to the left. *Source*: [1] Aquaron et al. (2002); [2] Dominguez-Gonzalez et al. (2017); [3] Duinker et al. (2020); [4] Afonso et al. (2021); [5] Lu et al. (2006); [6] Miyai et al. (2008); [7] Teas et al. (2007); [8] Francisco et al. (2018); [9] Combet et al. (2014); [10] Andersen et al. (2019); [11] Romarís-Hortas et al. (2011)

3.1.4 | Tolerable amounts of brown algae in human nutrition in terms of iodine content, considering both the iodine loss during processing and the iodine bioavailability

The tolerable amounts of brown algae, with respect to iodine, depend on the initial iodine content, the degree of processing and its resulting loss of iodine, and the specific bioavailability of each species. These data were available for *A. esculenta*, *L. digitata*, *L. japonica*, and *S. latissima* (Table 4).

For *A. esculenta*, between 0.4 and 1.1 g of kelp amounted to 150-μg iodine. For *L. digitata*, *S. japonica*, and *S. latissima*, 0.2–1.6, 0.1–1.4, and $<$ 0.1–3 g amounted to 150 μg

TABLE 4 The amount of brown alga (g dw) needed for an intake of 150 and 600 μg based on reported residual iodine content after processing and in vivo bioavailability[a]

Taxonomy	Processing method	Iodine after processing (ug/g dw)	Bioavailability of iodine (%)	Bioavailable iodine post-processing (ug/g dw)	Seaweed (g dw) equaling 150-ug iodine	Seaweed (g dw) equaling 600-ug iodine	Reference	
							Bioavailability	Processing
L. digitata	Blanched	1143	66	690	0.2	0.9	[1]	[2]
		1127	66	680	0.2	0.9	[1]	[2]
	Soaked	245	66	150	1.0	4.1	[1]	[2]
		157	66	90	1.6	6.4	[1]	[2]
	Soaked and boiled	333	66	200	0.8	3.0	[1]	[2]
		179	66	110	1.4	5.6	[1]	[2]
S. japonica	Blanched	3946	71	2400	0.1	0.3	[3]	[2]
	Soaked	909	71	550	0.3	1.1	[3]	[2]
	Soaked and boiled	182	71	110	1.4	5.5	[3]	[2]
S. latissima	Blanched	290	78	180	0.9	3.4	[4]	[5]
		320	78	190	0.8	3.1	[4]	[5]
		390	78	230	0.6	2.6	[4]	[5]
		1010	78	610	0.2	1.0	[4]	[5]
	Boiled	~90	78	54	3	11	[4]	[6]
		1620	78	970	0.2	0.6	[4]	[7]
	Boiled and fermented	900	78	540	0.3	1.1	[4]	[7]
	Dried	3000	78	1800	0.1	0.3	[4]	[8]
		4900	78	2900	0.1	0.2	[4]	[8]
		5700	78	3400	0.0	0.2	[4]	[8]
	Soaked	~1000	78	600	0.3	1.0	[4]	[9]
A. esculenta	Rehydrated	230	60	140	1.1	4.4	[10]	[11]
	Rehydrated and boiled	170	60	100	1.5	6.1	[10]	[11]
	Washed	270	60	160	0.9	3.7	[10]	[11]
	Washed and dried	670	60	400	0.4	1.5	[10]	[11]

[a]In the calculation, it was assumed that the bioavailability (%) remained the same regardless of processing. In cases where more than one in vivo bioavailability result was found, the highest bioavailability result was chosen since a lower bioavailability may be expressed in persons with insufficient iodine status.

Source: [1] Lu et al. (2006); [2] Ownsworth et al. (2019); [3] Miyai et al. (2008); [4] Duinker et al. (2020); [5] Nielsen et al. (2020); [6] Lüning and Mortensen (2015); [7] Bruhn et al. (2019); [8] Stévant, Indergård et al. (2018); [9] Stévant, Marfaing et al. (2018); [1] Teas et al. (2007); [11] Nitschke and Stengel (2016).

iodine. Generally, more processing in a liquid phase (e.g., soaking, boiling) resulted in a higher algal biomass needed to yield 150-μg iodine, according to the tendencies outlined in Section 4.2. In some cases, deviations from this general tendency occurred. This was the case during the boiling of *S. latissima*, wherein the amount of kelp equaling 150-μg iodine was 3 g, based on data from Lüning and Mortensen (2015), who used *S. latissima* with low initial iodine content and experienced a loss of around 77% iodine and 0.2 g based on data from Bruhn et al. (2019), who used *S. latissima* with average iodine content but experienced a lower iodine loss, only 38% during processing. Thus, it is difficult to extrapolate any expected results based on the species and degree of processing alone. Until more information is confirmed regarding which factors account for these differences and how much the different factors contribute to the loss of iodine, batch-specific data for the iodine content after processing should be used for calculations of tolerable amounts.

3.2 | Discussion

3.2.1 | Effect of choice of method for determination of iodine bioavailability

In vitro versus in vivo methodology

The bioavailability and bioaccessibility of iodine from brown algae ranged from 2% to 90%, depending on methodology and species (Figure 3). In vitro bioavailability studies using dialysis ranged from 2% to 28% (Combet et al., 2014; Domínguez-González et al., 2017; Romarís-Hortas et al., 2011) and using cell cultures from 2% to 7% (Domínguez-González et al., 2017). In contrast, in vivo bioavailability studies have yielded results ranging from 31% to 90% (Andersen et al., 2019; Aquaron et al., 2002; Combet et al., 2014; Duinker et al., 2020; Miyai et al., 2008; Teas et al., 2007). Thus, there is no overlap between in vitro bioavailability and in vivo bioavailability results.

