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COMPREHENSIVE REVIEW

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Consequences of acute and long-term excessive iodine intake: A literature review focusing on seaweed as a potential dietary iodine source

Marthe Jordbrekk Blikra[1] | **Inger Aakre**[2] | **Jessica Rigutto-Farebrother**[3]

[1]Department of Processing Technology, Seafood Division, Nofima AS, Stavanger, Norway

[2]Department of seafood and nutrition, Institute of Marine Research, Bergen, Norway

[3]Laboratory of Nutrition and Metabolic Epigenetics, Institute of Food, Nutrition and Health, ETH Zürich, Zürich, Switzerland

Correspondence
Marthe Jordbrekk Blikra, Department of Processing Technology, Seafood Division, Nofima AS, PO Box 8034, NO-4068 Stavanger, Norway.
Email: marthe.blikra@nofima.no

Inger Aakre, Department of Seafood and Nutrition, Institute of Marine Research, PO Box 1870 Nordnes, NO-5817 Bergen, Norway. Email: inger.aakre@hi.no

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Abstract

Macroalgae, also called seaweed, are becoming more widespread as food in Western diets. Seaweed can accumulate iodine, an essential nutrient for humans. However, some species of seaweed may contain very high amounts of iodine, and therefore, iodine has been identified as one of the major hazards in the seaweed food chain. Macroalgae may be consumed regularly, though many consumers report eating macroalgae only occasionally. The aim of this paper is to explore possible health consequences of excessive iodine intake according to long-term (chronic) or occasional (acute) excessive exposure to iodine, relating to a regular (chronic) or occasional (acute) seaweed intake, respectively. Furthermore, through a modeling exercise, we add different amounts of seaweed to the diet in a population group to explore the possible safe amounts that can be added without exceeding excessive iodine intakes and risking detrimental health effects. Chronic excessive iodine intakes were associated with several negative health outcomes at variable doses in various studies. For acute excessive iodine exposure, negative health effects seemed to be associated with higher iodine exposures. However, the research on this topic was limited. The chronic and acute iodine exposures needed to result in negative health outcomes may easily be ingested by macroalgae consumption. Adding seaweed to the diet must be done thoughtfully to avoid the risk of exceeding thresholds for excessive iodine intake.

KEYWORDS
excessive iodine intake, health outcomes, iodine, macroalgae, seaweed

1 | INTRODUCTION

Edible seaweeds, or macroalgae, have been incorporated into the diet for decades and have been commonly consumed in many Asian cultures, especially in Japan, China, and Korea (Bangmei & Abbott, 1987; McHugh, 2003; Rhee et al., 2011; Zava & Zava, 2011), but also other parts of the world, such as Ireland (Morrissey et al., 2001) and Portugal

(Paiva et al., 2014). In recent years, dietary seaweeds have entered the global food market and are increasingly popular in the Western diet, including Europe (Aakre et al., 2021; Bouga & Combet, 2015; MacArtain et al., 2007). Seaweeds provide a low-trophic food source rich in taste, which can add functionality to the food, such as texture, and reduce the overall salt content (Blikra et al., 2021; Gullón et al., 2021; Rioux et al., 2017; Vilar et al., 2020).

Macroalgae belong to three different phyla, typically characterized as red, green, and brown macroalgae. Although the chemical composition of macroalgae varies greatly depending on species, season, and environmental conditions and may include several nutrients (Cherry et al., 2019), the contribution to recommended daily intakes depends on portion sizes. Iodine is a trace element that may be highly concentrated in macroalgae, especially the commonly consumed brown algal species such as *Saccharina japonica* (kombu), *Saccharina latissima* (sugar kelp), or *Laminaria hyperborea* (tangle) (Blikra, Henjum, et al., 2022). Kelp species have a highly effective iodine uptake and concentrate iodine up to 30,000 times compared to seawater concentrations (Gall et al., 2004) due to its function as an inorganic antioxidant (Küpper et al., 2008). Iodine may also be found in significant amounts in some red and green species (Aakre et al., 2021; Duinker et al., 2020). As summarized in our previous review, iodine from algae is bioavailable, that is, it is taken up during digestion and enters the circulation (Blikra, Henjum, et al., 2022). Iodine is an essential micronutrient for humans throughout life, and a regular dietary supply of iodine is required in trace amounts (Zimmermann, 2009). The physiological role of iodine is as a component of the thyroid hormones thyroxine (T4) and triiodothyronine (T3), produced in the thyroid gland. The thyroid hormones regulate a wide range of cellular and physiological functions through gene transcription, and most cells in the body have thyroid hormone receptors (Brent, 2012). Like most hormones, the release of thyroid hormones from the thyroid gland is regulated through a negative feedback system (Chiamolera & Wondisford, 2009). If levels of thyroid hormones in the blood fall, the pituitary gland releases thyroid-stimulating hormone (TSH), which stimulates the uptake of iodine from the circulation and thyroid hormone production. TSH may, therefore, be used as a biomarker of thyroid function and is routinely measured in clinical settings. Thyroid hormones are essential for metabolic regulation. Moreover, during fetal life, they are important regulators of brain development as they are involved in cell differentiation, migration, signaling, and myelination and are, therefore, critical for normal fetal growth and development (Bernal, 2005).

Both too low and too high iodine intakes may increase the risk of adverse health consequences, and the relationship between intake and risk is therefore considered to be U-shaped (Laurberg et al., 2009). The negative health consequences of severe iodine deficiency are well documented in scientific literature and are collectively referred to as iodine-deficiency disorders (IDDs) (Hetzel, 1983). The IDDs vary with life stages and may include hypo- and hyperthyroidism, goiter, cretinism, increased infant mortality, and impaired child growth and development (Zimmermann, 2009). The effect of iodine deficiency acts through the thyroid hormones, and even though both iodine deficiency and excess are known to affect thyroid hormone synthesis, the health consequences of iodine excess are supported by less evidence.

Iodine intake recommendations are based on the amount of iodine needed to prevent goiter and maintain normal thyroid function (WHO, 2007a). The World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the Iodine Global Network (IGN) recommend a daily iodine intake of 150 μg/day for adults and between 90 and 120 μg/day for children, depending on age. For pregnant and lactating women, the recommendation is 250 μg/day (WHO, 2007b). Iodine is found in only a few foods, mainly from animal origin, such as milk, dairy products, and marine fish (Haldimann et al., 2005), and, with an increasing interest in plant-based diets, macroalgae could be an important iodine source for those who are omitting fish and animal-source foods. However, consumption of macroalgae may also cause excessive iodine intake, which applies especially to the brown algae species. The European Food Safety Authority (EFSA) recently published a risk assessment on macroalgal consumption in Europe and concluded that iodine intakes could be highly excessive among macroalgal consumers (EFSA et al., 2023). The tolerable upper intake level (UL) endorsed by EFSA is 600 μg/day and is defined as "the maximum level of total chronic intake of a nutrient from all sources judged to be unlikely to pose a risk of adverse health effects in humans." The UL is based on the no observed adverse effect level (NOAEL) of 1800 μg/day, with an uncertainty factor added (EFSA, 2018). If consumed on a regular basis, macroalgal species with high iodine content could result in chronic excessive iodine intakes; however, if consumed only occasionally, the excessive iodine exposure could be acute, not chronic.

The aim of this paper is to explore the health consequences of excessive iodine intake related to long-term, regular (chronic), and occasional (acute) excessive exposure to iodine. By contextualizing the findings to an occasional or habitual intake of seaweed, this review is of relevance to the emergence of edible macroalgae in the global food market. Finally, through a modeling exercise, we demonstrate iodine intakes in various scenarios of its addition to food in an attempt to find safe amounts of seaweed added per portion of food.

2 | MATERIALS AND METHODS

2.1 | Literature review

This is a narrative literature review that includes both primary and secondary sources, as well as gray literature. We searched relevant databases, including PubMed and Web of Science, for primary studies and secondary (review) articles. In addition, reference lists of selected papers were screened for relevant studies. We searched for papers covering iodine consumption correlated with health outcomes. We specifically aimed to group studies based on either chronic (i.e., long-term) or acute (i.e., one incidence or occasional) high iodine exposure to map knowledge regarding possible risks associated with either consumption pattern. For chronic excessive iodine exposure, we categorized the findings on health outcomes based on the following topics previously known from the literature: goiter formation, thyroid function, cancer prevalence, birth outcomes and fertility, and child development. We took a more investigative approach to acute iodine exposure and looked for any data describing effects on thyroid function and possible acute effects of single iodine exposures, especially those describing intakes well above recommendations.

We aimed to include all intervention studies retrieved that described seaweed as a source of iodine intake if they also measured an effect on health outcomes. Where the literature on seaweed was scarce, we included other sources as exposure. We have included both primary studies and reviews and tried, to the best of our ability, to summarize the information most relevant to the seaweed food sector and research within this field. Even if this has not been a systematic approach, we have followed some eligibility criteria when including, summarized in Table 1, and the included studies are detailed in Tables S1 and S2.

2.2 | Estimations of iodine content in raw and processed seaweed

Seaweed may be added as an ingredient to various foods, such as bread, pasta, soups, condiments, spice mixes, or snacks. Some typical food applications include (from smaller to larger estimated portions of seaweed):

1. Small amount (1 g dry), for example, spice/condiment or tea;
2. Medium amount (8 g dry), for example, food ingredients including use in soups (MacArtain et al., 2007);
3. Medium amount (25 g fresh), for example, a small side dish (Noahsen et al., 2020).

We calculated amounts of ingested iodine per portion size for six popularly consumed algae species based on the above portion sizes. The following information was used for assessing the loss, or extraction, of iodine during processing: 90% was extracted during blanching of *S. latissima* (Nielsen et al., 2020); 62%, 15%, and 10% were extracted during rehydration of *Alaria esculenta*, *Palmaria palmata*, and *Ulva*, respectively (Nitschke & Stengel, 2016); and 44% was extracted during washing of *Fucus vesiculosus* (Martinelango et al., 2006). No documentation was found for the effect of processing on the extraction of iodine from *Porphyra* spp. tissue during cooking operations. For calculations of the iodine content in fresh seaweed, a water content of 70% was assumed for all species—a conservative amount, based on data from Holdt and Kraan (2011). Data for iodine content in both unprocessed and processed seaweed are based on the 75% percentile iodine content (semiconservative approach) (Duinker et al., 2020).

2.3 | Modeling of scenarios for iodine inclusion levels in foods

Modeling of iodine exposure following various inclusion levels for iodine in foods was performed probabilistically using @Risk version 8.5.1 (Build 5), which is an add-on to Excel. The baseline data for iodine intake were taken from the report by the Norwegian Scientific Committee on Food and The Environment (Henjum et al., 2020), using data from the nationally representative Norkost study (Table 7.3.1.1-1, p. 118). The population iodine intake was estimated using a Pert function, with the median (P50) as the typical value, whereas the 5th and 95th percentiles (P05 and P95) were applied as the minimum and maximum values, respectively.

