Iodine content of dietary supplements available on the Norwegian market

Master Thesis in Clinical Nutrition

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Bergen, May 2021
Lina Midtgaard Nilsen

Abstract

Background: Insufficient iodine intake has been reported in groups of the Norwegian population. This is of concern, as iodine is an essential nutrient required throughout life. With few dietary sources of iodine, supplementation is recommended for individuals with a low intake of milk, dairy products and/or lean fish. However, no study has analysed the iodine content in supplements on the Norwegian market. Since legislation allows for deviation from labelled values of iodine content in dietary supplements, the use of these supplements could result in inadequate or excessive intake of iodine.

Aim: To analyse iodine content in dietary supplements available on the Norwegian market and compare the results to the labelled content.

Methods: Iodine containing dietary supplements were collected from pharmacies, health food stores, grocery stores, and online fitness stores in Norway. Three batches of each supplement product were purchased to account for variation in iodine content. During homogenisation and sample preparation, four samples from each batch were collected. Therefore, iodine was determined in a total of 12 samples from each supplement product by Inductively Coupled Plasma Mass Spectrometry. Mean analysed iodine content in each product was compared with the labelled iodine content.

Results: A total of 52 supplements were included in the study, and 58% of the supplements were within ±10% of complete accordance with labelled iodine content. The mean iodine content of all supplements was 150 µg/recommended dose ± 60 µg/recommended dose, with minimum and maximum iodine of 32 µg/recommended dose and 421 µg/recommended dose, respectively. Two products were below the lower tolerance limit of -20% of labelled iodine content and two products exceeded the upper tolerance limit of +45% of labelled iodine content recommended by the European Commission. None of the supplements had iodine content below the minimum allowed iodine content of 23 µg per recommended daily dose.

Conclusion: Our findings shows that the iodine content of approximately 60% of the supplements included in this present study is in accordance with the iodine content labelled on the product. However, the analysed iodine content of all included supplements was at a safe level and are unlikely to be harmful for most consumers. Yet, the labelling information of a few products could cause incorrect use of supplements and may result in excess iodine intake.

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Abbreviations

AR	Average Requirement
EC	European Commission
EFSA	European Food Safety Authority
FFQ	Food Frequency Questionnaire
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IMR	Institute of Marine Research
IOM	Institute of Medicine
LI	Lower Intake Level
LIMS	Laboratory Information Management System
LOD	Level of Detection
LOQ	Level of Quantification
MU	Measurement Uncertainty
NNR	Nordic Nutrition Recommendations
RI	Recommended Intake
RSD	Relative Standard Deviation
SD	Standard Deviation
T3	Triiodothyronine
T4	Thyroxine
TMAH	Tetramethyl Ammonium Hydroxide
TSH	Thyroid Stimulating Hormone
UIC	Urinary Iodine Concentration
UL	Upper Intake Level
WHO	World Health Organization

1. Introduction

The Norwegian population has been considered iodine sufficient for decades, however recent research suggests insufficient iodine intake in certain population groups (1, 2). There are few iodine sources in the diet and supplementation is recommended for individuals that cannot attain sufficient iodine intake from foods (3, 4). Difference between labelled iodine content of dietary supplements and analysed content may be a potential risk of either insufficient or excess intake but is allowed in current regulations.

1.1 Iodine functions and effects of deficiency and excess

Iodine is an essential trace mineral required for the synthesis of the thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4) in the thyroid gland. The thyroid hormones have a vital role in several physiological functions in the body and are essential throughout life (5). The thyroid hormones regulate metabolic rate and affect nearly all organs of the body and control heart, muscle and digestive function (5). In the foetus and young infant, these hormones are crucial for the development and maturation of the nervous system and brain (6, 7). Ingested iodine from foods or supplements is effectively absorbed in the gastrointestinal tract and transported in the circulation (8, 9). Uptake of iodine from the circulation is more effective in the thyroid gland, compared to other tissues, resulting in accumulation of iodine (10). In the thyroid, iodine undergoes a series of reactions to produce T_3 and T_4 (11). Iodine uptake and thyroid hormone production is regulated by thyroid stimulating hormone (TSH) concentrations as illustrated in **Figure 1**. Normal thyroid hormone concentrations are maintained by TSH release as a response to decreased content of thyroid hormones in the circulation (8, 11)