For example, the in vivo bioavailability of iodine from *A. nodosum* was between 31% and 46% in human intervention studies (Andersen et al., 2019; Combet et al., 2014). An in vitro bioavailability study of iodine from the same species, assessed using dialysis, found a much lower bioavailability of only 5% after simulated digestion in the small intestines (Combet et al., 2014). Other direct comparisons between in vitro and in vivo bioavailability of the same species cannot be made, no further overlap was found in the literature.

In summary, in vitro bioavailability results are consistently lower than in vivo bioavailability results from studies using the same or genetically similar species, and in vivo bioavailability results yield 5 to 30 times higher results relative to in vitro bioavailability results. In contrast, in vitro bioaccessibility results are in the same range as in vivo bioavailability results from studies of genetically similar species. Such findings strongly indicate that in vitro bioaccessibility studies could offer a much better representation of the in vivo bioavailability than the in vitro bioavailability results. For the time being, in vitro bioavailability results should therefore not be trusted to truly represent the human bioavailability of iodine from brown algae, unless validated using human intervention studies.

In vivo methods of sample collection

In all the studies that investigated seaweed iodine bioavailability in humans, only the iodine that entered the body and the iodine excreted in the urine within a certain time (total urine) or after a certain time (Urinary Iodine Concentration (UIC)/g creatinine) were measured. Since humans can store iodine for up to 3 months, it is expected that iodine-insufficient persons will add more of the bioavailable iodine to their depleting iodine storage, and therefore excrete less iodine than sufficient persons, even though their uptake from the food during digestion may be identical. Thus, the "bioavailability" measured by these studies may be lower than the fraction that was absorbed into the body.

Another issue that is worth noting related to in vivo iodine bioavailability studies is sampling. Combet et al. (2014) found that iodine ingested from *A. nodosum* was more slowly excreted than iodine from pure sodium iodide (KI), with a peak in excretion 2 to 5 h after seaweed consumption and 0 to 2 h after KI consumption. This indicates differences in digestion and ease of accessibility of iodine from the two matrices. In practice, this implies that the timing of sample collection is highly important unless all urine for the following 1 to 3 days is collected. In the studies found, only two studies used continuous sampling after seaweed ingestion. Combet et al. (2014) collected 24-h urine samples following seaweed ingestion, and Teas et al. (2007) collected 48-h urine samples following seaweed ingestion. In the study by Miyai et al. (2008), a portion of the urine was collected after each urination for the duration of the study period. In the studies by Aquaron et al. (2002) and Andersen et al. (2019), six spot urine samples were collected following seaweed ingestion. The first sample was collected after 4 h in the study by Aquaron et al. (2002) and after 6 h in the study by Andersen et al. (2019). Thus, the differences in the sampling methods used in the mentioned studies may have affected the results (Table S2).

3.2.2 | Effect of iodine speciation on iodine bioavailability

It has been suggested that the chemical speciation of iodine is a co-factor in determining the bioavailability of iodine from food (Hou, 2009). In a study by Domínguez-González et al. (2017), the apparent permeability of various iodine species across an intestinal cell membrane was measured. They found that I^- passed more readily across the membrane than the other iodine species, in the following order: I^- > MIT > IO_3^- > DIT. This finding is consistent with the in vivo bioavailability results of this review (Figure 2c). The in vivo bioavailability of iodine from species containing 88% to 98% I^- was 57% to 90%, and the in vivo bioavailability of iodine from species containing less iodine was lower (31% to 60%). Our correlation analysis thus suggests that I^- content may be used as an indicator of the bioavailability of iodine from brown algae.

A human intervention study ($n = 1$) to determine the bioavailability of iodine from pure iodine compounds found higher bioavailability from inorganic iodine (potassium iodide, KI, 96%) than organic iodine (MIT, 80%); however, other results from the same study are contradictory (Aquaron et al., 2002). The iodine bioavailability from *L. hyperborea*, containing most of its iodine in the form of I^- (98%; Lu et al., 2006), and *Gracilaria verrucosa* (red alga), containing mostly organically bound iodine (approx. 80% according to the authors), was assessed (Aquaron et al., 2002). The bioavailability of iodine from *G. verrucosa* was 101%, compared to 90% from *L. hyperborea*, in iodine-sufficient persons. For iodine-insufficient persons, it was 85%, compared to 61.5% (Aquaron et al., 2002). The results indicate that other factors aside from iodine speciation and iodine sufficiency also influence the bioavailability of iodine from seaweeds. It has been suggested that the iodine of brown algae is "trapped" in the complex fiber network of brown algae, which contains primarily alginate, and therefore less available than iodine from red algae, which contains different primary fibers (agar and carrageenan). However, the bioavailability is still very high for *L. hyperborea* (> 61.5%). To assess the effect of iodine speciation alone, a comparison of the iodine bioavailability from brown algal species with similar alginate structure and content and different iodine speciation could be useful. For the time being, such data could not be found.

3.2.3 | Effects of processing on iodine bioavailability

Brown algae species with higher proportions of iodine in the form of I^-, lost iodine more readily during processing than species with lower proportions of I^- (Figure 2b). Based on this data, it would appear that I^- is removed more readily via processing than other species of iodine. This suggests the fraction of remaining I^- after processing would be lower than the fraction prior to processing. If this is indeed the case, this could result in reduced bioavailability of the residual fraction of iodine after processing, compared to its raw state, if the iodine bioavailability from I^- is higher than from other chemical forms, which was suggested in Figure 2c. Conversely, changes in the structure of the algae, such as the loosening of the fiber matrix, could increase the bioavailability of iodine from processed brown algae, compared to raw brown algae. Currently, there is minimal data available to support or refute these speculations. No in vivo bioavailability studies have thus far assessed the effect of processing on the bioavailability of the remaining iodine fraction, and further investigations into how processing affects the bioavailability of iodine from brown algae are warranted.