Three iodine inclusion levels in food items containing seaweed were chosen for the scenario modeling (Table 2), namely low–medium (50–150 µg iodine/portion), high (150–600 µg iodine/portion), and extreme inclusion (2500–10,000 µg iodine/portion). Examples of the first two categories could be foods where seaweed is added for iodine fortification purposes or as a taste enhancer/spice. Since food manufacturers typically would add as much seaweed as possible without posing a health risk, the typical inclusion value was modeled as equaling the maximum value for these cases. For the extreme inclusion, this scenario portrays consumers adding seaweed with high iodine

TABLE 1 Overview of studies selected in the review.

Parameter	Description
Study design	• Human experimental studies (randomized controlled trials and other controlled studies) • Human observational studies (cross-sectional studies, case–controlle studies, and cohort studies) • Secondary literature (reviews) on both humans and (when relevant) animals
Population	• All age groups, males and females • For the outcome "cancer," one review summarizing both human and animal studies was included
Exposure	• Oral iodine intake • Exposure in prioritized order: 1. Exposure from seaweeds (chronic and acute) 2. Exposure from other sources, for example, water (chronic) and contrast media (acute)
Outcome of interest—chronic	• Thyroid size (goiter, thyroid volume) • Thyroid function (hypo- and hyperthyroidism, TSH, free thyroid hormones [fT3, fT4] thyroid antibodies) • Cancer prevalence (thyroid cancer) • Birth outcomes (stillbirth, premature birth, fertility) • Child development (developmental scores, IQ, growth, weight)
Outcome of interest—acute	• Thyroid function (hypo- and hyperthyroidism, TSH, fT3, fT4, thyroid antibodies) • Acute reactions
Publication type	• Scientific publications and reports • Gray literature

TABLE 2 Modeling parameters (iodine content [µg/portion]) for the various inclusion levels in foods.

	Iodine content (µg/portion) in the different scenarios		
	Low–medium scenario	**High scenario**	**Extreme scenario**
Minimum	50	150	2500
Maximum	150	600	10,000
Typical value	150	600	5000
Function type	Pert[a]	Pert	Pert

[a]The Pert function is a smoothed triangular function.

content in their day-to-day cooking, or consumption across multiple foods per day. The scenario exemplifies the consumption of 1 g of nonblanched, dried sugar kelp one to three times per day.

The model was run in three simulations, portraying different consumer behaviors (no seaweed intake, 1 item/day, and 1–3 items/day). The consumers eating one to three items were modeled using a Pert function with a typical value of 2. The different scenarios were used to assess the percentage of the population that consumed more than the UL of 600 µg/day and the NOAEL of 1800 µg/day. This part of the modeling only looked at one relevant population group, namely women (18–70 years) who take supplements. This consumer group was chosen since young women are vulnerable to iodine excess while also benefiting from small doses of iodine fortification. Supplement users were chosen in this scenario to take into account the higher background exposure in this group. The model was run using 10,000 iterations. A summary is included in Table 3.

3 | RESULTS

3.1 | Consequences of long-term excessive iodine exposure

3.1.1 | Goiter

Goiter is a visible manifestation of iodine deficiency, where the lack of iodine may stimulate thyroid follicular cell growth, causing thyroid gland enlargement (Zimmermann et al., 2008). It is established that both iodine deficiency and excess can lead to the formation of goiter (Laurberg et al., 2009). The incidence of increased thyroidal volume and goiter upon increased iodine intake has been thoroughly reviewed elsewhere (Farebrother et al., 2019). Specific studies of seaweed intake and goiter are scarce in the Western parts of the world, but several studies have been conducted in Japan on the topic. In a study from 1965, the occurrence of goiter was high in school children living in the coastal areas of Hokkaido in Japan, where the

TABLE 3 Summary of the scenario modeling.

	Details
Inclusion level	1. Low–medium (50–150 µg/portion) 2. High (150–600 µg/portion) 3. Extreme inclusion (2500–10,000 µg/portion)
Population group	Women (18–70 years) using iodine supplements
Consumer behavior	1. No seaweed intake 2. 1 item/day 3. 1–3 items/day
Output	Distribution graphs and percent of the population group ingesting more than 600 tolerable upper intake level (UL) and 1800 µg iodine/day, which corresponds to the no observed adverse effect level (NOAEL)[a]

[a] EFSA (2018).

prevalence of visible goiter was 6.6% in Hidaka and 9.0% in Rishiri Island. In comparison, the prevalence of goiter was 1.3% in the control area of Sapporo city. The regions with high goiter prevalence had traditionally high intakes of kelp, and for some of the cases, withdrawal of kelp from the usual diet decreased the size of the goiter (Suzuki et al., 1965). The high prevalence of goiter in the coastal areas of Hokkaido has been referred to as "endemic coast goiter" in the areas of Hidaka and Rishiri Island (Suzuki et al., 1965). A second study was conducted in the Hokkaido area five years later, where the same association between high seaweed intake and goiter was found (Suzuki, 1973). In a third large epidemiological study in Ishikawa district, Japan, between 1972 and 1975, the prevalence of goiter was 2.7% and 3.0% in Kanazawa City and Wajima City, which was considerably lower than in the previous survey from 1965. However, they found that abnormalities in thyroid gland consistency were more prevalent among girls living in coastal areas than in urban areas (Inoue et al., 1975).

The intake threshold at which iodine excess increases the risk of goiter has been uncertain. In 2005, Zimmermann and colleagues found that UIC (urinary iodine concentration) between 300 and 500 µg/L was not associated with increased thyroid volume in children, while a UIC above 500 µg/L was associated with an increase (Zimmermann et al., 2005). In 2021, a meta-analysis was performed to explore the development of goiter associated with either high iodine concentrations in drinking water or high UICs in China (Xu et al., 2021), revealing that goiter risk increased with a UIC above 300 µg/day or with an iodine concentration in drinking water above 100 µg/L for school children.

3.1.2 | Thyroid function

Excess iodine may lead to altered thyroid function, such as hyperthyroidism (Roti & Uberti, 2001) and hypothyroidism (Markou et al., 2001). Such findings have been found in studies investigating excessive iodine intake from kelp. In a Korean cohort, the iodine intake over 1 year was assessed, along with urinary iodine excretion (UIE), in 184 patients diagnosed with thyroid disorders and 207 controls with normal thyroid function (Kim & Kim, 2000). Both the iodine intake and UIE were higher in patients with thyroid disease than the euthyroid control subjects, and the main dietary iodine sources were seaweed. Prolonged (>2 weeks) iodine supplementation of 356 µg, through seaweeds (*Ascophyllum nodosum*), though below the UL, resulted in elevated TSH in two out of 42 healthy British women of childbearing age (Combet et al., 2014). The increase may be associated with iodine-induced hypothyroidism (Combet et al., 2014). A double-blind, randomized crossover study of 25 women using a slightly higher iodine content (475 µg) from another brown alga (*A. esculenta*) for 7 weeks found significantly increased serum TSH (Teas et al., 2007). A cross-sectional population study from Japan found that most subjects with hypothyroidism also reported an almost daily kelp intake (Konno et al., 1994). Thyroid dysfunction has previously been found in other Japanese studies, using seaweed as an intervention (Miyai et al., 2008; Takase et al., 2020). Miyai et al. (2008) gave healthy adults between 35,000 and 70,000 µg iodine through kombu (*S. japonica*[1]) daily for 7–87 days. This resulted in a significant increase in TSH and a slight but statistically nonsignificant decrease in free T3 and T4 (fT3 and fT4). During the longest period of intake (87 days), the elevated TSH was sustained, while fT3 and fT4 were almost unchanged. In the other Japanese intervention study (Takase et al., 2020), blood lipids were the primary outcome. Participants were given capsules with *P. palmata* daily for 8 weeks, resulting in an iodine intake of 2000 µg/day. The intervention group had increased TSH compared with the control group, who received placebo

[1] Formerly referred to as *Laminaria japonica* (Lane, C. E., Mayes, C., Druehl, L. D., & Saunders, G. W. (2006). A multi-gene molecular investigation of the kelp (Laminariales, Phaeophyceae) supports substantial taxonomic re-organization. *Journal of Phycology*, *42*(2), 493–512.).

capsules (Takase et al., 2020). Whether hypothyroidism can be reversed by restricting iodine intake was studied in a clinical trial in patients with spontaneously occurring hypothyroidism. Twelve of the patients (55%) became euthyroid after restricted iodine intake for 3 weeks, while in the remaining 10 patients, the thyroid function did not improve (Tajiri et al., 1986).

Excessive iodine intake may also result in hyperthyroidism, which is characterized by a low or suppressed TSH (Roti & Uberti, 2001). Several case reports have shown iodine-induced thyrotoxicosis or hyperthyroidism after ingestion of kelp (de Smet et al., 1990; Eliason, 1998; Gherbon et al., 2019; Müssig et al., 2006; Shilo & Hirsch, 1986). The iodine doses ingested through kelp varied from an estimated 580–990 μg/day (Müssig et al., 2006) to 2800–4200 μg/day (Shilo & Hirsch, 1986) and 336 μg/day (Gherbon et al., 2019), and in two of the case reports, the iodine content of the kelp supplements was not known (de Smet et al., 1990; Eliason, 1998). In all the studies, the supplements were ingested for a relatively long period of time (4 weeks to several months). Similarly, dietary supplements containing kelp and seaweed from Norway were linked to hyperthyroidism (two cases) in the 1970s and 1980s, as summarized in a 34-year-old review (Pennington, 1990). In studies where iodine intake has changed rapidly due to iodine fortification of salt, changes in thyroid function have been observed. This has been seen in studies from, for example, Denmark, Zimbabwe, and Austria (Bülow Pedersen et al., 2006; Mostbeck et al., 1998; Todd et al., 1995); however, all these populations were iodine deficient before fortification, and prolonged iodine deficiency has been suggested to result in susceptibility to thyroid disease upon increased iodine intake (Laurberg et al., 2001).