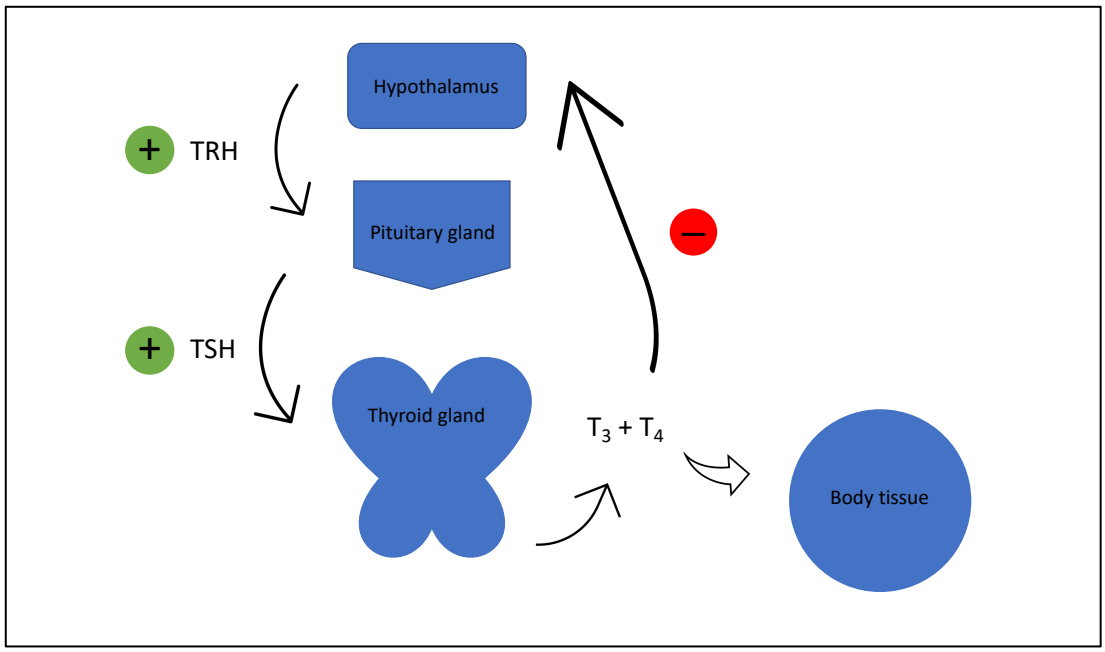

Figure 1. Regulation thyroid hormones. Thyroid stimulating hormone from the pituitary gland stimulate thyroid hormone production in the thyroid. Negative feedback from the thyroid hormones T_3 and T_4 maintain normal levels.

With prolonged iodine deficiency or excess, the thyroid can no longer maintain normal thyroid hormone synthesis. The association between intake and risk of adverse health implications can be described as U-shaped (**Figure 2**), as both deficiency and excess are associated with thyroid dysfunction (12, 13). Inadequate thyroid hormone production (hypothyroidism), due to insufficient iodine intake, may lead to a range of conditions, known as iodine deficiency disorders (14). Enlargement of the thyroid gland, called goitre is seen in severe iodine deficiency (14, 15). Severe iodine deficiency and goitre is no longer prevalent in Norway, but mild-to-moderate deficiency has been reported in certain groups of the Norwegian population, including women of childbearing age (2, 16). Research suggests that mild-to-moderate iodine deficiency during pregnancy is associated with impaired cognitive outcomes in the child (17-22). Documentation on the health consequences of excessive iodine intake is limited (23). Excessive iodine intake may cause a transient reduction in thyroid hormone production as a mechanism to protect against hyperthyroidism (24). It has been proposed that the thyroid of vulnerable individuals and the foetus may have difficulty escaping this effect, prolonging the state of hypothyroidism (25-27). Absence of these protective mechanisms has been reported in vulnerable individuals, such as those who have previously been exposed to iodine deficiency, resulting in excess production of thyroid hormones (hyperthyroidism) (8, 23, 28).

