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Iodine Biofortification of Vegetables Could Improve Iodine Supplementation Status

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Abstract: Iodine is an essential trace element for both humans and animals. It is essential to produce important hormones by the thyroid gland. In most inland areas, the soils are iodine deficient and its amount is insufficient to produce agricultural crops with adequate iodine content to cover the recommended daily intake. In connection with the occurrence of iodine deficiency disorders (IDDs), it has been the subject of intensive research in the past. However, following the introduction of iodized table salt in the food industry, problems related to IDD were not solved and studies on iodine mobility and bioavailability from soils are rare even today and have remained insufficiently investigated. In many countries, mainly in Europe, the prescription rate of medicaments used to treat goiter is still high. Thus, there are a considerable amount of studies looking for alternative methods for iodine supplementation in foodstuffs among the use of iodized table salt. In most cases, the subject of these studies are agricultural crops. This mini review presents the consequences of inadequate and excess iodine intake, the current status of iodine supplementation and the most recent alternative methods of the application of iodine in agriculture and its effect on the quality of used plant species.

Keywords: iodine; biofortification; nutrition; vegetables; iodine deficiency

1. Introduction

Iodine is an essential micronutrient in humans, and although its deficiency-related disorders were a serious problem in the past, they still persist in some areas and have an endemic character. In the 1920s, the US [1] and Switzerland [2] were the first countries where table salt fortification with iodine began. Since the 1990s, several fortification programs were implemented and more than 70% of the world's population is estimated to be well supplied [3]. Still, the program seems to fail for several reasons in some other countries. Despite several existing methods battling iodine deficiency, this issue is still widespread, and it has reappeared in Australia and the UK. While in some countries only table salt is iodized, others also include iodine in salt for specific products (e.g., bread salt) [4]. A major goal is to fortify products in the food industry, but there is a misperception that the addition of fortified salt to processed food alters taste and color [5].

Rasmussen et al. [6] investigated through an 11-year follow-up study the effectiveness of the Danish iodine fortification program by evaluating urinary iodine excretion. They examined factors that could change iodine intake, such as dietary habits, education, lifestyle factors, and health parameters. Median urinary iodine concentration in the population had increased significantly during investigated years in all age and gender groups, but it was still below the recommended amount. The study showed that the increase in iodine excretion was positively associated with the usage of iodine supplements, the consumption of bread with iodine-fortified salt, and the higher milk intake, which is a natural source of iodine, thus, the iodine content there might be elevated due to cattle supplementation [7]. The strategy to combat iodine deficiency in Denmark seems to be working, however, the level of iodine fortification of salt is too low [6].

Charlton et al. [8] stated that mandatory fortification in Australia could be effective. However, there is inadequate knowledge about iodine requirements among the population. Overall knowledge regarding health implications of iodine deficiency was poor and dietary intake alone was insufficient to meet the increased needs of women during pregnancy. Only women taking iodine-containing supplements had adequate urinary iodine levels [8]. Since the mandatory salt iodization program in several countries started, the number of iodine-deficient countries in the world has decreased from 54 in 2003 to 32 in 2011. Surprisingly, 11 (34%) of these countries are developed countries in Europe [9]. During the year 2013, the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) performed a postal survey requesting information on the iodine status from the most affected areas in West and Central European regions. The results showed that at least 400 million people from 20 countries have no or limited access to iodized salt. Only 13 European countries responded that salt iodization is mandatory [4]. It is alarming that Europe has the most iodine-deficient countries from any continent [9]. This is a particularly important issue for iodine nutrition requirements during pregnancy and breastfeeding. In the past decade, the mild to moderate iodine deficiency in the first trimester of pregnancy among pregnant women in the UK was associated with a decrease in the intelligence quotient of offspring with a major negative impact on the verbal intelligence quotient [10]. Thyroid screening tests in Hungary among schoolchildren revealed that 21% of children had an enlarged thyroid gland, with significantly higher occurrence in boys (24.9%) than in girls (17.1%). Along with the occurrence of goiter, the median value of urinary iodide in half of the subjects showed a slight iodine deficiency [11]. The number of iodine-deficient countries worldwide divided into regions is listed in Table 1. The data clearly show that the current iodine supplementation is not sufficient, and the strategies for iodine status improvement worldwide should be changed. Insufficient or excessive iodine intake causes abortion, stillbirths, prenatal mortality, cretinism, goiter, endemic mental retardation, impaired mental function, hypo- and hyperthyroidism, autoimmune thyroid diseases, and increased susceptibility of the thyroid gland to nuclear radiation [12,13]. The recommended daily iodine intake for school-age children is listed in Table 2.