3.2.4 | Safe consumption of brown algae

The bioavailability of iodine from brown algae is generally high, with in vivo bioavailability ranging from 31% to 90%. Around 90% of the absorbed iodine is generally assumed to be excreted in urine after consumption in iodine-sufficient individuals (WHO, 2007). Since the bioavailability of iodine from seaweed can reach 90%, it might be debatable whether the bioavailability should be considered at all when calculating the amount of brown algae that can safely be consumed. In the present work, bioavailability was nonetheless considered in the calculation to indicate a maximum amount of brown algae, which can safely be consumed.

The amount of brown algal biomass equaling a specific amount of iodine is highly variable. The maximum recommended intake of iodine for adults (600 μg) can be calculated by ingesting between 0.2—11 g processed, dry brown algae (Table 4). Although there are some species-specific and processing-specific tendencies, it is not possible to predict the result based on the species and type of processing. Currently, the safe consumption of brown algae is therefore heavily reliant on specific measurements of algae from each location and each set of processing conditions, as well as the homogeneity of the raw material. Care should be taken to provide representative samples for iodine analysis to avoid significant variability between the iodine content provided on the food packaging and the actual iodine content, an issue relevant to many food products containing seaweeds on the market today (Aakre et al., 2021).

Seaweed is a new dietary component that remains undiscovered by many Western consumers, but out of those who include seaweed as a component of their diet, many may consume substantially higher doses of iodine than the recommended maximum intake. A recent observational study of iodine intake among seaweed consumers in Norway (Aakre et al., 2020) assessed iodine uptake after the consumption of a single seaweed meal, which the participants prepared themselves at home according to their regular practice. The study found that the median iodine intake in the group (n = 44) was 2430 μg/day, which exceeded the tolerable upper intake level of 600 μg/day set by SCF (2002) and the lowest observable adverse effect level for iodine intake (1800 μg/day; Russell et al., 2001; Scientific Committee on Food, 2002). Similar findings were observed previously in a small group of vegans and vegetarians consuming seaweeds as part of their habitual diet (n = 35; Groufh-Jacobsen et al., 2020). In the latter study, the intake ranged from 521 to 1467 μg/day, with a mean value of 866 μg/day. Thus, in these population groups, there is a risk of developing thyroid disorders as a consequence of excessive iodine intake. The iodine content in seaweed food products on the market is often high, and values up to 12,000 μg/g were found in a study assessing the iodine content of commercially available products (Aakre et al., 2021). Thus, it is not surprising that consumers of seaweed can have higher intakes than the recommended maximum intake.

Safe consumption of brown algae requires both that the iodine content is within the tolerable amounts per serving size per day and the availability of information on iodine content on the food packaging. Many seaweed products contain excessive iodine (Aakre et al., 2021; Bouga & Combet, 2015), and the majority of consumers are unaware of the importance of avoiding excessive iodine in their diet. The market availability of many seaweed products thus introduces a risk of excessive iodine consumption. This may further impose health risks on a population level, especially for vulnerable groups, such as pregnant women. In most European countries, including Norway, it is not mandatory to declare the iodine content of seaweed products. The iodine content is rarely indicated on the packaging of seaweed products available in and from Norway today, and when it is provided, it often deviates from the measured values of iodine content (Aakre et al., 2021). Insufficient labelling or declarations have also been observed by others (Bouga & Combet, 2015). This is unfortunate since the failure to provide accurate data renders it impossible for consumers to make informed decisions regarding their iodine intake. This should therefore be a focus area, both industrially and for food retailers.

The iodine content of macroalgae or foods containing macroalgae is currently not regulated in the European Union (EU) or Norway. However, regulations are being discussed both on national and international levels, and changes might be implemented during the next few years. As of now (September 2021), regulating the iodine content in foods containing brown algae is up to the industry producing foods containing seaweeds; this requires a great awareness of these issues and a commitment to providing healthy foods for the consumers. However, in the case of a lack of specific regulations, this may signify to food producers that iodine consumption is safe and does not need to be specifically controlled, particularly if this is combined with insufficient communication between food authorities and food producers regarding these issues. In our opinion, this could have unfortunate consequences, as it may encourage the unregulated introduction of foods containing high iodine contents in the market.

4 | CONCLUSION AND FUTURE PERSPECTIVES

Brown algae are strong iodine accumulators and contain higher amounts of iodine than any other known food group. Iodine in brown algae is mostly in the form of I^-, but organically bound iodine and $IO_3^-$are also present in some species. The bioavailability of iodine from brown algae is high and varies between 31% and 90% when measured using in vivo bioavailability studies. Measurements using in vitro bioaccessibility techniques have yielded similar results relative to the in vivo bioavailability studies for similar species; they, therefore, appear to provide reliable results. In contrast, in vitro bioavailability measurements consistently yield much lower results than in vivo bioavailability measurements; therefore, in vitro bioavailability methods as they are today should not be trusted to provide accurate results regarding the bioavailability of iodine from brown algae. Although processing strategies may reduce the iodine content of brown algae significantly, the iodine content is still high after processing. The tolerable amount of brown algae per day is thus also quite low, with 0.2–11 g dw providing 600-μg iodine. Furthermore, the loss of iodine content during processing is currently not predictable, and in many cases, low amounts of brown algae are sufficient to exceed the recommended intakes and tolerable upper intake level of iodine.

4.1 | Future perspectives

We believe that the above-mentioned findings demonstrate that many brown algal species are currently unsuitable for mass consumption. More research on developing cultivation strategies or processing schemes aimed at reducing the iodine content is, therefore, necessary to produce safe and predictable products for consumers. In the meantime, brown algae should be consumed with caution and in small quantities to avoid excessive intake of iodine. Further regulations of foods containing seaweeds with regards to allowable iodine contents per serving size should be considered both on an EU level and on a national level.