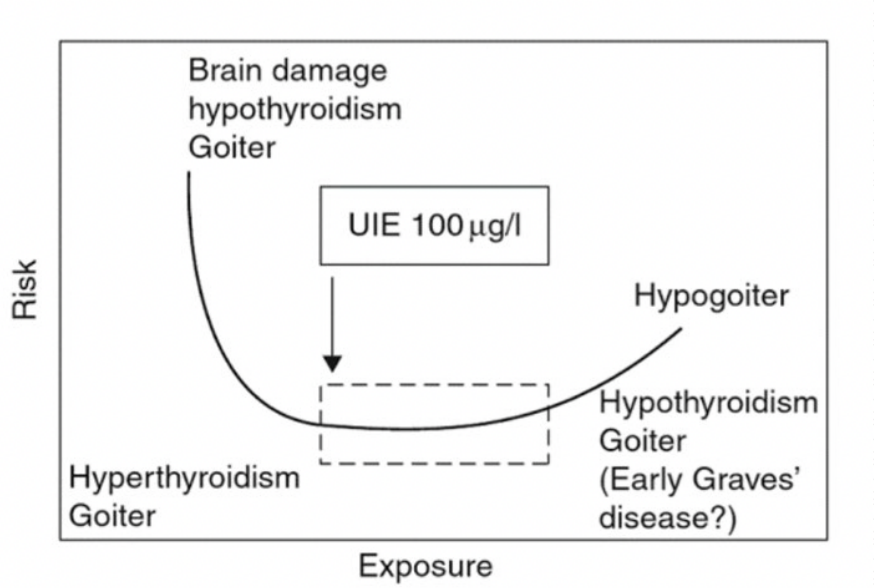

Figure 2. The association between intake and risk of adverse health implications is U-shaped. Both iodine deficiency and excess are associated with thyroid dysfunction. The range of optimal intake is small and illustrated by a dotted box. Retrieved from Laurberg et al, 2002.

1.2 Biomarkers of iodine status

Approximately 90% of ingested iodine is excreted in urine within 24-48 hours (29, 30). Thus, urinary iodine concentration (UIC), reflects recent iodine intake and is used to assess iodine status of populations (31). The use of UIC as a biomarker of habitual iodine intake in individuals is limited due to the variability in iodine intake from day to day (32, 33). These variations level out when used in large population samples, and when repeated in individuals. Studies have proposed that ten repeated spot urine samples are required to establish an individual's iodine status (34, 35). Other biomarkers that are affected by iodine status include serum concentrations of TSH and T_4. With iodine deficiency, TSH is elevated to stimulate thyroid hormone production (8, 31, 32). As iodine deficiency progresses, the thyroid reaches a threshold for thyroid hormone production and serum T_4 concentrations decrease (31). Serum levels of these markers may be within normal range in mild-to-moderate iodine deficiency and is affected by other factors than iodine status, such as illness and pregnancy (32). Hence, these markers are not considered reliable markers of iodine status in individuals and should be used along with other tests. Thyroglobulin is considered a sensitive biomarker for long-term iodine status, but its validity is limited in pregnancy and in individuals with anti-thyroglobulin antibodies (32, 36).

Unfortunately, reliable and cost-effective biomarkers of iodine status in individuals are limited, particularly in mild-to-moderate iodine deficiency (32). Iodine must come through the diet, and iodine intake can be estimated by assessing dietary patterns and supplement use. Estimation of salt intake is difficult therefore the use of dietary assessment is limited in areas where iodine from salt contributes greatly to the total iodine intake. In Norway, iodised salt is limited to household use, and iodisation level of salt is low (3). Thus, dietary assessment is suitable for estimating iodine intake in the Norwegian population. The primary tools for estimating nutrient intake are food frequency questionnaires (FFQs), 24-h recall interviews and food records (31). FFQs record the participants consumption frequency and portions sizes of iodine rich foods within a defined time period. In the 24h-recall, a trained interviewer acquires detailed information on dietary intake of the previous day. To account for the high day-to-day variability in iodine intake, a large sample size or repeated interviews should be applied. Food records collect self-reported food intake over a specified time period, usually days. All of the mentioned dietary assessment tools rely on accurate food composition data and are limited by the natural variability in iodine content of foods. Labelled iodine content may be used for estimating iodine intake from supplements (37). Thus, deviance from labelled iodine content in supplements, could potentially contribute to inaccurate estimations of iodine intake.

1.3 Dietary reference values for iodine

Dietary reference values are an umbrella term for a set of nutrient reference values. Dietary reference values for iodine from different health authorities vary somewhat and are presented in **Table 1.** The Nordic Nutrition Recommendations (NNR) are used in Norway, and includes avenge requirement (AR), recommended intake (RI), upper intake level (UL) and lower intake level (LI) (38). The term recommended intake (RI) refers to the amount of a nutrient that meets the known requirement and maintains good nutritional status among practically all healthy individuals in a particular life stage or gender group (38). The recommended intake (RI) for adults of 150 µg/day includes a safety margin for goitrogenic substances (38). Iodine requirements are higher during pregnancy due to increased production of thyroid hormones, transfer of thyroid hormones and iodine to the foetus, and increased urinary excretion of iodine (6, 27, 39). The urinary excretion returns to normal after pregnancy, but requirements increase during lactation due to the excretion of iodine in breast milk (11, 39, 40). The recommended intake (RI) during pregnancy and lactation is 175 µg/day and 200 µg/day, respectively (38).