Table 1. Country data on median urinary iodine concentrations and urinary iodine concentrations in school-age children by region [13].

Region	Severe Iodine Deficiency [<20 $\mu g \cdot L^{-1}$]	Moderate Iodine Deficiency [20–49 $\mu g \cdot L^{-1}$]	Mild Iodine Deficiency [50–99 $\mu g \cdot L^{-1}$]	Optimal Iodine Nutrition [100–199 $\mu g \cdot L^{-1}$]	Risk of IIH in Susceptible Groups [200–299 $\mu g \cdot L^{-1}$]	Risk of Adverse Health Consequences [≥300 $\mu g \cdot L^{-1}$]	No Data
Africa	0	6	10	13	2	2	15
Asia	1	4	12	12	0	0	13
Europe	0	1	15	14	0	0	11
Latin America and the Caribbean	0	1	1	3	3	3	14
Northern America	0	0	0	0	0	0	1
Oceania	0	1	2	1	0	0	12
Total	1	13	40	43	5	5	60

Table 2. Criteria for assessing adequate daily iodine intake based on median urinary iodine (UI) concentrations in school-age children [13].

Median UI [μg L^{-1}]	Iodine Intake	Nutrition
<20	Insufficient	Severe iodine deficiency
20201349	Insufficient	Moderate iodine deficiency
50–99	Insufficient	Mild iodine deficiency
100–199	Adequate	Optimal iodine nutrition
200–299	More than adequate	Risk of iodine-induced hyperthyroidism in susceptible groups
>300	Excessive	Risk of adverse health consequences

2. Iodine in Foodstuffs

Table salt is the main target for iodine fortification in the human diet. According to the WHO [14], some assumptions must be taken into account for salt iodination strategy, such as iodine loss during storage and cooking. Almost 20% of iodine is lost during transport from production site to the household, and another 20% before consumption during the cooking process. Therefore, in order to provide a daily 150 μg iodine intake via iodized salt, the initial iodine concentration in the salt at the point of production must be within the range of 20–40 mg·kg^{-1}. With this and iodine intake only from the iodized salt, the urinary iodine levels should be 100–200 μg·L^{-1} [14].

In Europe, the permitted sources of iodine in table salt are KI, KIO_3, or NaI. In some countries, bread and processed food fortification is also mandatory [15]. For example, the use of iodinated bread salt has been mandatory since 2000 in Denmark because these foods are consumed by nearly everyone. Since then, it has been legal to sell non-fortified bread and salt only if they are produced in another country [6]. The main source of iodine in the diet is seafood. However, in inland regions, where the source of iodine is external to soils [16], it is mostly milk and dairy products, meat, and to a lesser extent, plants.

As indicated, cooking processes can affect the quantity of iodine in food due to its volatile nature. Goindi et al. [17] evaluated iodine loss during several different cooking procedures through several traditional recipes. They found out that the mean losses of iodine during the different procedures used, in descending order, were boiling (37%), shallow frying (27%), pressure cooking (22%), deep frying (20%), steaming (20%), and roasting (6%) [17]. However, Meinhardt et al. [18] did not observe significant iodine loss during cooking when using salt fortified with KIO_3 and concluded that waxy potatoes cut into small pieces and egg pasta showed the highest iodine uptake potential during cooking. The daily intake should not be much more than the recommended daily intake or maximum permitted level to prevent consequences of excessive intake [19]. The main sources of iodine in foodstuffs are presented in Table 3.

Table 3. Iodine content is selected foodstuffs.