Other potentially toxic elements (cadmium, inorganic arsenic, mercury, and lead) also need to be considered for the determination of the safe amounts of brown macroalgae, which can be consumed each day for each species of brown algae in future studies. Furthermore, there are several species within the group of red and green macroalgae, which are edible and may be considered for human consumption.

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AUTHOR CONTRIBUTION

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest to declare.

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REFERENCES

Aakre, I., Solli, D. D., Markhus, M. W., Mæhre, H. K., Dahl, L., Henjum, S., Alexander, J., Korneliussen, P. -A., Madsen, L., & Kjellevold, M. (2021). Commercially available kelp and seaweed products–valuable iodine source or risk of excess intake? *Food & Nutrition Research*, *65*. https://doi.org/10.29219/fnr.v65.7584

Aakre, I., Strand, T. A., Bjøro, T., Norheim, I., Barikmo, I., Ares, S., Alcorta, M. D., & Henjum, S. (2016). Thyroid function among breastfed children with chronically excessive iodine intakes. *Nutrients*, *8*(7), 398. https://doi.org/10.3390/nu8070398

Aakre, I., Tveito Evensen, L., Kjellevold, M., Dahl, L., Henjum, S., Alexander, J., Madsen, L., & Markhus, M. W. (2020). Iodine status and thyroid function in a group of seaweed consumers in Norway. *Nutrients*, *12*(11), 3483. https://doi.org/10.3390/nu12113483

Abel, M. H., Brandlistuen, R. E., Caspersen, I. H., Aase, H., Torheim, L. E., Meltzer, H. M., & Brantsaeter, A. L. (2019). Language delay and poorer school performance in children of mothers with inadequate iodine intake in pregnancy: Results from follow-up at 8 years in the Norwegian Mother and Child Cohort Study. *European Journal of Nutrition*, *58*(8), 3047–3058. https://doi.org/10.1007/s00394-018-1850-7

Afonso, C., Matos, J., Campos, A. M., Gomes, R., Delgado, I., Coelho, I., Castanheira, I., Bandarra, N. M., & Cardoso, C. (2021). Elemental composition and bioaccessibility of three insufficiently studied Azorean macroalgae. *International Journal of Food Science and Technology*, *56*(1), 330–341. https://doi.org/10.1111/ijfs.14647

Andersen, S., Noahsen, P., Rex, K. F., Florian-Sørensen, H. C., & Mulvad, G. (2019). Iodine in edible seaweed, its absorption, dietary use, and relation to iodine nutrition in Arctic people. *Journal of Medicinal Food*, *22*(4), 421–426. https://doi.org/10.1089/jmf.2018.0187

Ar Gall, E., Küpper, F. C., & Kloareg, B. (2004). A survey of iodine content in *Laminaria digitata*. *Botanica Marina*, *47*(1), 30–37. https://doi.org/10.1515/BOT.2004.004

Aquaron, R., Delange, F., Marchal, P., Lognoné, V., & Ninane, L. (2002). Bioavailability of seaweed iodine in human beings. *Cellular and Molecular Biology (Noisy-le-Grand, France)*, *48*(5), 563–569.

Bak, U. G. (2019). *Seaweed cultivation in the Faroe Islands: An investigation of the biochemical composition of selected macroalgal species, optimised seeding technics, and open-ocean cultivation methods from a commercial perspective* (Doctoral dissertation), Kongens Lyngby, Denmark. Technical University of Denmark.

Bath, S. C., Steer, C. D., Golding, J., Emmett, P., & Rayman, M. P. (2013). Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: Results from the Avon Longitudinal Study of Parents and Children (ALSPAC). *The Lancet*, *382*(9889), 331–337. https://doi.org/10.1016/S0140-6736(13)60436-5

Biancarosa, I., Belghit, I., Bruckner, C. G., Liland, N. S., Waagbø, R., Amlund, H., Heesch, S., & Lock, E. J. (2018). Chemical characterization of 21 species of marine macroalgae common in Norwegian waters: Benefits of and limitations to their potential use in food and feed. *Journal of the Science of Food and Agriculture*, *98*(5), 2035–2042. https://doi.org/10.1002/jsfa.8798

Bouga, M., & Combet, E. (2015). Emergence of seaweed and seaweed-containing foods in the UK: Focus on labeling, iodine content, toxicity and nutrition. *Foods*, *4*(2), 240–253. https://doi.org/10.3390/foods4020240

Brent, G. A. (2012). Mechanisms of thyroid hormone action. *The Journal of Clinical Investigation*, *122*(9), 3035–3043. https://doi.org/10.1172/JCI60047

Brown, E. M., Allsopp, P. J., Magee, P. J., Gill, C. I., Nitecki, S., Strain, C. R., & McSorley, E. M. (2014). Seaweed and human health. *Nutrition Reviews*, *72*(3), 205–216. https://doi.org/10.1111/nure.12091

Bruhn, A., Brynning, G., Johansen, A., Lindegaard, M. S., Sveigaard, H. H., Aarup, B., Fonager, L., Andersen, L. L., Rasmussen, M. B., & Larsen, M. M. (2019). Fermentation of sugar kelp (*Saccharina latissima*)—effects on sensory properties, and content of minerals and metals. *Journal of Applied Phycology*, *31*(5), 3175–3187. https://doi.org/10.1007/s10811-019-01827-4

Bürgi, H. (2010). Iodine excess. *Best Practice & Research Clinical Endocrinology & Metabolism*, *24*(1), 107–115. https://doi.org/10.1016/j.beem.2009.08.010

Cao, J., Peng, L. -Q., Xu, J. -J., Du, L. -J., & Zhang, Q. -D. (2016). Simultaneous microextraction of inorganic iodine and iodinated amino acids by miniaturized matrix solid-phase dispersion with molecular sieves and ionic liquids. *Journal of Chromatography A*, *1477*, 1–10. https://doi.org/10.1016/j.chroma.2016.11.053