Two of the population groups that are particularly vulnerable to excessive iodine consumption are the fetus and infants. Several studies describing this risk are reported from Asian cultures. Studies have indicated that excessive iodine intake from seaweed by mothers during pregnancy or lactation was associated with hyperthyrotropinemia or hypothyroidism in their infants (Emder & Jack, 2011; Hamby et al., 2018; Nishiyama et al., 2004). The studies by Emder and Jack (2011) and Hamby et al. (2018) are case reports, where mothers have ingested seaweed soup during and/or after pregnancy, causing thyroid dysfunction in the infants. In the study by Nishiyama et al. (2004), 34 Korean infants who were positive for congenital hypothyroidism screening were selected, among whom 15 infants were diagnosed with hyperthyrotropinemia due to excess iodine consumption by the mothers during pregnancy. The mothers had consumed kombu, other seaweeds, and seaweed soup, at an estimated iodine intake of between 820 and 3200 μg/day. Another Korean study found that subclinical hypothyroidism in preterm infants was associated with high iodine levels in breast milk, mostly due to seaweed consumption (Chung et al., 2009), where the median iodine content in the breast milk was 2529 μg/L. This breast milk iodine concentration is excessive compared to what is required to maintain a sufficient infant iodine intake, and a breast milk iodine concentration of 150 and 71 μg/L in colostrum and mature breast milk, respectively, has been suggested to ensure sufficient iodine intake by others (Nazeri et al., 2018).

There are also studies where excessive iodine intakes have not been associated with any negative effects on thyroid function. A large multicenter study from Kenya and Tanzania, including 4636 participants from several population groups (school-aged children, women of reproductive age, pregnant and lactating women, and infants), found chronic excessive iodine intakes (indicated by a UIC of >300 μg/L) in all the population groups (Farebrother et al., 2018). The iodine exposure in this study was not from seaweed but mainly from iodized salt and groundwater. This study showed little effect on thyroid function, except for a <15% prevalence of subclinical hyperthyroidism and hypothyroxinemia in women of reproductive age and pregnant women, respectively. Thyroglobulin (T_g) concentrations were, however, elevated in all groups. A Korean study with 349 mother–infant pairs found that women in the highest quartile of iodine intake during pregnancy (≥647 μg/day) had similar thyroid function as the women with lower iodine intake (Ju et al., 2023). Seaweed and seaweed soup were major dietary iodine sources. The thyroid function among the infant pairs was not reported in the study.

3.1.3 | Cancer prevalence

Some Asian studies have investigated the association between iodine intake (by assessing UIC) and cancer prevalence. A retrospective analysis of South Korean patients with thyroid nodules concluded that patients with relatively low (<300 μg/L) or extremely excessive (≥2500 μg/L) UIC were more likely to have thyroid cancer compared to patients with UIC between 300 and 2500 μg/L (these were more likely to have benign nodules) (Kim et al., 2017). Only patients with thyroid nodules were included (no controls). According to WHO guidelines, over half the patients had excessive iodine status (≥300 μg/L). A more recent case–control study, also from South Korea, found a higher prevalence of excessive iodine status (UIC of ≥300 μg/L) in patients with papillary thyroid cancer than in controls, and excessive iodine intake was identified as a risk factor for papillary thyroid cancer (Kim et al., 2021). However, a question was raised about whether UIC can rightly be used as an indicator for iodine intake in this patient group, after a meta-analysis performed by

Yan et al. (2019). Their study suggested that the high UIC associated with papillary thyroid cancer was a characteristic of the disease and not a risk factor. Among others, the aforementioned primary studies were used in the meta-analysis.

Two studies from Japan investigated the association between seaweed intake and thyroid cancer. These studies characterized seaweed consumption in terms of days per week (not in terms of iodine content), with 2 days or less being the lowest consumption rate. The first study, conducted by Michikawa et al. (2012), found an increased risk of thyroid cancer for postmenopausal women consuming seaweeds three times a week or more compared to those consuming seaweeds two times a week or less. There was no association for premenopausal women. In contrast, the second study, conducted by Wang et al. (2016), found no association between seaweed consumption rate and thyroid cancer risk. The latter study also attempted to investigate the effects in men, but the incidence rate for men was too low. Both studies were prospective studies with over 30,000 women and a mean follow-up period of ≥12 years.

Due to the complexity of this issue, a more mechanistic understanding could be beneficial for assessing causalities. In this respect, Zimmermann and Galetti (2015) conducted a thorough review of iodine intake and thyroid cancer, including both human and animal studies. They found that studies performed on rats or mice typically found no association between excessive iodine intake and cancer prevalence in these animals. It should be noted that rats have a much higher tolerance for excessive iodine than humans and will not respond to iodine excess with increasing TSH levels, as observed in humans (Lee et al., 2015). During simultaneous exposure to either excess or deficient iodine alongside a carcinogen, the number of instances of thyroid cancer increased. Based on these observations, the authors suggested that iodine excess functions as a promoter rather than a carcinogen itself (Zimmermann & Galetti, 2015). Furthermore, the authors compared iodine status in various populations with the incidence of thyroid cancer over time. Based on these historical data, they concluded that a correlation between iodine excess and thyroid cancer, in general, could not be found, but that evidence is more convincing for a shift in thyroid cancer type upon increasing iodine status in a population. Specifically, a shift from anaplastic thyroid cancer and follicular thyroid cancer to papillary thyroid cancer has been observed, which in turn decreases mortality from thyroid cancer in general. This was also pointed out in an earlier review study by Feldt-Rasmussen (2001), and a more recent review by Kitahara and Schneider (2022) on the epidemiology of thyroid cancer refers to the same conclusions.

3.1.4 | Birth outcomes and fertility

No studies assessing the effect of seaweed intake were found on this topic, so we summarized information on other iodine sources. Adverse consequences on birth outcomes (e.g., stillbirth, premature birth) have been associated with severe iodine deficiency (Zimmermann, 2009). Given iodine's U-shaped relationship between intake and risk of negative health consequences (Laurberg et al., 2009), such outcomes may also occur as a consequence of iodine excess. As summarized in a 34-year-old review, case reports from the 1940s to the 1970s report that large doses of iodine supplied as potassium iodide or Lugol's solution (e.g., as a treatment for asthma, hyperthyroidism, and tachycardia) to pregnant women resulted in adverse effects on infants including death (six cases), respiratory distress, brain damage, goiter, and hypothyroidism (Pennington, 1990). More recently, a study of 1569 pregnant women found that more than adequate or excessive iodine intakes (UIC > 250 μg/L) were linked to an increased risk of macrosomia (Xiao et al., 2018). In another study, high iodine status (UIC > 249 μg/L) had a higher rate of abnormal amniotic fluid (Yang et al., 2018). Iodine status has also been found to affect fertility in males. Both iodine deficiency and excess were associated with reduced semen quality (semen volume and semen concentration) in Chinese men (Sun et al., 2020). A correlation between low fertility and higher median urinary iodine content has also been reported elsewhere (Partal-Lorente et al., 2017).

3.1.5 | Child development

Iodine deficiency has been named as one of the main risk factors for preventing children from attaining their developmental potential (Walker et al., 2011), and there is general agreement that correcting iodine deficiency is beneficial for child development (Aburto et al., 2014; Bougma et al., 2013). Even though both iodine deficiency and excess are known to affect thyroid hormone synthesis similarly, very little research has been dedicated to excessive iodine intake and child development.

Fetuses and young children may be particularly vulnerable to inadequate iodine intake and, thus, also to excessive seaweed consumption. In Japan and Korea, seaweeds are incorporated into the dietary culture, and seaweed intake is perceived as good for pregnancy and lactation (Orito et al., 2009; Rhee et al., 2011). Thyroid dysfunction in newborns and young children after maternal seaweed consumption has been reported (Chung et al., 2009; Emder & Jack, 2011; Nishiyama et al., 2004); however, few studies have been found related to outcomes on child development. One study of Japanese pregnant women showed a wide variation in UIC, and a positive correlation was seen between maternal UIC and TSH levels. However, no apparent negative effects were seen on fetal maturation scores or developmental testing of the infants at 3, 6, 9, and 12 months (Orito et al., 2009).

Since the literature reporting risks of child developmental outcomes in correlation with seaweed consumption is limited, studies reporting risks associated with other iodine sources are also described here. China has areas with both iodine excess and deficiency, due to variable levels of iodine in drinking water (Du et al., 2014). Several Chinese studies have investigated the relationship between iodine excess and children's intelligence. However, many of these are only published in Chinese. A review and meta-analyses published in 2021 summarized findings from 17 studies published between 1985 and 2020 (16 published in Chinese and one in English) on the effect of iodine excess on children's intelligence in China (Li et al., 2022). They concluded that the intelligence level of children who were exposed to high iodine concentrations was reduced. However, the results from the primary studies showed inconsistency in this association, and the authors underline the lack of conclusive evidence to confirm the effect of iodine excess on children's IQ (Li et al., 2022). In a recent Chinese study published in 2023, maternal iodine nutrition above requirements (UIC $\geq$ 250 µg/L or total serum iodine more than the 90th percentile) negatively affected infant language development and fine motor skills (Wu et al., 2023). In Australia and New Zealand, table salt and salt used in bread are iodized; in addition, pregnant women are advised to take iodine supplements during pregnancy. This has raised concern regarding potential high iodine intakes in this population group (Sullivan et al., 2024). In a prospective cohort of 699 pregnant women and young children from Australia, they found that both too low and too high iodine intakes in pregnancy were associated with poor outcomes related to neurodevelopment, where language and cognitive scores were negatively affected by iodine intakes >350 µg/day (Sullivan et al., 2024). As highlighted in a systematic review on the effect of iodine supplementation during pregnancy (Dineva et al., 2020), some observational studies have found that a sudden change in iodine intake in pregnancy, through supplementation, is negatively associated with child development, such as motor development, behavioral problems, and attention deficit hyperactivity disorder (ADHD) diagnosis (Abel, Caspersen, et al., 2017; Abel, Ystrom, et al., 2017; Markhus et al., 2018).

Less discussed are the effects on physical growth that may be associated with excessive iodine intake (Rigutto-Farebrother, 2023). Stunting is a recognized IDD, with the potential mechanism for this resulting from changes to thyroid hormone synthesis (hypothyroidism) due to exposure to inadequate iodine intakes in early life. Considering that at high intakes, similar changes to thyroid hormone production may occur as at low intakes, it follows that physiological growth may also be affected. Thyroid hormones act on the skeleton; thyroid hormone receptors have been identified in osteoblast cell lines and human bone samples, indicating a direct role in skeletal development (Yen, 2001). Moreover, indirect mechanisms via Growth Hormone and Insulin-like Growth Factors also promote skeletal growth controlled, in part, by thyroid hormone (Cabello & Wrutniak, 1989; Laron, 2003; Robson et al., 2002).