Food	Iodine Concentration	Source
Milk	242 mg·kg^{-1}	[19]
Yogurt	266 mg·kg^{-1}	[19]
Cottage cheese	490 mg·kg^{-1}	[19]
Cheese	265 mg·kg^{-1}	[19]
Poultry meat	130 mg·kg^{-1}	[19]
Beef meat	113 mg·kg^{-1}	[19]
Fish	315 mg·kg^{-1}	[19]
Eggs	50–100 mg·kg^{-1}	[20]
Bread	2.2–584 μg per slice	[21]
Processed meat products	50–400 mg·kg^{-1}	[19]

3. Risk of Iodine-Induced Hyperthyroidism

Iodine-induced hyperthyroidism is related to the rapidity of the increase in iodine intake and occurs in populations that already have severe iodine deficiency. It usually disappears in due course with the correction of the iodine deficiency, and it appears in patients who have pre-existing autonomous nodular goiter and in subjects with latent Graves' disease [14]. The main substances which induce excessive iodine intake are listed in Table 4. To prevent iodine-induced hyperthyroidism, an adequate iodine intake for normal thyroid function is required [22], and kelp supplements containing more than 500 µg iodine should not be taken daily by patients with an iodine deficit [23]. Even the use of iodized salt can result in hyperthyroidism in deficient areas, probably from autoimmune origin [24]. Several iodine supplements, including iodinated contrast agents used for radiologic studies, contain iodine in much higher (several thousand-fold) concentrations than the recommended maximum daily intake. In susceptible individuals, these supplements can cause thyroid dysfunction after a single exposure, such as in patients with specific risk factors, including those with pre-existing thyroid disease among the elderly, fetuses, and neonates [25].

Table 4. Sources of excess iodine intake with potential thyroid disfunction risk.

Supplement/Food	Amount of Iodine	Source
Kelp	16–8165 $\mu g \cdot g^{-1}$	[25]
Prenatal vitamins	Non-prescription 11–610 per daily serving Prescription 26–220 µg per daily serving	[26,27]
Iodinated contrast	13,500 µg per CT scan	[24]
Saturated solution of potassium iodide	50,000 µg per drop	[24]

4. Iodine Biofortification in Plants

Plant iodine content is generally low, but still considered as an important source of dietary iodine for humans and grazing livestock [28]. Generally, iodine is toxic to plants but can be beneficial at low concentrations [29,30]. Its detrimental effects to specific plants depend on applied iodine species, mechanism of its uptake and transport by the plant, the sensitivity of the exposed organism and the mechanism of resistance, application method, and the properties of the used substrate [31]. The most effective method is foliar application for leafy vegetables [32].

Tonacchera et al. [33] proved that the consumption of biofortified vegetables mildly, but significantly, elevates urinary iodine concentration. The first successful in situ experiment on iodine biofortification was conducted by Jiang et al. [34]. Approximately 37,000 people were treated during this experiment. Potassium iodate was dripped into irrigation water on tilled land for four years. At the end of the experiment, the concentration of water-soluble iodine in the soil was three-fold higher than the concentration in the irrigation water, which declined subsequently with a half-life of two to four months, and declined to the level of neighboring non-treated soil iodine concentrations two years after the last dripping. Besides the increase in water-soluble soil iodine concentration, the uptake of iodine by plants (wheat, cabbage, maize, etc.) increased and persisted through three growing seasons. The thyroidal concentration of iodine increased three-fold in crop-fed chickens and sheep, but the increase was also observed in meat, eggs, and milk. Urinary iodine had increased significantly in all age groups and infant mortality decreased by 50% [34]. A similar study was conducted by the same authors a few years before this extensive field experiment with similarly positive results, thus, this method is considered as a cost-effective method of supplying iodine in areas dependent on irrigation [35]. Ren et al. [36] also used irrigation water treated with potassium iodate to soil fortification where, after a single application, soil iodine content increased two-fold and was available for more than four years after application.

Various studies proved that tomato is a suitable target plant for iodine biofortification and it can accumulate up to 10 mg of iodine per kg of tomato fresh weight [37] Iodide and iodate, having no serious detrimental effects on plant growth and development or fruit yield, were shown to be suitable for tomato biofortification, covering the recommended daily intake [38]. Mild phytotoxic symptoms were observed, including leaf chlorosis, wilting, and epinasty. However, probably due to sorption phenomena, the organic matter-rich soil alleviated the adverse effects, while only a mild reduction of accumulated iodine in fruits was observed [37]. The addition of exogenous humic acids, which are great iodine sorbents [39] and, thus, play a main role in its soil retention, also prevents the deleterious effects of iodine on plants [40,41]. Furthermore, biofortification did not affect the quality of tomato, and storage had no effect on the iodine content in biofortified tomato fruit. Surprisingly, boiling did not affect the iodine content, while peeling lowered its content in fruits, as the peel alone contained a significant amount of iodine [37]. Usually, fruit contains the least iodine, as its concentration in plants usually follows the sequence roots > leaves > stems > fruits [42].