Chen, R., Li, Q., Cui, W., Wang, X., Gao, Q., Zhong, C., Sun, G., Chen, X., Xiong, G., & Yang, X. (2018). Maternal iodine insufficiency and excess are associated with adverse effects on fetal growth: A prospective cohort study in Wuhan, China. *The Journal of Nutrition*, *148*(11), 1814–1820. https://doi.org/10.1093/jn/nxy182

Chung, H. R., Shin, C. H., Yang, S. W., Choi, C. W., & Kim, B. I. (2009). Subclinical hypothyroidism in Korean preterm infants associated with high levels of iodine in breast milk. *The Journal of Clinical Endocrinology & Metabolism*, *94*(11), 4444–4447. https://doi.org/10.1210/jc.2009-0632

Combet, E., Ma, Z. F., Cousins, F., Thompson, B., & Lean, M. E. (2014). Low-level seaweed supplementation improves iodine status in iodine-insufficient women. *British Journal of Nutrition*, *112*(5), 753–761. https://doi.org/10.1017/S0007114514001573

Commission, E. (2018). Commission recommendation (EU) 2018/464 of 19 March 2018 on the monitoring of metals and iodine in seaweed, halophytes and products based on seaweed. Official Journal of the European Union *78*, 16–18. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018H0464&from=DE

Davis, T. A., Volesky, B., & Mucci, A. (2003). A review of the biochemistry of heavy metal biosorption by brown algae. *Water Research*, *37*(18), 4311–4330. https://doi.org/10.1016/S0043-1354(03)00293-8

Dawczynski, C., Schaefer, U., Leiterer, M., & Jahreis, G. (2007). Nutritional and toxicological importance of macro, trace, and ultra-trace elements in algae food products. *Journal of Agricultural and Food Chemistry*, *55*(25), 10470–10475. https://doi.org/10.1021/jf0721500

Domínguez-González, M. R., Chiocchetti, G. M., Herbello-Hermelo, P., Vélez, D., Devesa, V., & Bermejo-Barrera, P. (2017). Evaluation of iodine bioavailability in seaweed using in vitro methods. *Journal of Agricultural and Food Chemistry*, *65*(38), 8435–8442. https://doi.org/10.1021/acs.jafc.7b02151

Duinker, A., Kleppe, M., Fjære, E., Biancarosa, I., Heldal, H. E., Dahl, L., & Lunestad, B. T. (2020). *Knowledge update on macroalgae food and feed safety—based on data generated in the period 2014–2019 by the Institute of Marine Research, Norway*. National Institute of Nutrition and Seafood Research (NIFES).

Eastman, C. J. (2017). Mild to moderate iodine deficiency. In E. N. Pearce (Ed.), *Iodine deficiency disorders and their elimination*. 59–74. Springer.

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). (2014). Scientific opinion on dietary reference values for iodine. *EFSA Journal*, *12*(5), 3660.

Emder, P. J., & Jack, M. M. (2011). Iodine-induced neonatal hypothyroidism secondary to maternal seaweed consumption: A common practice in some Asian cultures to promote breast milk supply. *Journal of Paediatrics and Child Health*, *47*(10), 750–752. https://doi.org/10.1111/j.1440-1754.2010.01972.

Francisco, J., Cardoso, C., Bandarra, N., Brito, P., Horta, A., Pedrosa, R., Gil, M. M., Delgado, I. M., Castanheira, I., & Afonso, C. (2018). Bioaccessibility of target essential elements and contaminants from F*ucus spiralis*. *Journal of Food Composition and Analysis*, *74*, 10–17. https://doi.org/10.1016/j.jfca.2018.08.003

Granby, K., Amlund, H., Valente, L. M. P., Dias, J., Adoff, G., Sousa, V., Marques, A., Sloth, J. J., & Larsen, B. K. (2020). Growth performance, bioavailability of toxic and essential elements and nutrients, and biofortification of iodine of rainbow trout (*Onchorynchus mykiss*) fed blends with sugar kelp (*Saccharina latissima*). *Food and Chemical Toxicology*, *141*, 111387. https://doi.org/10.1016/j.fct.2020.111387

Scientific Committee on Food (2002). *Opinion of the scientific committee on food on the tolerable upper intake level of iodine*. European Commission.

Ar Gall, E. A., Küpper, F. C., & Kloareg, B. (2004). A survey of iodine content in *Laminaria digitata*. *Botanica Marina*, *47*(1), 30–37. https://doi.org/10.1515/BOT.2004.004

Gamallo-Lorenzo, D., Barciela-Alonso, M. D. C., Moreda-Piñeiro, A., Bermejo-Barrera, A., & Bermejo-Barrera, P. (2005). Microwave-assisted alkaline digestion combined with microwave-assisted distillation for the determination of iodide and total iodine in edible seaweed by catalytic spectrophotometry. *Analytica Chimica Acta*, *542*(2), 287–295. https://doi.org/10.1016/j.aca.2005.04.002

Groufh-Jacobsen, S., Hess, S. Y., Aakre, I., Folven Gjengedal, E. L., Blandhoel Pettersen, K., & Henjum, S. (2020). Vegans, vegetarians and pescatarians are at risk of iodine deficiency in Norway. *Nutrients*, *12*(11), 3555. https://doi.org/10.3390/nu12113555

Guiry, M. D., & Guiry, G. M. (2021). *AlgaeBase. World-wide electronic publication*. National University of Ireland. http://www.algaebase.org.