The upper intake level (UL) is defined as the maximum level of long-term (months or years) daily nutrient intake that is unlikely to pose a risk of adverse health effects in humans (38). UL for iodine has not been established in the NNR. The Scientific committee on food (SCF) established UL for iodine based on elevation in serum TSH and enhanced TSH response to TRH at an iodine intake equivalent to 1800 µg/day (41). These effects were considered to be of biochemical nature and no adverse health effects were observed. An uncertainty factor of 3 was considered adequate, providing an UL of 600 µg/d. Established ULs for iodine from health authorities are presented in **Table 2.**

Table 1. Recommended iodine intake for different life stages by health authorities (15, 30, 38, 42)

NNR, Nordic		**IOM, USA**		**EFSA, Europe**		**WHO**	
Life stage	µg/day	Life stage	µg/day	Life stage	µg/day	Life stage	µg/day
-	-	< 6 months	110	-	-	0-5 years	90
6-11 months	50	7-12 months	130	6-11 months	50	6-12 years	120
1-1.9 years	70	1-8 years	90	1-3 years	70	>13 years	150
2-5 years	90	-	-	4-6 years	90	-	-
6-9 years	120	9 -13 years	120	7-10 years	100	-	-
-	-	-	-	11-14 years	120	-	-
>10 years	150	>14 years	150	>15 years	130	-	-
Pregnancy	175	Pregnancy	220	pregnancy	130	Pregnancy	250
Lactation	200	Lactation	290	Lactation	160	Lactation	250

Abbreviations: NNR, Nordic Nutrition Recommendations; IOM, Institute of Medicine; EFSA, European Food Safety Authority; WHO, World Health Organization.

Table 2. Upper intake levels of iodine for different life stages by health authorities(30, 40, 41)

EFSA, Europe		**IOM, USA**		**WHO**	
Life stage	µg/day	Life stage	µg/day	Life stage	µg/day
1-3 years	200	1-3 years	200	0-2 years	180
4-6 years	250	4-8 years	300	-	-
7-10	300	9-13 years	300	-	-
11-14 years	450	14-18 years	900		
15-17 years	500	-	-	-	-
≥ 18 years	600	≥ 19 years	1100	-	-
-		Pregnancy 14-18 years	900	-	-
-		Pregnancy ≥ 19 years	1100		
Pregnancy	600	Lactation 14- 18 years	900	Pregnancy	500
Lactation	600	Lactation ≥ 19 years	1100	Lactation	500

Abbreviations: EFSA, European Food Safety Authority; IOM, Institute of Medicine; WHO, World Health Organization.

1.4 Dietary sources of iodine

Iodine in the earth's surface will leach from soil to seawater in areas susceptible to erosion. Crops and drinking water from iodine replete areas, including Norway, will consequently be low in iodine (43). This results in few natural iodine sources in the Norwegian diet.

Iodine is abundant in seawater and is concentrated in sea-living organisms such as fish, shellfish and algae (43). The iodine content of species varies, with a higher content in lean fish (3). The iodine content of algae is highly variable and may pose a risk of excess intake (38, 44). Milk and dairy products are important iodine sources of the Norwegian population. Mandatory fortification of cow fodder was introduced in the 1950s and was initially intended to meet the iodine requirements of the animal but led to milk with high iodine content (1, 8). Egg is another food high in iodine due to the fortification of chicken feed. (3). Universal salt iodisation has been considered the prime intervention to eradicate iodine deficiency since the 1980s and was officially recommended by WHO/UNICEF in 1994 (15, 45). Norway only has iodised salt available for household use at a low concentration of 5 µg/g salt, hence the overall iodine contribution from salt intake is not significant (8). Iodine containing dietary supplements are readily available on the Norwegian market and constitute an important iodine source (46). Accordingly, the most important iodine sources in Norway are milk and dairy products, seafood, eggs, and dietary supplements.

1.5 Iodine status and dietary iodine intake in Norway

Norway has been considered iodine sufficient for decades, but recent research suggests insufficient iodine status in certain population groups (2, 16, 47). A decline in consumption of milk and fish has been observed in the last decades and could explain the insufficient iodine status in groups of the Norwegian population (2, 48). Iodine intake has been estimated from intake of iodine rich foods in the Norkost 3 dietary survey (49, 50). The median iodine intake in the study population was 202 µg/day, though there was a great variation in intake ranging from 15-1462 µg/day. Men had significantly higher intake of iodine than women, and 5% of men had intakes above upper intake level of 600 µg/day for adults. In contrast, only 41% of women had iodine intake above RI, with 46% of younger women having high risk of inadequate iodine intake, and very few women exceeded UL. It was confirmed that milk and fish are the major iodine sources in the Norwegian population, and that intake of these foods are lower in younger age groups compared to older age groups. Reported use of iodine containing supplements was 16% in women and 11% in men, contributing to 95 µg/day and 117 µg/day, respectively (8).