Besides tomato, Li et al. [43] suggested that strawberries are also a suitable target for biofortification, with an accumulation of iodine up to 4000 $\mu g \cdot kg^{-1}$ of fresh weight. Therefore, one serving of the biofortified strawberries can easily cover the daily recommended intake (150 $\mu g \cdot day^{-1}$). Potassium iodide treatment also had several positive effects on the fruit quality of strawberry, such as increased biomass per plant and increased vitamin C and soluble sugar contents, however, the high concentrations had detrimental effects on plant growth [43].

Biofortification was also successfully implemented on the fruit of pepper plants, which accumulated up to 1330 $\mu g \cdot kg^{-1}$ from iodide solution during hydroponic experiments. In addition, some qualitative parameters such as ascorbic acid and soluble sugar contents increased slightly when the maximum iodine content of the solution did not exceed 1 $mg \cdot L^{-1}$. Additionally, positive changes in photosynthetic activity in leaves and antioxidant capacity were observed. This enhanced the tolerance of pepper to elevated concentrations of exogenous iodine [42].

Irrigation water supplemented with iodine was also applied on rice. However, the accumulation rate of iodine by the grain was not sufficient, thus, the authors suggested that feeding farm animals with straw residues to enhance iodine content in meat and milk is a more plausible strategy [44]. Among other crops, carrots and lettuce are also good targets for iodine biofortification, as highlighted in Table 5. Generally, leafy vegetables are more convenient for dietary iodine intake because they are consumed raw, thus, the loss during cooking is eliminated and are easy to fortify via foliar application [41,45–47].

Table 5. List of studies on iodine biofortification of crops and the respective bioaccumulation efficiency related to the recommended daily intake per 100 g of fresh weight.

Crop	Iodine Dosage	Applied Iodine Form	Type of Application	Iodine Content Per 100 g of Fresh Weight (μg)	% of RDI (Recommended Daily Intake)	Source
Carrot	10–150 $mg \cdot kg^{-1}$	KI	Soil pot	0–5000	0–3333	[48]
Celery	10–150 $mg \cdot kg^{-1}$	KI	Soil pot	500–16,000	333–10,667	[49]
Cucumber	12–150 $mg \cdot m^{-2}$	Kelp fertilizer	Soil	30–120	20–80	[50]
Lettuce	0.5–2 $kg \cdot ha^{-1}$	KIO_3	Foliar application	45–300	30–200	[51]
Pepper	10–150 $mg \cdot kg^{-1}$	KI	Soil pot	100–500	67–333	[49]
Potato	0.05–0.5%	KIO_3	Irrigation water	1870–3400	1247–2267	[52]
Radish	10–150 $mg \cdot kg^{-1}$	Kelp fertilizer	Soil pot	100–1300	67–867	[53]
Strawberry	0.25–5 $mg \cdot L^{-1}$	KI, KIO_3	Hydroponic	400–4133	400–2755	[43]
Spinach	0.5–2 $mg \cdot kg^{-1}$	KIO_3	Soil pot	6–824	4–549	[54]
Tomato	12–64 $mg \cdot dm^{-3}$	KI	Soil pot	200–1000	133–667	[37]

5. Influence of Soil and Agronomic Factors on Iodine Biofortification

Iodine biofortification can be applied by addition of its dominant inorganic species, iodide and iodate, to water solutions, irrigation water, or soil. Except for these inorganic species, iodine-rich seaweed-based fertilizers were also successfully used for iodine biofortification [48,49,55]. Still, the foliar application of water solutions is the easiest way to biofortify crops with iodine. This method is most efficient when applied to leafy vegetables [51]. It was successfully tested on lettuce [51], fruit trees [56], kohlrabi [51], potato, carrot, and onion [57]. Iodine biofortification via hydroponic solutions also provided promising outcomes that were reported for spinach [58,59], lettuce [45], strawberry [43], tomato [60], and pepper [42]. In all cases, the bioaccumulation efficiency of iodine from hydroponic solutions was superior to other exposure methods. Still, the biofortification strategies from soils can be more beneficial due to the soil buffer ability driven by the interactions between iodine species and soil components, which alleviate the iodine toxic effects. The presence of humic acids in growth solutions can reduce the deleterious effects of iodine on plants by preventing its rapid and extensive uptake due to sorptive mechanisms which, on the other hand, can prevent the high accumulation rate of iodine in the plant tissues [40].