Holdt, S. L., & Kraan, S. (2011). Bioactive compounds in seaweed: Functional food applications and legislation. *Journal of Applied Phycology*, *23*(3), 543–597. https://doi.org/10.1007/s10811-010-9632-5

Hou, X. (2009). Iodine speciation in foodstuffs, tissues, and environmental samples: Iodine species and analytical method. In V. R. Preedy, G. N. Burrow, & R. R. Watson (Eds.), *Comprehensive handbook of iodine: Nutritional, biochemical, pathological and therapeutic aspects*. (pp. 139–150). Academic Press.

Hou, X., Chai, C., Qian, Q., Yan, X., & Fan, X. (1997). Determination of chemical species of iodine in some seaweeds (I). *Science of the Total Environment*, *204*(3), 215–221. https://doi.org/10.1016/S0048-9697(97)00182-4

Hou, X., Yan, X., & Chai, C. (2000). Chemical species of iodine in some seaweeds II. Iodine-bound biological macromolecules. *Journal of Radioanalytical and Nuclear Chemistry*, *245*(3), 461–467. https://doi.org/10.1023/a:1006728420096

Hynes, K. L., Otahal, P., Hay, I., & Burgess, J. R. (2013). Mild iodine deficiency during pregnancy is associated with reduced educational outcomes in the offspring: 9-year follow-up of the gestational iodine cohort. *The Journal of Clinical Endocrinology & Metabolism*, *98*(5), 1954–1962. https://doi.org/10.1210/jc.2012-4249

Katagiri, R., Yuan, X., Kobayashi, S., & Sasaki, S. (2017). Effect of excess iodine intake on thyroid diseases in different populations: A systematic review and meta-analyses including observational studies. *Plos One*, *12*(3), e0173722. https://doi.org/10.1371/journal.pone.0173722

Konno, N., Makita, H., Yuri, K., Iizuka, N., & Kawasaki, K. (1994). Association between dietary iodine intake and prevalence of subclinical hypothyroidism in the coastal regions of Japan. *The Journal of Clinical Endocrinology & Metabolism*, *78*(2), 393–397. https://doi.org/10.1210/jcem.78.2.8106628

Kreissig, K. J., Hansen, L. T., Jensen, P. E., Wegeberg, S., Geertz-Hansen, O., & Sloth, J. J. (2021). Characterisation and chemometric evaluation of 17 elements in ten seaweed species from Greenland. *Plos One*, *16*(2), e0243672. https://doi.org/10.1371/journal.pone.0243672

Küpper, F. C., Carpenter, L. J., Leblanc, C., Toyama, C., Uchida, Y., Maskrey, B. H., Robinson, J., Verhaeghe, E. F., Malin, G., & Luther, G. W. III. (2013). In vivo speciation studies and antioxidant properties of bromine in Laminaria digitata reinforce the significance of iodine accumulation for kelps. *Journal of Experimental Botany*, *64*(10), 2653–2664. https://doi.org/10.1093/jxb/ert110

Küpper, F. C., Carpenter, L. J., McFiggans, G. B., Palmer, C. J., Waite, T. J., Boneberg, E. -M., Woitsch, S., Weiller, M., Abela, R., & Grolimund, D. (2008). Iodide accumulation provides kelp with an inorganic antioxidant impacting atmospheric chemistry. *Proceedings of the National Academy of Sciences*, *105*(19), 6954–6958. https://doi.org/10.1073/pnas.0709959105

Küpper, F. C., Feiters, M. C., Olofsson, B., Kaiho, T., Yanagida, S., Zimmermann, M. B., Carpenter, L. J., Luther, G. W., Lu, Z. III, Jonsson, M., & Kloo, L. (2011), Commemorating two centuries of iodine research: An interdisciplinary overview of current research. *Angewandte Chemie International Edition*, *50*, 11598–11620.

Küpper, F. C., Schweigert, N., ArGall, E., Legendre, J. M., Vilter, H., & Kloareg, B. (1998). Iodine uptake in Laminariales involves extracellular, haloperoxidase-mediated oxidation of iodide. *Planta*, *207*, 163–171. https://doi.org/10.1007/s004250050469

Laurberg, P., Pedersen, I., Carlé, A., Andersen, S., Knudsen, N., Ovesen, L., & Rasmussen, L. B. (2009). The U-shaped curve of iodine intake and thyroid disorders. In V. Preedy, G. Burrow, & R. Watson (Eds.), *Comprehensive handbook on iodine: Nutritional, endocrine and pathological aspects* (pp. 449–455). Elsevier Inc.

Leblanc, C., Colin, C., Cosse, A., Delage, L., La Barre, S., Morin, P., Fiévet, B., Voiseux, C., Ambroise, Y., & Verhaeghe, E. (2006). Iodine transfers in the coastal marine environment: The key role of brown algae and of their vanadium-dependent haloperoxidases. *Biochimie*, *88*(11), 1773–1785. https://doi.org/10.1016/j.biochi.2006.09.001

Leung, A. (2017). The effects of iodine excess. In E. N. Pearce (Ed.), *Iodine deficiency disorders and their elimination*. (pp. 75–89). Springer.