As described previously, chronic iodine excess may cause hypo- or hyperthyroidism. In China, in an area of high iodine water intake (range 150–963 µg/L), children were found to be 4 cm taller than their counterparts in areas with water with normal iodine concentrations (range 13–51 µg/L); however, thyroid disorders were more prevalent in the high iodine cohort, and an increased thyroid volume was correlated with increasing iodine intake. A UIC of $\geq$600 µg/L was independently associated with subclinical hypothyroidism (Sang et al., 2013). Though reporting from literature without a direct growth outcome, it is important to note that a further consequence of chronic excess iodine exposure is the potential earlier development of Graves' disease in subjects with a genetic disposition, as seen in younger age groups in Iceland when compared to a population in Denmark with low-to-average iodine intake, where hypothyroidism prevalence was associated with multinodular toxic goiter and single toxic adenoma rather than autoimmunity (Laurberg et al., 1991). This is of concern in younger populations, since Graves' disease in pregnancy can increase the risk of low birth weight and intrauterine growth restriction (Nguyen et al., 2018), and in childhood, it can lead to a shorter adult stature due to accelerated growth rates causing premature closure of epiphyses and/or cranial plates (Bassett & Williams, 2016; Williams, 2013).

3.2 | Consequences of acute and occasional excessive iodine exposure

No studies describing the consequences of acute iodine exposure in humans from seaweed containing iodine levels above the ULs were found during our explorations. One study describing the consequences of a single exposure below the UL was found (Noahsen et al., 2020), where seaweed containing a maximum of 300 µg iodine in each portion (25 g Greenlandic *F. vesiculosus* salad) was used. After consumption of this amount, the TSH increased in participants (n = 3), but none had levels above normal values, and the levels returned to normal by day 2.

Other dietary sources of acute iodine exposure include potassium iodine (KI) taken at infrequent intervals. An intervention study from 1998 administered KI in various intervals (ranging from biweekly to yearly) in 304 schoolchildren aged 7–13 in an iodine-deficient area, in doses ranging from 8700–993,000 µg (Todd & Dunn, 1998). Since the area was severely iodine deficient, having a control group was considered unethical and, therefore, was not included. The study reported no adverse effects. However, some children in all study groups complained of sore throat, headache, and abdominal pain. The number of children with TSH levels above normal in the group receiving 993,000 µg KI once per year ($n = 50$) was changed from 4 at baseline to 6 after 13 months. In comparison, for children receiving 8700 µg KI every other week ($n = 52$), the number of children with elevated TSH went from 8 at baseline to 3 after 13 months. The thyroid volume decreased for children receiving 8700 µg KI biweekly or 29,700 µg KI monthly, but not for the remaining participants in groups receiving other doses.

Another source of acute iodine exposure is radiographic iodinated contrast media (ICM), which are commonly administered intravenously to hospital patients prior to computed tomography (CT) scans. A relatively recent review summarized the risk for ICM-induced thyroid dysfunction (Lee et al., 2015). They found that the typical doses for CT scans range from 2500 to 5000 µg of bioavailable iodine and 15–37 g of total iodine (including nonbioavailable iodine). According to the authors, thyroid dysfunction may arise after a single ICM use. In patients without preexisting thyroid disease, the risk of developing hypo- or hyperthyroidism increased 1.6–3.0 times after a single ICM exposure. Although the dysfunctions were normally transient, some patients developed permanent hypothyroidism following the administration of ICM. In euthyroid patients (50–84 years), TSH decreased following a single ICM administration when measured at 4 and 8 weeks after administration (Conn et al., 1996). In the latter study, two out of 73 patients developed hyperthyroidism, and one developed atrial fibrillation in response to abnormal thyroid values.

Some older case studies describe the acute effects of intentional or unintentional acute iodine exposure through tinctures or medical solutions. These were previously summarized by Pennington (1990), but a brief summary is included here. Very high, acute exposure to iodine is characterized as poisoning and may, in the worst case, lead to death. The reported cases outlined intentional poisoning by tinctures of iodine (18 cases), and death usually occurred within 48 h. The doses were reported in nine of the cases and ranged from 1184 to over 9000 mg iodine. Other reported acute effects of very high doses of iodine include vomiting, abdominal cramps, anuria, acute renal fever, hemolytic anemia, metabolic acidosis, delirium, weak pulse, fever, collapse, coma, and cyanosis, among others (Pennington, 1990).

3.3 | Seaweed as food ingredients

The iodine content in seaweed is affected by the cooking and processing methods applied. Examples of common methods include washing, blanching, boiling, fermentation, steaming, pulsed electric field processing, drying, and rehydration (Blikra et al., 2021). The iodine content is typically reduced during processing, with steps involving immersion in warm water being more efficient (Blikra et al., 2024; Blikra, Skipnes, et al., 2022; Bruhn et al., 2019; Correia et al., 2021; Nielsen et al., 2020; Nitschke & Stengel, 2016; Stévant et al., 2018; Sun et al., 2022). For sugar kelp, a loss of iodine of about 90% has been achieved using blanching (Nielsen et al., 2020). For species containing less iodine, such as *P. palmata* and *Ulva*, smaller losses (10%–15%) in iodine content have been found (Nitschke & Stengel, 2016). Thus, the degree of processing is highly important for the iodine content in the seaweed used for consumption, especially for brown algae.

The estimations made in the present work show that iodine amounts can be high compared to both daily requirements and the UL, especially for dry, unprocessed brown algae (Table 4). Although processing greatly reduces the ingested amount of iodine per portion size, the amounts of iodine present may still be very large, as exemplified by one portion of 8 g blanched, dry *S. latissima* containing 3700 µg iodine (Table 4).

A recent project report described the fate of the iodine content in 55 g fermented *S. latissima* cooked in 200 mL tap water (Stévant et al., 2021), which could exemplify one portion of seaweed soup. Prior to cooking, the portion of kelp contained a total of ~21,000 µg iodine, whereas after cooking, only ~3000 µg iodine (14%) was found in the kelp. Based on measurements of the iodine content in the liquid fraction, and mass balance calculations, they concluded that most of the extracted iodine was still present in the liquid fraction after 15 min of boiling (~15,000 µg or 72%; i.e., low-to-negligible evaporation). This iodine may be ingested in the case of soup.

3.4 | Scenarios for iodine inclusion levels in foods

The Norwegian, dietary supplement-consuming women (18-70 years) used in this scenario showed an adequate iodine status (baseline exposure) (Figure 1a). Additional

TABLE 4 Iodine contents in unprocessed and processed popular seaweed species, with estimations of ingested iodine per portion size.

Phylogeny	Species	Iodine (P25–P75; µg/g dw) Unprocessed[1]	Processed[2]	Portion size (g)	Ingested iodine (µg)[4] Unprocessed[1]	Processed[2]
Brown	*Saccharina latissima*	2600–4600	260–460	1 g dry	4600	460
				8 g dry	37,000	3700
				25 g fresh[3]	1600	160
	Alaria esculenta	450–1100	170–420	1 g dry	1100	420
				8 g dry	8800	3300
				25 g fresh	390	150
	Fucus vesiculosus	210–520	120–290	1 g dry	520	290
				8 g dry	4200	2300
				25 g fresh	190	100
Red	*Palmaria palmata*	130–430	110–370	1 g dry	430	370
				8 g dry	3400	2900
				25 g fresh	150	130
	Porphyra spp.	15–100	n.a.	1 g dry	100	n.a.
				8 g dry	800	n.a.
				25 g fresh	40	n.a.
Green	*Ulva* spp.	29–290	30–260	1 g dry	290	260
				8 g dry	2300	2100
				25 g fresh	100	90

Note: [1] Using data from Duinker et al. (2020); [2] Assuming 90 % reduction during blanching of S. latissima (Nielsen et al., 2020), 62, 15 and 10 % reduction during rehydration of A. esculenta, P. palmataand Ulva, respectively (Nitschke & Stengel, 2016), and 44 %reduction during washing of F.vesiculosis (Martinelango et al., 2006). [3] Assuming 70 % water contentfor all spp. - a conservative amount, based on data from Holdt and Kraan (2011). [4] Calculated using the 75 %percentile iodine content.

TABLE 5 Population (%) above the tolerable upper intake level (UL) and no observed adverse effect level (NOAEL) for iodine in women aged 18–70 consuming supplements.

Threshold levels	Consumer behavior	Population (%) exceeding threshold values for iodine intake: Low–medium (50–150 µg/portion)	High (150–600 µg/portion)	Extreme (2500–10,000 µg/portion)
>600 µg/day[a]	No seaweed intake	0.0	0.0	0.0
	1 item/day	0.0	77.8	100.0
	1–3 items/day	7.9	91.6	100.0
>1800 µg/day[b]	No seaweed intake	0.0	0.0	0.0
	1 item/day	0.0	0.0	100.0
	1–3 items/day	0.0	5.9	100.0

[a]Recommended maximum daily intake level.
[b]NOAEL.

iodine intake through food items containing 50–150 µg iodine/portion (low-medium scenario) shifted the total iodine intake predictably, but for consumers eating one portion per day, the intake remained below the maximum recommended intake per day of 600 µg. For consumers eating between 1 and 3 items/day, 88% had an iodine intake above 600 µg/day (Table 5). Substituting the added iodine content with 150–600 µg iodine/portion (high scenario) shifted the tendency considerably (to the right) for consumers, and >77% of those eating one portion per day exceeded the intake limit of 600 µg/day. Looking at consumers having a more frequent intake of seaweed food items (1–3 portions/day), 92% ingested more than 600 µg of iodine, whereas roughly 6% had an iodine intake above NOAEL in the high scenario (Figure 1b). This tendency is more exaggerated for iodine additions of 2500–10,000 µg/day, which is included as a scenario to portray consumers of unprocessed, dried, high-iodine-containing seaweed such as sugar kelp. In this case, portions of 1 g sugar kelp eaten 1 or 1–3 times/day are modeled to repre-

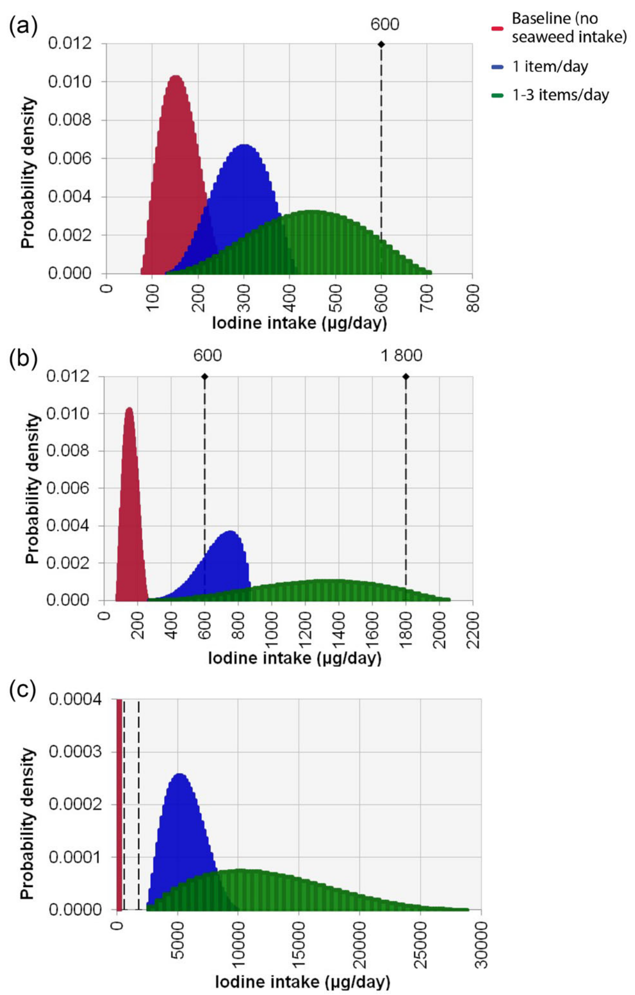

FIGURE 1 The probability density for daily iodine intake for women aged 18–70 consuming supplements modeled for three seaweed inclusion rates in food items: (a) low-to-medium, (b) high, and (c) extreme seaweed scenarios. The simulation was run for the three consumption behaviors (baseline [no seaweed intake], 1 item/day, and 1–3 items/day).

sent addition as a spice/condiment during home cooking. For the latter case, both consumer behaviors represent intakes above the NOAEL (Figure 1c).