In soils, the application of iodate is more favorable than fortification using iodide. The uptake of iodate from soils was shown to be more successful by several studies, probably due to its slower uptake by plants [31]. Iodate is not as readily bioavailable as iodide, but probably has to be reduced to iodide prior to its uptake. This is very likely biologically mediated by roots or microbially in the rhizosphere [61]. Alternatively, interaction with humic substances can also lead to iodate reduction due to the presence of free redox active groups in their structure [62].

Still, iodide exposure was shown to have various adverse effects on plants. Lawson et al. [51] reported a 20% decrease in crop yield for lettuce and kohlrabi and common toxicity symptoms such as chlorosis and necrotic spots on the leaves, which were observed in the presence of iodine. However, at low concentrations, iodine can act as a growth enhancer and positively affect some quantitative and nutritional parameters of crops, which are important from an agricultural point of view and can make iodine biofortification attractive for farmers. Iodine increased the levels of glucose, fructose, and total sugar in edible parts of carrot [46] and tomato [63]. It enhanced antioxidant levels in leaves of lettuce [45], improved its response to salinity stress [64], increased the ascorbic acid content in edible parts of pepper, lettuce, barbary fig, and tomato [42,63,65,66], and decreased levels of ammonium and lead accumulation in spinach, while the overall accumulation of nitrates and chlorides increased [67].

6. Simultaneous Biofortification with Selenium Could Improve Global Thyroid Status

In cases when the soil environment is deficient in more micronutrients that govern similar biological processes, plant biofortification with various micronutrients is an advantageous strategy. This is the case of iodine and selenium; and while iodine is needed as the constituent of thyroid hormones (triiodothyronine and tetraiodothyronine), selenium is also essential for the biosynthesis and function of a small number of selenocysteine-containing selenoproteins implicated in thyroid hormone metabolism and gland function. Selenium also has a role in the prevention of autoimmune thyroid diseases in women of childbearing age [68]. Several studies confirmed that patients treated with 200 μg of selenium had improved patient thyroid condition. It decreased the amount of thyroid peroxidase (TPO) antibodies in patients with autoimmune thyroiditis and Hashimoto's thyroiditis [69] and decreased the incidence of postpartum thyroiditis in women positively tested for TPO antibodies [70].

Rasmussen et al. [71] investigated the association between blood serum selenium concentration, thyroid volume, and risk of an enlarged thyroid gland in an area where mild iodine deficiency was eliminated after introducing iodine fortification. They found that low serum selenium concentration was associated with a larger thyroid volume and a higher prevalence of thyroid enlargement [71]. A similar study was conducted in Ethiopia in children with selenium deficiency. They also found that serum selenium is negatively associated with tetraiodothyronine hormone level in children and concluded that selenium deficiency in the area may endanger the effectiveness of the salt iodization program [72]. To improve thyroid status, selenium could also be biofortified along with iodine. There have only been a few attempts at the simultaneous biofortification of iodine and selenium. Smolen et al. [73] presented that the application of salicylic acid improves the efficiency of the uptake of both elements by lettuce. Despite the fact that selenium is not essential for plants, similarly to iodine, it has a positive impact on plant development and production parameters, such as increased seed production in canola [74]. Therefore, the simultaneous biofortification of iodine and selenium could be attractive to farmers if enough information is available to work out a proper biofortification strategy [75].

However, an extensive field research is still needed to establish the most optimal conditions for such an approach.

7. Conclusions

The elimination of iodine deficiency and iodine supplementation are still serious health issues, mainly in European countries. The daily intake should be adequate according to the recommended daily intake and the consumption of supplements and vitamins is not recommended to avoid adverse effects of excess iodine intake. In the right chemical form and application, iodine biofortification of crops is an attractive and cost-effective alternative approach to increase daily intake of iodine in order to eliminate iodine deficiency disorders. Plants such as lettuce, tomato, strawberries, potato, carrots, radish, and cucumber are good targets for iodine fortification, which could be simultaneously fortified with selenium in order to provide better support for thyroid health, as both elements are important for the healthy function of the thyroid gland. With more studies that are persuasive towards the public, the iodine biofortification of crops shows promising results, and together with the use of iodinated salt, it may significantly improve iodinedaily intake by humans without the risk of excessive iodine intake.

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