Liu, H. -L., Lam, L. T., Zeng, Q., Han, S. -Q., Fu, G., & Hou, C. -C. (2009). Effects of drinking water with high iodine concentration on the intelligence of children in Tianjin. *China. Journal of Public Health*, *31*(1), 32–38. https://doi.org/10.1093/pubmed/fdn097

Lu, Y., Suliman, S., Hansen, H. R., & Feldmann, J. (2006). Iodine excretion and accumulation in seaweed-eating sheep from Orkney. *Scotland. Environmental Chemistry*, *3*(5), 338–344. https://doi.org/10.1071/EN06041

Lüning, K., & Mortensen, L. (2015). European aquaculture of sugar kelp (*Saccharina latissima*) for food industries: Iodine content and epiphytic animals as major problems. *Botanica Marina*, *58*(6), 449–455. https://doi.org/10.1515/bot-2015-0036

MacArtain, P., Gill, C. I., Brooks, M., Campbell, R., & Rowland, I. R. (2007). Nutritional value of edible seaweeds. *Nutrition Reviews*, *65*(12), 535–543. https://doi.org/10.1111/j.1753-4887.2007.tb00278.x

Markhus, M. W., Dahl, L., Moe, V., Abel, M. H., Brantsæter, A. L., Øyen, J., Meltzer, H. M., Stormark, K. M., Graff, I. E., & Smith, L. (2018). Maternal iodine status is associated with offspring language skills in infancy and toddlerhood. *Nutrients*, *10*(9), 1270. https://doi.org/10.3390/nu10091270

Martinelango, P. K., Tian, K., & Dasgupta, P. K. (2006). Perchlorate in seawater: Bioconcentration of iodide and perchlorate by various seaweed species. *Analytica Chimica Acta*, *567*(1), 100–107. https://doi.org/10.1016/j.aca.2006.02.015Get

Miyai, K., Tokushige, T., Kondo, M., & Group, I. R. (2008). Suppression of thyroid function during ingestion of seaweed "Kombu" (*Laminaria japonoca*) in normal Japanese adults. *Endocrine Journal*, *55*(6), 1103–1108. https://doi.org/10.1507/endocrj.K08E-125

Mæhre, H. K., Malde, M. K., Eilertsen, K. E., & Elvevoll, E. O. (2014). Characterization of protein, lipid and mineral contents in common Norwegian seaweeds and evaluation of their potential as food and feed. *Journal of the Science of Food and Agriculture*, *94*(15), 3281–3290. https://doi.org/10.1002/jsfa.6681

Nielsen, C. W., Holdt, S. L., Sloth, J. J., Marinho, G. S., Sæther, M., Funderud, J., & Rustad, T. (2020). Reducing the high iodine content of *Saccharina latissima* and improving the profile of other valuable compounds by water blanching. *Foods*, *9*(5), 569. https://doi.org/10.3390/foods9050569

Nielsen, C. W., Rustad, T., & Holdt, S. L. (2021). Vitamin C from seaweed: A review assessing seaweed as contributor to daily intake. *Foods*, *10*(1), 198. https://doi.org/10.3390/foods10010198

Nitschke, U., & Stengel, D. B. (2015). A new HPLC method for the detection of iodine applied to natural samples of edible seaweeds and commercial seaweed food products. *Food Chemistry*, *172*, 326–334. https://doi.org/10.1016/j.foodchem.2014.09.030

Nitschke, U., & Stengel, D. B. (2016). Quantification of iodine loss in edible Irish seaweeds during processing. *Journal of Applied Phycology*, *28*(6), 3527–3533. https://doi.org/10.1007/s10811-016-0868-6

Nova, P., Martins, A. P., Teixeira, C., Abreu, H., Silva, J. G., Silva, A. M., Freitas, A. C., & Gomes, A. M. (2020). Foods with microalgae and seaweeds fostering consumers health: A review on scientific and market innovations. *Journal of Applied Phycology*, *32*, 1789–1802. https://doi.org/10.1007/s10811-020-02129-w

Ownsworth, E., Selby, D., Ottley, C. J., Unsworth, E., Raab, A., Feldmann, J., Sproson, A. D., Kuroda, J., Faidutti, C., & Bücker, P. (2019). Tracing the natural and anthropogenic influence on the trace elemental chemistry of estuarine macroalgae and the implications for human consumption. *Science of the Total Environment*, *685*, 259–272. https://doi.org/10.1016/j.scitotenv.2019.05.263

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, *372*, n71. https://doi.org/10.1136/bmj.n71

Phaneuf, D., Côté, I., Dumas, P., Ferron, L. A., & LeBlanc, A. (1999). Evaluation of the contamination of marine algae (seaweed) from the St. Lawrence River and likely to be consumed by humans. *Environmental Research*, *80*(2), S175–S182. https://doi.org/10.1006/enrs.1998.3915

Ren, S., & Zhong, Z. (2014). Meta-analysis on the relationship between Chinese children's intelligence and excessive iodine [Chinese]. *Wei sheng yan jiu [English: Journal of Hygiene Research]*, *43*(1), 133–138.

Roleda, M. Y., Skjermo, J., Marfaing, H., Jónsdóttir, R., Rebours, C., Gietl, A., Stengel, D. B., & Nitschke, U. (2018). Iodine content in bulk biomass of wild-harvested and cultivated edible seaweeds: Inherent variations determine species-specific daily allowable consumption. *Food Chemistry*, *254*, 333–339. https://doi.org/10.1016/j.foodchem.2018.02.024

Romarís-Hortas, V., Bermejo-Barrera, P., & Moreda-Piñeiro, A. (2012). Development of anion-exchange/reversed-phase high performance liquid chromatography–inductively coupled plasma-mass spectrometry methods for the speciation of bio-available iodine and bromine from edible seaweed. *Journal of Chromatography A*, *1236*, 164–176. https://doi.org/10.1016/j.chroma.2012.03.019

Romarís-Hortas, V., Bermejo-Barrera, P., & Moreda-Piñeiro, A. (2013). Ultrasound-assisted enzymatic hydrolysis for iodinated amino acid extraction from edible seaweed before reversed-phase high performance liquid chromatography–inductively coupled plasma-mass spectrometry. *Journal of Chromatography A*, *1309*, 33–40. https://doi.org/10.1016/j.chroma.2013.08.022

Romarís-Hortas, V., Bermejo-Barrera, P., Moreda-Piñeiro, J., & Moreda-Piñeiro, A. (2012). Speciation of the bio-available iodine and bromine forms in edible seaweed by high performance liquid chromatography hyphenated with inductively coupled plasma-mass spectrometry. *Analytica Chimica Acta*, *745*, 24–32. https://doi.org/10.1016/j.aca.2012.07.035