4 | DISCUSSION

4.1 | Consequences of chronic and acute excessive iodine exposure

Studies on the consequences of chronic excessive iodine exposure from seaweed were found for goiter, thyroid function, and cancer, but for birth outcomes and child development, we did not find any studies on seaweed intake. Therefore, other exposures were included. As seen from the results, negative health effects have been reported after excessive iodine intake from seaweed at variable levels. As noted already by Pennington in 1990, an iodine intake of ≤1000 µg/day could be tolerated by many, but intakes in the range between 200 and 1000 µg/day may cause harmful effects in some individuals depending on a range of factors (Pennington, 1990). The negative health outcomes from iodine excess are thought to be mediated through the thyroid hormones (including TSH). Several studies with an experimental design have found associations between iodine excess and thyroid function, and the outcome is often a mild and transient rise in TSH (Combet et al., 2014; Miyai et al., 2008; Teas et al., 2007). However, variations in TSH, even within reference ranges, have been associated with adverse health outcomes (Taylor et al., 2013). Furthermore, other studies reported more severe effects on thyroid function (Chung et al., 2009; Nishiyama et al., 2004; Takase et al., 2020), and physiological changes may be triggered in susceptible groups, especially pregnant women, infants, and those previously exposed to iodine deficiency (Farebrother et al., 2019).

As such, conflicting evidence exists on chronic excessive iodine intake. Regarding goiter and thyroid function, large studies in different population groups have not seen any adverse effects on thyroid function from chronic excessive iodine intakes (Farebrother et al., 2018; Ju et al., 2023). Excessive iodine intake in relation to cancer is, however, a complex issue, and findings point in different directions. A review on iodine intake and thyroid cancer pointed out that a correlation between iodine excess and thyroid cancer, in general, cannot be found, though some evidence supports a shift in thyroid cancer type when the population's iodine status is increased (Zimmermann & Galetti, 2015). For birth outcomes, studies on the consequences of iodine excess are scarce. However, evidence on the association between thyroid function and birth outcomes is more established, which might be seen as an indirect effect of iodine excess. A systematic review and meta-analysis examining 10,736 pregnant women exposed to iodine intake above requirements found that six of the nine studies included reported hypothyroidism during pregnancy; however, subclinical and overt hyperthyroidism, as well as hypothyroxinemia, were also reported (Candido et al., 2023). Thus, it seems that the increased risk of thyroid disorders (indirect effect of iodine excess), including subclinical disorders, increases the risk of negative birth outcomes. Thyroid dysfunction has been found to give an increased risk of complications during pregnancy, including pre-eclampsia, perinatal mortality, (recurrent) miscarriage, and preterm delivery (van den Boogaard et al., 2011; Yang et al., 2018). For child development, several observational studies have found an association with excessive iodine intake (Li et al., 2022; Sullivan et al., 2024; Wu et al., 2023). However, since these studies are of observational design, other factors cannot be excluded, and well-designed randomized controlled trials are warranted on this topic.

Regarding acute or occasionally high iodine exposure, ICM use could increase the risk of developing iodine-induced thyroid dysfunction, even in euthyroid individuals (Lee et al., 2015). These authors found that typical doses for CT scans range from 2500 to 5000 µg of bioavailable iodine and 15 to 37 g of total iodine. For comparison, the bioavailable portion of the administered iodine is in the range of an 8-g portion of processed, dried *S. latissima*, *A. esculenta*, or *P. palmata*, or 1 g dry unprocessed *S. latissima* (Table 4). As summarized in our previous review, iodine from brown algae is bioavailable (Blikra, Henjum, et al., 2022). Thus, we cannot rule out that certain species of seaweed could induce acute toxic effects, if not used with caution.

The risk for developing iodine-induced hypothyroidism after acute iodine exposure is higher for fetuses and neonates, and even transient fetal and neonatal hypothyroidism can be detrimental to neurodevelopment (e.g., Lee et al., 2015). Older people are at risk of other serious complications, including atrial fibrillation and coma. Apart from low and high age, risk factors for developing thyroid dysfunction following acute iodine exposure include long-standing iodine deficiency, latent thyroid disease, or having a history of thyroid disease. In some cases of ICM administration, preventive therapy using antithyroid drugs, for example, methimazole, is given (Lee et al., 2015), illustrating that the risks following acute iodine exposure are acknowledged in medical fields.

Seaweed is a diverse group, and the iodine content may vary widely between species (Duinker et al., 2020); however, a large variety of seaweed does not accumulate high amounts of iodine content. The risk of consuming excessive iodine from seaweed will, therefore, depend on the species and amounts consumed. From this review, it seems that adverse health effects from acute excessive iodine exposure may emerge at higher doses than those seen in the studies on chronic excessive iodine exposure. However, the evidence is limited. The UL for iodine is the maximum level of total chronic intake. Since seaweed is consumed infrequently by many, this could result in occasional, rather than chronic, high iodine intakes. Whether an occasional iodine intake above the UL could pose a risk is a topic that needs further investigation. To the best of our knowledge, no safe upper intake level is established for acute iodine exposure. According to the literature on ICM administration, intakes ranging from 2500 to 5000 µg of bioavailable iodine increase the risk of thyroid dysfunction, even if ingested once or occasionally (Lee et al., 2015). Extreme iodine intakes (>2500 µg, equivalent to 1 g unprocessed, dry sugar kelp) could, therefore, cause a health risk even for occasional seaweed consumers. However, data for occasional high iodine exposure are lacking, and the safe upper limit for occasional high iodine intake may be well below 2500 µg.

4.2 | Seaweed inclusion levels in foods

Adding seaweed to foods must be done thoughtfully to avoid the risk of exceeding thresholds for iodine intake. By exceeding the UL, the risk of an adverse health effect increases. The NOAEL is the highest concentration of a substance where no adverse effect has been detected in the studied populations; thus, by exceeding this limit, the risk of an adverse health effect would increase further. Indeed, adverse effects have been observed with iodine intakes above the NOAEL for iodine. In the modeled scenarios for iodine inclusion, the addition of 50–150 µg of iodine per portion size resulted in most of the women (>92%) remaining below the threshold of 600 µg iodine/day if consuming between one and three portions of seaweed-containing foods per day (Table 5). As shown in Table 4, the addition of 1 g of dried seaweed per portion size easily surpasses 50–150 µg of iodine, even when applying processed seaweeds. This suggests that both species- and processing-specific calculations are needed to determine appropriate inclusion levels of seaweed in foods. High inclusion rates of 150–600 µg iodine/portion led to most women (>97%) surpassing the maximum recommended daily intake and some exceeding the NOAEL of 1800 µg/day (5%–12%).

Some population groups should be especially careful with excessive iodine consumption, including persons with underlying thyroid disease, neonates, pregnant and lactating women, and older persons. According to a meta-analysis conducted by Garmendia Madariaga et al. (2014), 6.7% of the European population had undiagnosed thyroid dysfunction assessed biochemically, including hypo- and hyperthyroidism, with most cases being subclinical. The proportion of the European population estimated to be pregnant (numbers from 2021) was 0.9%.[2] Thus, it can be estimated that 5%–10% of the European population is especially susceptible to iodine excess. High iodine inclusion rates in food items (i.e., 150–600 µg iodine/portion) could pose a health risk for these consumers.

In Norway, it is currently not mandatory to label seaweed food products with iodine content. This has, however, been a concern for decades, and already in 1991, a paper in the journal for the Norwegian Medical Association concluded that "nature products" contain-

[2] Calculated based on the number of born children, that is, not factoring multiple pregnancies or loss during pregnancy or birth.

ing iodine should be subject to public control and that the iodine content should be regulated. In the same paper, several cases of hypo- and hyperthyroidism were found in Norwegian patients following the consumption of iodine-containing supplements or seaweeds, though all cases normalized after discontinuing these products (Jørgensen & Svindland, 1991). The Norwegian Food Safety Authority (NFSA) published, in 2024, guidance on the production and marketing of seaweed and kelp as food (NFSA, 2024). Regarding iodine, as well as metals, the NFSA recommends developing a plan for sampling and analyses to control the content of iodine in the products. The heterogeneity of the analyte needs to be considered in such a plan. For iodine, the content may vary both within and between species and may also vary considerably with different processing techniques (Blikra, Henjum, et al., 2022). These aspects are important to consider when choosing sampling methods and analyzing the results. The EU recommendation (EU) 2018/464 on monitoring metals and iodine in seaweeds used as food and feed (European Commission, 2018) refers to the sampling procedures for iodine stating that they must be conducted in accordance with Commission Regulation (EC) No 333/2007.

It is also appropriate to mention that although these inclusion levels of seaweed in food are small, they can still contribute to taste and functionality beyond iodine fortification (e.g., Blikra et al., 2021; Gullón et al., 2021; Rioux et al., 2017; Vilar et al., 2020). Seaweed can thus provide a useful food ingredient, but it is necessary to monitor and control the iodine content in the resulting food products to avoid excessive intake.

4.3 | Limitations of the study

This narrative review does not employ the rigorous approach of a systematic review, and therefore, the results presented cannot be considered as a summarization of evidence with a degree of certainty. Though we are confident to have obtained relevant literature to enlighten this topic, since no systematic search was done, we cannot rule out that important studies were left out. We have included studies of variable size and design, most of which are of observational design and therefore not optimal to assess causal relationships between iodine intake and health consequences. Furthermore, no risk of bias assessment has been made; thus, we cannot account for potential bias in the included studies. Yet, even if this review cannot be compared to the evidence of a systematic review, we believe that this work highlights some important topics and provides considerable insights into this field of emerging consumer importance. Additionally, if taking a hazard identification approach, adverse effects have been reported from excessive iodine intakes, which implies that precaution should be applied and further investigations should be conducted.

4.4 | Recommendations for future research

We highlight that the literature on chronic and acute iodine exposure from seaweed remains scarce, and conflicting results exist. To be able to assess the burden of evidence in this area, we call for robust systematic reviews on both acute and chronic exposure in relation to the different outcomes outlined in this paper. As there are several difficulties in assessing the potential risk of excessive iodine intake in randomized controlled trials, we believe studies of both experimental and observational design should be included. In addition, studies quantifying the health risks of chronic/acute excessive iodine consumption and studies enabling or performing modeling of the risk/benefit of seaweed inclusion in the diet (e.g., DALYs), considering both iodine deficiency/excess and other constituents (e.g., heavy metals, bioactive components, fiber, etc.), are called for.

5 | CONCLUSION

Macroalgae concentrate iodine, and many species contain high amounts of iodine. Negative health outcomes for both chronic and acute iodine exposures were found in this review. Vulnerable groups, including persons with underlying thyroid disease and pregnant women are especially susceptible and estimated to be in the range of 5%–10% of the European population. The chronic and acute iodine exposures needed to result in negative health outcomes may easily be ingested by macroalgae consumption. Thus, we believe there are good reasons to be cautious when recommending macroalgae to the general population. However, the addition of macroalgae to food could be done in such a way that safe limits are not surpassed, such as by the addition of small amounts of processed algae of a species with a preferably lower iodine content. As of now, macroalgae is treated as a collective term, and in the future, it might be useful to divide recommendations into different species, since the iodine content in different species varies dramatically. The ambiguity of seaweed as a healthy food item is, however, difficult to communicate to the general public, and industrial applications may be easier to envisage than domestic use, since even small amounts of seaweed may provide functionality beyond iodine fortification and taste.

AUTHOR CONTRIBUTIONS

Marthe Jordbrekk Blikra: Conceptualization; methodology; software; data curation; investigation; formal analysis; funding acquisition; visualization; writing—original draft; writing—review and editing. **Inger Aakre**: Conceptualization; methodology; data curation; investigation; validation; funding acquisition; visualization; writing—original draft; writing—review and editing; project administration. **Jessica Rigutto-Farebrother**: Conceptualization; data curation; investigation; supervision; validation; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

ORCID

Marthe Jordbrekk Blikra https://orcid.org/0000-0002-9666-0067
Inger Aakre https://orcid.org/0000-0002-3046-1823

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. https://doi.org/10.29219/fnr.v65.7584

Abel, M. H., Caspersen, I. H., Meltzer, H. M., Haugen, M., Brandlistuen, R. E., Aase, H., Alexander, J., Torheim, L. E., & Brantsæter, A. L. (2017). Suboptimal maternal iodine intake is associated with impaired child neurodevelopment at 3 years of age in the Norwegian mother and child cohort study. *Journal of Nutrition*, *147*(7), 1314–1324. https://doi.org/10.3945/jn.117.250456

Abel, M. H., Ystrom, E., Caspersen, I. H., Meltzer, H. M., Aase, H., Torheim, L. E., Askeland, R. B., Reichborn-Kjennerud, T., & Brantsæter, A. L. (2017). Maternal iodine intake and offspring attention-deficit/hyperactivity disorder: Results from a large prospective cohort study. *Nutrients*, *9*(11), Article 1239. https://doi.org/10.3390/nu9111239

Aburto, N. J., Abudou, M., Candeias, V., Wu, T., & Organization, W. H. (2014). *Effect and safety of salt iodization to prevent iodine deficiency disorders: A systematic review with meta-analyses*. World Health Organization.

Bangmei, X., & Abbott, I. A. (1987). Edible seaweeds of China and their place in the Chinese diet. *Economic Botany*, *41*(3), 341–353. https://doi.org/10.1007/BF02859049

Bassett, J. H. D., & Williams, G. R. (2016). Role of thyroid hormones in skeletal development and bone maintenance. *Endocrine Reviews*, *37*(2), 135–187. https://doi.org/10.1210/er.2015-1106

Bernal, J. (2005). Thyroid hormones and brain development. *Vitamins & Hormones*, *71*, 95–122.

Blikra, M. J., Altintzoglou, T., Løvdal, T., Rognså, G., Skipnes, D., Skåra, T., Sivertsvik, M., & Noriega Fernández, E. (2021). Seaweed products for the future: Using current tools to develop a sustainable food industry. *Trends in Food Science & Technology*, *118*, 765–776. https://doi.org/10.1016/j.tifs.2021.11.002

Blikra, M. J., Henjum, S., & Aakre, I. (2022). Iodine from brown algae in human nutrition, with an emphasis on bioaccessibility, bioavailability, chemistry, and effects of processing: A systematic review. *Comprehensive Reviews in Food Science and Food Safety*, *21*(2), 1517–1536. https://doi.org/10.1111/1541-4337.12918

Blikra, M. J., Rode, T. M., Skåra, T., Maribu, I., Sund, R., Risa Vaka, M., & Skipnes, D. (2024). Processing of sugar kelp: Effects on mass balance, nutrient composition, and color. *LWT - Food Science and Technology*, *203*, Article 116402. https://doi.org/10.1016/j.lwt.2024.116402

Blikra, M. J., Skipnes, D., & Skåra, T. (2022). On the use of pulsed electric field technology as a pretreatment to reduce the content of potentially toxic elements in dried *Saccharina latissima*. *LWT - Food Science and Technology*, *169*, Article 114033. https://doi.org/10.1016/j.lwt.2022.114033

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

Bougma, K., Aboud, F. E., Harding, K. B., & Marquis, G. S. (2013). Iodine and mental development of children 5 years old and under: A systematic review and meta-analysis. *Nutrients*, *5*(4), 1384–1416. https://doi.org/10.3390/nu5041384

Brent, G. A. (2012). Mechanisms of thyroid hormone action. *Journal of Clinical Investigation*, *122*(9), 3035–3043.

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

Bülow Pedersen, I., Laurberg, P., Knudsen, N., Jørgensen, T., Perrild, H., Ovesen, L., & Rasmussen, L. B. (2006). Increase in incidence of hyperthyroidism predominantly occurs in young people after iodine fortification of salt in Denmark. *The Journal of Clinical Endocrinology & Metabolism*, *91*(10), 3830–3834. https://doi.org/10.1210/jc.2006-0652

Cabello, G., & Wrutniak, C. (1989). Thyroid hormone and growth: Relationships with growth hormone effects and regulation. *Reproduction Nutrition Development*, *29*(4), 387–402.

Candido, A. C., Vieira, A. A., de Souza Ferreira, E., Moreira, T. R., do Carmo Castro Franceschini, S., & Cotta, R. M. M. (2023). Prevalence of excessive iodine intake in pregnancy and its health consequences: Systematic review and meta-analysis. *Biological Trace Element Research*, *201*(6), 2784–2794. https://doi.org/10.1007/s12011-022-03401-5

Cherry, P., O'Hara, C., Magee, P. J., McSorley, E. M., & Allsopp, P. J. (2019). Risks and benefits of consuming edible seaweeds. *Nutrition Reviews*, *77*(5), 307–329. https://doi.org/10.1093/nutrit/nuy066

Chiamolera, M. I., & Wondisford, F. E. (2009). Thyrotropin-releasing hormone and the thyroid hormone feedback mechanism. *Endocrinology*, *150*(3), 1091–1096.

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

Conn, J. J., Sebastian, M. J., Deam, D., Tam, M., & Martin, F. (1996). A prospective study of the effect of nonionic contrast media on thyroid function. *Thyroid*, *6*(2), 107–110.

Correia, H., Soares, C., Morais, S., Pinto, E., Marques, A., Nunes, M. L., Almeida, A., & Delerue-Matos, C. (2021). Seaweeds rehydration and boiling: Impact on iodine, sodium, potassium, selenium, and total arsenic contents and health benefits for consumption. *Food and Chemical Toxicology*, *155*, Article 112385. https://doi.org/10.1016/j.fct.2021.112385

de Smet, P. A., Stricker, B. H., Wilderink, F., & Wiersinga, W. M. (1990). Hyperthyroidism during treatment with kelp tablets [In Dutch]. *Ned Tijdschr Geneeskd*, *134*(21), 1058–1059.

Dineva, M., Fishpool, H., Rayman, M. P., Mendis, J., & Bath, S. C. (2020). Systematic review and meta-analysis of the effects of iodine supplementation on thyroid function and child neurodevelopment in mildly-to-moderately iodine-deficient pregnant women. *The American Journal of Clinical Nutrition*, *112*(2), 389–412.

Du, Y., Gao, Y., Meng, F., Liu, S., Fan, Z., Wu, J., & Sun, D. (2014). Iodine deficiency and excess coexist in China and induce thyroid dysfunction and disease: A cross-sectional study. *PLoS ONE*, *9*(11), Article e111937. https://doi.org/10.1371/journal.pone.0111937

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).

European Food Safety Authority (EFSA). Dujardin, B., Ferreira de Sousa, R., & Gómez Ruiz, J. A.. (2023). Dietary exposure to heavy metals and iodine intake via consumption of seaweeds and halophytes in the European population. *EFSA Journal*, *21*(1), Article e07798. https://doi.org/10.2903/j.efsa.2023.7798

European Food Safety Authority (EFSA). (2018). *Overview on tolerable upper intake levels as derived by the Scientific Committee on Food (SCF) and the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)*. Author.

Eliason, B. C. (1998). Transient hyperthyroidism in a patient taking dietary supplements containing kelp. *The Journal of the American Board of Family Practice*, *11*(6), 478–480. https://doi.org/10.3122/jabfm.11.6.478

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.x

European Commission. (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*, *L 78*, 16–18.

Farebrother, J., Zimmermann, M. B., & Andersson, M. (2019). Excess iodine intake: Sources, assessment, and effects on thyroid function. *Annals of the New York Academy of Sciences*, *1446*(1), 44–65.