Romarís-Hortas, V., García-Sartal, C., del Carmen Barciela-Alonso, M., Domínguez-González, R., Moreda-Piñeiro, A., & Bermejo-Barrera, P. (2011). Bioavailability study using an in-vitro method of iodine and bromine in edible seaweed. *Food Chemistry*, *124*(4), 1747–1752. https://doi.org/10.1016/j.foodchem.2010.07.117

Russell, R., Beard, J. L., Cousins, R. J., Dunn, J. T., Ferland, G., Hambidge, K., Lynch, S., Penland, J., Ross, A. & Stoecker, B. (2001). Dietary reference intakes for vitamin A, vitamin k, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium and zinc: A report of the Panel on Micronutrients, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. National Academies Press. http://www.peirsoncenter.com/uploads/6/0/5/5/6055321/10026.pdf

Shah, M., Wuilloud, R. G., Kannamkumarath, S. S., & Caruso, J. A. (2005). Iodine speciation studies in commercially available seaweed by coupling different chromatographic techniques with UV and ICP-MS detection. *Journal of Analytical Atomic Spectrometry*, *20*(3), 176–182. https://doi.org/10.1039/B415756G

Sharma, S., Neves, L., Funderud, J., Mydland, L. T., Øverland, M., & Horn, S. J. (2018). Seasonal and depth variations in the chemical composition of cultivated *Saccharina latissima*. *Algal Research*, *32*, 107–112. https://doi.org/10.1016/j.algal.2018.03.012

Stévant, P., Indergård, E., Ólafsdóttir, A., Marfaing, H., Larssen, W. E., Fleurence, J., Roleda, M. Y., Rustad, T., Slizyte, R., & Nordtvedt, T. S. (2018). Effects of drying on the nutrient content and physicochemical and sensory characteristics of the edible kelp *Saccharina latissima*. *Journal of Applied Phycology*, *30*(4), 2587–2599. https://doi.org/10.1007/s10811-018-1451-0

Stévant, P., Marfaing, H., Duinker, A., Fleurence, J., Rustad, T., Sandbakken, I., & Chapman, A. (2018). Biomass soaking treatments to reduce potentially undesirable compounds in the edible seaweeds sugar kelp (*Saccharina latissima*) and winged kelp (*Alaria esculenta*) and health risk estimation for human consumption. *Journal of Applied Phycology*, *30*(3), 2047–2060. https://doi.org/10.1007/s10811-017-1343-8

Suzuki, H., Higuchi, T., Sawa, K., Ohtaki, S., & Horiuchi, Y. (1965). "Endemic coast goitre" in Hokkaido, Japan. *European Journal of Endocrinology*, *50*(2), 161–176. https://doi.org/10.1530/acta.0.0500161

Teas, J., Pino, S., Critchley, A., & Braverman, L. E. (2004). Variability of iodine content in common commercially available edible seaweeds. *Thyroid: Official Journal of the American Thyroid Association*, *14*(10), 836–841. https://doi.org/10.1089/1050725045041293

Teas, J., Braverman, L. E., Kurzer, M. S., Pino, S., Hurley, T. G., & Hebert, J. R. (2007). Seaweed and soy: Companion foods in Asian cuisine and their effects on thyroid function in American women. *Journal of Medicinal Food*, *10*(1), 90–100. https://doi.org/10.1089/jmf.2005.056

van Netten, C., Cann, S. A. H., Morley, D. R., & van Netten, J. P. (2000). Elemental and radioactive analysis of commercially available seaweed. *Science of the Total Environment*, *255*(1-3), 169–175. https://doi.org/10.1016/s0048-9697(00)00467-8

Verhaeghe, E. F., Fraysse, A., Guerquin-Kern, J. -L., Wu, T. -D., Devès, G., Mioskowski, C., Leblanc, C., Ortega, R., Ambroise, Y., & Potin, P. (2008). Microchemical imaging of iodine distribution in the brown alga *Laminaria digitata* suggests a new mechanism for its accumulation. *JBIC Journal of Biological Inorganic Chemistry*, *13*(2), 257–269. https://doi.org/10.1007/s00775-007-0319-6

World Health Organisation, United Nations Children's Fund, International Council for Control of Iodine Deficiency Disorders. (2007) Assessment of Iodine Deficiency Disorders and Monitoring their Elimination. A guide for programme managers. Geneva: WHO; 2007. http://apps.who.int/iris/bitstream/handle/10665/43781/9789241595827_eng.pdf;jsessionid=0AF20DC3D8168907B72F73474618EFBE?sequence=1

Yang, M., Her, N., Ryu, J., & Yoon, Y. (2014). Determination of perchlorate and iodide concentrations in edible seaweeds. *International Journal of Environmental Science and Technology*, *11*(3), 565–570. https://doi.org/10.1007/s13762-013-0263-7

Yeh, T. S., Hung, N. H., & Lin, T. C. (2014). Analysis of iodine content in seaweed by GC-ECD and estimation of iodine intake. *Journal of Food and Drug Analysis*, *22*(2), 189–196. https://doi.org/10.1016/j.jfda.2014.01.014

Zhou, S. J., Condo, D., Ryan, P., Skeaff, S. A., Howell, S., Anderson, P. J., McPhee, A. J., & Makrides, M. (2019). Association between maternal iodine intake in pregnancy and childhood neurodevelopment at age 18 months. *American Journal of Epidemiology*, *188*(2), 332–338. https://doi.org/10.1093/aje/kwy225

Zimmermann, M. B. (2009). Iodine deficiency. *Endocrine Reviews*, *30*(4), 376–408. https://doi.org/10.1210/er.2009-0011

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