Farebrother, J., Zimmermann, M. B., Abdallah, F., Assey, V., Fingerhut, R., Gichohi-Wainaina, W. N., Hussein, I., Makokha, A., Sagno, K., Untoro, J., Watts, M., & Andersson, M. (2018). Effect of excess iodine intake from iodized salt and/or groundwater iodine on thyroid function in nonpregnant and pregnant women, infants, and children: A multicenter study in East Africa. *Thyroid*, *28*(9), 1198–1210. https://doi.org/10.1089/thy.2018.0234

Feldt-Rasmussen, U. (2001). Iodine and cancer. *Thyroid*, *11*(5), 483–486. https://doi.org/10.1089/105072501300176435

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

Garmendia Madariaga, A., Santos Palacios, S., Guillén-Grima, F., & Galofré, J. C. (2014). The incidence and prevalence of thyroid dysfunction in Europe: A meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*, *99*(3), 923–931. https://doi.org/10.1210/jc.2013-2409

Gherbon, A., Frandes, M., Lungeanu, D., Nicula, M., & Timar, R. (2019). Transient hyperthyroidism following the ingestion of complementary medications containing kelp seaweed: A case-report. *Medicine*, *98*(37), Article e17058. https://doi.org/10.1097/md.0000000000017058

Gullón, P., Astray, G., Gullón, B., Franco, D., Campagnol, P. C. B., & Lorenzo, J. M. (2021). Inclusion of seaweeds as healthy approach to formulate new low-salt meat products. *Current Opinion in Food Science*, *40*, 20–25. https://doi.org/10.1016/j.cofs.2020.05.005

Haldimann, M., Alt, A., Blanc, A., & Blondeau, K. (2005). Iodine content of food groups. *Journal of Food Composition and Analysis*, *18*(6), 461–471. https://doi.org/10.1016/j.jfca.2004.06.003

Hamby, T., Kunnel, N., Dallas, J. S., & Wilson, D. P. (2018). Maternal iodine excess: An uncommon cause of acquired neonatal hypothyroidism. *Journal of Pediatric Endocrinology and Metabolism*, *31*(9), 1061–1064. https://doi.org/10.1515/jpem-2018-0138

Henjum, S., Brantsæter, A. L., Holvik, K., Lillegaard, I. T. L., Mangschou, B., Parr, C. L., Starrfelt, J., Stea, T. H., Andersen, L. F., & Dahl, L. J. (2020). *Benefit and risk assessment of iodization of household salt and salt used in bread and bakery products. Opinion of the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of the Norwegian Scientific Committee for Food and Environment*. Norwegian Scientific Committee for Food and Environment (VKM).

Hetzel, B. S. (1983). Iodine deficiency disorders (IDD) and their eradication. *Lancet*, *2*(8359), 1126–1129.

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

Inoue, M., Taketani, N., Sato, T., & Nakajima, H. (1975). High incidence of chronic lymphocytic thyroiditis in apparently healthy school children: Epidemiological and clinical study. *Endocrinologia Japonica*, *22*(6), 483–488.

Ju, D. L., Cho, S. W., Chung, C. W., Lee, Y. A., Cheon, G. J., Park, Y. J., Shin, C. H., Jun, J. K., Chung, J.-K., Park, S. K., & Song, Y. (2023). High intakes of iodine among women during pregnancy and the postpartum period has no adverse effect on thyroid function. *European Journal of Nutrition*, *62*(1), 239–249. https://doi.org/10.1007/s00394-022-02960-6

Jørgensen, H., & Svindland, O. (1991). Hyper- and hypothyreosis due to iodine-containing "health products" [In Norwegian]. *Tidsskriftet Norske Lægeforening*, *111*, 3153–3155.

Kim, H. J., Kim, N. K., Park, H. K., Byun, D. W., Suh, K., Yoo, M. H., Min, Y. K., Kim, S. W., & Chung, J. H. (2017). Strong association of relatively low and extremely excessive iodine intakes with thyroid cancer in an iodine-replete area. *European Journal of Nutrition*, *56*(3), 965–971. https://doi.org/10.1007/s00394-015-1144-2

Kim, J. Y., & Kim, K. R. (2000). Dietary iodine intake and urinary iodine excretion in patients with thyroid diseases. *Yonsei Medical Journal*, *41*(1), 22–28. https://synapse.koreamed.org/upload/synapsedata/pdfdata/0069ymj/ymj-41-22.pdf

Kim, K., Cho, S. W., Park, Y. J., Lee, K. E., Lee, D. W., & Park, S. K. (2021). Association between iodine intake, thyroid function, and papillary thyroid cancer: A case-control study. *Endocrinology and Metabolism*, *36*(4), 790–799. https://doi.org/10.3803/EnM.2021.1034

Kitahara, C. M., & Schneider, A. B. (2022). Epidemiology of thyroid cancer. *Cancer Epidemiology, Biomarkers & Prevention*, *31*(7), 1284–1297. https://doi.org/10.1158/1055-9965.Epi-21-1440

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

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 of the United States of America*, *105*(19), 6954–6958. https://doi.org/10.1073/pnas.0709959105

Laron, Z. (2003). Interactions between the thyroid hormones and the hormones of the growth hormone axis. *Pediatric Endocrinology Reviews*, *1*(Suppl. 2), 244–249–discussion 250. http://europepmc.org/abstract/MED/16444165

Laurberg, P., Pedersen, I. B., Knudsen, N., Ovesen, L., & Andersen, S. (2001). Environmental iodine intake affects the type of nonmalignant thyroid disease. *Thyroid*, *11*(5), 457–469. https://doi.org/10.1089/105072501300176417

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. R. Preedy, G. N. Burrow, & R. Watson (Eds.), *Comprehensive handbook of iodine: Nutritional, biochemical, pathological and therapeutic aspects* (pp. 449–455). Elsevier Inc.

Laurberg, P., Pedersen, K. M., Vestergaard, H., & Sigurdsson, G. (1991). High incidence of multinodular toxic goitre in the elderly population in a low iodine intake area vs. high incidence of Graves' disease in the young in a high iodine intake area: Comparative surveys of thyrotoxicosis epidemiology in East-Jutland Denmark and Iceland. *Journal of Internal Medicine*, *229*(5), 415–420. https://doi.org/10.1111/j.1365-2796.1991.tb00368.x

Lee, S. Y., Rhee, C. M., Leung, A. M., Braverman, L. E., Brent, G. A., & Pearce, E. N. (2015). A review: Radiographic iodinated contrast media-induced thyroid dysfunction. *The Journal of Clinical Endocrinology & Metabolism*, *100*(2), 376–383. https://doi.org/10.1210/jc.2014-3292

Li, F., Wan, S., Zhang, L., Li, B., He, Y., Shen, H., & Liu, L. (2022). A meta-analysis of the effect of iodine excess on the intellectual development of children in areas with high iodine levels in their drinking water. *Biological Trace Element Research*, *200*(4), 1580–1590. https://doi.org/10.1007/s12011-021-02801-3

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), Article 1270. https://doi.org/10.3390/nu10091270

Markou, K., Georgopoulos, N., Kyriazopoulou, V., & Vagenakis, A. G. (2001). Iodine-induced hypothyroidism. *Thyroid*, *11*(5), 501–510. https://doi.org/10.1089/105072501300176462

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

McHugh, D. J. (2003). *A guide to the seaweed industry* (Fisheries Technical Paper No. 441). FAO.

Michikawa, T., Inoue, M., Shimazu, T., Sawada, N., Iwasaki, M., Sasazuki, S., Yamaji, T., Tsugane, S., & Japan Public Health Center-based Prospective Study Group. (2012). Seaweed consumption and the risk of thyroid cancer in women. *European Journal of Cancer Prevention*, *21*(3), 254–260. https://www.jstor.org/stable/48504137

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

Morrissey, J., Kraan, S., & Guiry, M. D. (2001). *A guide to commercially important seaweeds on the Irish coast*. Irish Bord Iascaigh Mhara/Irish Sea Fisheries Board. https://www.seaweed.ie/pdf/BIM%20Guide.pdf

Mostbeck, A., Galvan, G., Bauer, P., Eber, O., Atefie, K., Dam, K., Feichtinger, H., Fritzsche, H., Haydl, H., Köhn, H., König, B., Koriska, K., Kroiss, A., Lind, P., Markt, B., Maschek, W., Pesl, H., Ramschak-Schwarzer, S., Riccabona, G., … Zechmann, W. (1998). The incidence of hyperthyroidism in Austria from 1987 to 1995 before and after an increase in salt iodization in 1990. *European Journal of Nuclear Medicine*, *25*(4), 367–374. https://doi.org/10.1007/s002590050234

Müssig, K., Thamer, C., Bares, R., Lipp, H. P., Häring, H. U., & Gallwitz, B. (2006). Iodine-induced thyrotoxicosis after ingestion of kelp-containing tea. *Journal of General Internal Medicine*, *21*(6), C11–C14. https://doi.org/10.1111/j.1525-1497.2006.00416.x

Nazeri, P., Kabir, A., Dalili, H., Mirmiran, P., & Azizi, F. (2018). Breast-milk iodine concentrations and iodine levels of infants according to the iodine status of the country of residence: A systematic review and meta-analysis. *Thyroid*, *28*(1), 124–138. https://doi.org/10.1089/thy.2017.0403

Norwegian Food Safety Authority (NFSA). (2024). *Veileder om produksjon og omsetning av tang og tare som mat [Guidelines for production and sale of seaweed as food]*. https://www.mattilsynet.no/mat-og-drikke/matproduksjon/fisk-og-sjomat/veileder-om-produksjon-og-omsetting-av-tang-og-tare-som-mat

Nguyen, C. T., Sasso, E. B., Barton, L., & Mestman, J. H. (2018). Graves' hyperthyroidism in pregnancy: A clinical review. *Clinical Diabetes and Endocrinology*, *4*, Article 4. https://doi.org/10.1186/s40842-018-0054-7

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), Article 569. https://doi.org/10.3390/foods9050569

Nishiyama, S., Mikeda, T., Okada, T., Nakamura, K., Kotani, T., & Hishinuma, A. (2004). Transient hypothyroidism or persistent hyperthyrotropinemia in neonates born to mothers with excessive iodine intake. *Thyroid*, *14*(12), 1077–1083. https://doi.org/10.1089/thy.2004.14.1077

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

Noahsen, P., Kleist, I., Larsen, H. M., & Andersen, S. (2020). Intake of seaweed as part of a single sushi meal, iodine excretion and thyroid function in euthyroid subjects: A randomized dinner study. *Journal of Endocrinological Investigation*, *43*(4), 431–438. https://doi.org/10.1007/s40618-019-01122-6

Orito, Y., Oku, H., Kubota, S., Amino, N., Shimogaki, K., Hata, M., Manki, K., Tanaka, Y., Sugino, S., Ueta, M., Kawakita, K., Nunotani, T., Tatsumi, N., Ichihara, K., Miyauchi, A., & Miyake, M. (2009). Thyroid function in early pregnancy in Japanese healthy women: Relation to urinary iodine excretion, emesis, and fetal and child development. *The Journal of Clinical Endocrinology & Metabolism*, *94*(5), 1683–1688. https://doi.org/10.1210/jc.2008-2111

Paiva, L., Lima, E., Patarra, R. F., Neto, A. I., & Baptista, J. (2014). Edible Azorean macroalgae as source of rich nutrients with impact on human health. *Food Chemistry*, *164*, 128–135. https://doi.org/10.1016/j.foodchem.2014.04.119

Partal-Lorente, A. B., Maldonado-Ezequiel, V., Martinez-Navarro, L., Herrera-Contreras, I., Gutierrez-Repiso, C., García-Fuentes, E., & Santiago-Fernandez, P. (2017). Iodine is associated to semen quality in men who undergo consultations for infertility. *Reproductive Toxicology*, *73*, 1–7. https://doi.org/10.1016/j.reprotox.2017.07.020

Pennington, J. A. (1990). A review of iodine toxicity reports. *Journal of the American Dietetic Association*, *90*(11), 1571–1581.

Rhee, S. S., Braverman, L. E., Pino, S., He, X., & Pearce, E. N. (2011). High iodine content of Korean seaweed soup: A health risk for lactating women and their infants? *Thyroid*, *21*(8), 927–928. https://doi.org/10.1089/thy.2011.0084

Rigutto-Farebrother, J. (2023). Optimizing growth: The case for iodine. *Nutrients*, *15*(4), Article 814. https://doi.org/10.3390/nu15040814

Rioux, L.-E., Beaulieu, L., & Turgeon, S. L. (2017). Seaweeds: A traditional ingredients for new gastronomic sensation. *Food Hydrocolloids*, *68*, 255–265. https://doi.org/10.1016/j.foodhyd.2017.02.005

Robson, H., Siebler, T., Shalet, S. M., & Williams, G. R. (2002). Interactions between GH, IGF-I, glucocorticoids, and thyroid hormones during skeletal growth. *Pediatric Research*, *52*(2), 137–147. https://doi.org/10.1203/00006450-200208000-00003

Roti, E., & Uberti, E. D. (2001). Iodine excess and hyperthyroidism. *Thyroid*, *11*(5), 493–500. https://doi.org/10.1089/105072501300176453

Sang, Z., Chen, W., Shen, J., Tan, L., Zhao, N., Liu, H., Wen, S., Wei, W., Zhang, G., & Zhang, W. (2013). Long-term exposure to excessive iodine from water is associated with thyroid dysfunction in children. *Journal of Nutrition*, *143*(12), 2038–2043.

Shilo, S., & Hirsch, H. J. (1986). Iodine-induced hyperthyroidism in a patient with a normal thyroid gland. *Postgraduate Medical Journal*, *62*(729), 661–662. https://doi.org/10.1136/pgmj.62.729.661

Stévant, P., Duinker, A., Larssen, W. E., Krook, J. L., Birkeland, I. M., Bjelland, L. A. B., Chapman, A., Hogstad, S., McStay, R. N., & Sveier, H. (2021). *Methods for iodine-reduction of sugar kelp to produce safe, flavourful and nutritious ingredient to the food industry (Report 2115)*. Møreforsking. https://www.moreforsk.no/download.aspx?object_id=upload_images/C17991248E544C109705892363C306A6.pdf

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

Sullivan, T. R., Best, K. P., Gould, J., Zhou, S. J., Makrides, M., & Green, T. J. (2024). Too much too little: Clarifying the relationship between maternal iodine intake and neurodevelopmental outcomes. *The Journal of Nutrition*, *154*(1), 185–190. https://doi.org/10.1016/j.tjnut.2023.09.008

Sun, N., Sun, B., Li, C., Zhang, J., & Yang, W. (2022). Effects of different pretreatment methods and dietary factors on the form and bioavailability of iodine in Laminaria japonica. *Journal of Aquatic Food Product Technology*, *31*(2), 154–169. https://doi.org/10.1080/10498850.2021.2024313

Sun, Y., Chen, C., Liu, G. G., Wang, M., Shi, C., Yu, G., Lv, F., Wang, N., & Zhang, S. (2020). The association between iodine intake and semen quality among fertile men in China. *BMC Public Health*, *20*(1), Article 461. https://doi.org/10.1186/s12889-020-08547-2

Suzuki, H. (1973). Further studies of "Endemic coast goiter" in Hokkaido, Japan. *Iodine Metabolism and Thyroid Function*, 143–157.

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

Tajiri, J., Higashi, K., Morita, M., Umeda, T., & Sato, T. (1986). Studies of hypothyroidism in patients with high iodine intake. *The Journal of Clinical Endocrinology & Metabolism*, *63*(2), 412–417. https://doi.org/10.1210/jcem-63-2-412

Takase, T., Nakamura, A., Miyoshi, H., Koga, M., Toyomaki, A., Kusumi, I., Kino, R., Konishi, Y., Kiso, Y., & Atsumi, T. (2020). Effects of *Palmaria palmata* on lipid metabolism and glycemic control in participants with hypercholesterolemia in a randomized double-blind placebo-controlled trial. *Phytotherapy Research*, *34*(9), 2303–2312. https://doi.org/10.1002/ptr.6680

Taylor, P. N., Razvi, S., Pearce, S. H., & Dayan, C. M. (2013). A review of the clinical consequences of variation in thyroid function within the reference range. *The Journal of Clinical Endocrinology & Metabolism*, *98*(9), 3562–3571. https://doi.org/10.1210/jc.2013-1315

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

Todd, C. H., & Dunn, J. T. (1998). Intermittent oral administration of potassium iodide solution for the correction of iodine deficiency. *The American Journal of Clinical Nutrition*, *67*(6), 1279–1283. https://doi.org/10.1093/ajcn/67.6.1279

Todd, C. H., Allain, T., Gomo, Z. A., Hasler, J. A., Ndiweni, M., & Oken, E. (1995). Increase in thyrotoxicosis associated with iodine supplements in Zimbabwe. *Lancet*, *346*(8989), 1563–1564. https://doi.org/10.1016/s0140-6736(95)92095-1

van den Boogaard, E., Vissenberg, R., Land, J. A., van Wely, M., van der Post, J. A. M., Goddijn, M., & Bisschop, P. H. (2011). Significance of (sub)clinical thyroid dysfunction and thyroid autoimmunity before conception and in early pregnancy: A systematic review. *Human Reproduction Update*, *17*(5), 605–619. https://doi.org/10.1093/humupd/dmr024

Vilar, E. G., Ouyang, H., O'Sullivan, M. G., Kerry, J. P., Hamill, R. M., O'Grady, M. N., Mohammed, H. O., & Kilcawley, K. N. (2020). Effect of salt reduction and inclusion of 1% edible seaweeds on the chemical, sensory and volatile component profile of reformulated frankfurters. *Meat Science*, *161*, Article 108001. https://doi.org/10.1016/j.meatsci.2019.108001

Walker, S. P., Wachs, T. D., Grantham-McGregor, S., Black, M. M., Nelson, C. A., Huffman, S. L., Baker-Henningham, H., Chang, S. M., Hamadani, J. D., Lozoff, B., Gardner, J. M., Powell, C. A., Rahman, A., & Richter, L. (2011). Inequality in early childhood: Risk and protective factors for early child development. *Lancet*, *378*(9799), 1325–1338. https://doi.org/10.1016/s0140-6736(11)60555-2

Wang, C., Yatsuya, H., Li, Y., Ota, A., Tamakoshi, K., Fujino, Y., Mikami, H., Iso, H., & Tamakoshi, A. (2016). Prospective study of seaweed consumption and thyroid cancer incidence in women: The Japan collaborative cohort study. *European Journal of Cancer Prevention*, *25*(3), 239–245. https://doi.org/10.1097/cej.0000000000000168

World Health Organization (WHO). (2007a). *Assessment of iodine deficiency disorders and monitoring their elimination: A guide for programme managers*. Author.

World Health Organization (WHO). (2007b). *Iodine deficiency in Europe: A continuing public health problem*. Author.

Williams, G. R. (2013). Thyroid hormone actions in cartilage and bone. *European Thyroid Journal*, *2*(1), 3–13.

Wu, W., Chen, Y., Guo, W., Zhang, K., Chen, W., Fu, M., Pan, Z., Yang, Y., Zhang, N., & Zhang, W. (2023). The relationship between iodine excess and thyroid function during pregnancy and infantile neurodevelopment at 18–24 months. *The Journal of Nutrition*, *153*(8), 2320–2327. https://doi.org/10.1016/j.tjnut.2023.05.012

Xiao, Y., Sun, H., Li, C., Li, Y., Peng, S., Fan, C., Teng, W., & Shan, Z. (2018). Effect of iodine nutrition on pregnancy outcomes in an iodine-sufficient area in China. *Biological Trace Element Research*, *182*(2), 231–237. https://doi.org/10.1007/s12011-017-1101-4

Xu, T., Ren, Z., Li, S., Tan, L., & Zhang, W. (2021). The relationship of different levels of high iodine and goiter in school children: A meta-analysis. *Nutrition & Metabolism*, *18*(1), Article 46. https://doi.org/10.1186/s12986-021-00563-2

Yan, A. R., Zhang, X., Shen, H., Zhou, X., Li, R., & Yuan, Z. (2019). Urinary iodine is increased in papillary thyroid carcinoma but is not altered by regional population iodine intake status: A meta-analysis and implications. *Endocrine Journal*, *66*(6), 497–514. https://doi.org/10.1507/endocrj.EJ18-0532

Yang, J., Liu, Y., Liu, H., Zheng, H., Li, X., Zhu, L., & Wang, Z. (2018). Associations of maternal iodine status and thyroid function with adverse pregnancy outcomes in Henan Province of China. *Journal of Trace Elements in Medicine and Biology*, *47*, 104–110. https://doi.org/10.1016/j.jtemb.2018.01.013

Yen, P. M. (2001). Physiological and molecular basis of thyroid hormone action. *Physiological Reviews*, *81*(3), 1097–1142. https://doi.org/10.1152/physrev.2001.81.3.1097

Zava, T. T., & Zava, D. T. (2011). Assessment of Japanese iodine intake based on seaweed consumption in Japan: A literature-based analysis. *Thyroid Research*, *4*, Article 14. https://doi.org/10.1186/1756-6614-4-14

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

Zimmermann, M. B., & Galetti, V. (2015). Iodine intake as a risk factor for thyroid cancer: A comprehensive review of animal and human studies. *Thyroid Research*, *8*(1), Article 8. https://doi.org/10.1186/s13044-015-0020-8

Zimmermann, M. B., Ito, Y., Hess, S. Y., Fujieda, K., & Molinari, L. (2005). High thyroid volume in children with excess dietary iodine intakes. *The American Journal of Clinical Nutrition*, *81*(4), 840–844. https://doi.org/10.1093/ajcn/81.4.840

Zimmermann, M. B., Jooste, P. L., & Pandav, C. S. (2008). Iodine-deficiency disorders. *The Lancet*, *372*(9645), 1251–1262. https://doi.org/10.1016/S0140-6736(08)61005-3

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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