Pregnant and lactating women are particularly at risk of iodine deficiency due to increased iodine requirements. This is of concern as their children are at risk of suboptimal development, if iodine intake is not sufficient (51). Measurements of UIC in women of childbearing age and pregnant women substantiate the concern of insufficient iodine intake in this group (22, 52, 53). In studies assessing iodine status among pregnant women in Norway 15-32% of participants reported the use of iodine containing supplements (18, 52, 54, 55). Individuals that limit their consumption of milk or fish voluntarily or due to health concerns may be at risk of insufficient iodine intake. This includes vegans as well as individuals with allergies to fish and/or dairy products (56). Vegan diets exclude all foods from animal origin, thereby fish and milk. UIC measurements among vegans and vegetarians indicate insufficient intake (16, 57). There is also concern that ethnic minorities in Norway may have insufficient iodine intake due to lactose intolerance and food cultures low in milk and fish. Madar et al. found through dietary assessment and UIC that Somali immigrants in Norway had insufficient iodine intake (58). Children and men in Norway generally have a sufficient iodine intake (2, 16, 59, 60). Iodine supplementation in these groups may result in excess iodine intake. However, men and children with low intake of fish and milk are most likely at risk of insufficient intake.

These studies highlight that iodine requirements are not secured by food in all population groups, particularly women of childbearing age, vegans and ethnic minorities. Iodine supplementation may therefore be necessary to ensure sufficient intake in the population.

1.6 Recommendations for iodine supplementation

In Norway iodine supplementation is recommended in individuals that cannot attain sufficient iodine intake from their diet. Recommendations of iodine containing supplements for groups at risk of deficiency are presented in **Table 3.** The recommended iodine supplementation is 100-150 µg/day dependant on life stage and iodine intake from food.

Table 3. Recommended iodine supplementation for populations groups at risk of iodine deficiency from the Norwegian Institute of Public health (4)

Population group	**Iodine intake from food**	**Recommended iodine supplementation (µg/day)**
Women of childbearing age	< 3 dl milk/yogurt daily with regular intake of lean saltwater fish or <5 dl milk/yogurt daily with little or no intake of lean saltwater fish	100
Pregnant and lactating women	< 6 dl milk/yogurt daily with regular intake of lean saltwater fish or < 8 dl milk/yogurt daily with little or no intake of lean saltwater fish	150
Allergic, vegetarians and others	< 3-5 dl milk/yoghurt daily (depending on fish intake)	100-150

The World Health Organization (WHO) recommend supplementation during pregnancy in countries without universal salt iodisation, but not in iodine sufficient populations (15). Several countries, including USA, Australia and New Zealand, recommend supplementation of 150 µg iodine daily in all pregnancies (61-63).

Iodine supplementation during pregnancy has been reported to improve maternal iodine status and appears to be safe for the child (64). However, the effects of supplementation in pregnant women with mild-to-moderate iodine deficiency on child neurodevelopment are inconsistent (65, 66). A systematic review found that there is currently not enough evidence to support recommendation of iodine supplementation in all pregnancies (63). The limited evidence of positive outcomes from maternal iodine supplementation could be explained by late initiation as sufficient iodine is required early in foetus development (67-69). Hence, sufficient iodine status should be attained prior to conception (64, 70). Many pregnancies are unplanned, and iodine status in women of childbearing age is a public health concern.

1.7 Regulations on dietary supplements

The Norwegian regulation on nutrient supplements is adopted from the Directive 2002/46/EC (71, 72). In this regulation it is stated that "the declared values on supplement packaging should be average values based on the manufacturers analysis of the product». When establishing the nutrient content of a supplement, the manufacturer should take upper safe intake limits and intake from other dietary sources into account. The minimum limit for iodine content in dietary supplements is 23 µg per daily dose. Norway previously had a maximum limit for iodine content in dietary supplements of 225 µg/recommended dose. This was repealed in 2017 as the European Commission (EC) is working on establishing joint maximum limits. However, this work is halted indefinitely. The Norwegian Food Safety Authority has assigned The Norwegian Scientific Committee for Food and Environment to conduct an independent risk assessment for consequences of establishing new national maximum limits (73).

When analysing a dietary supplement, the labelled value may vary from the analytical value. The EC has published a guidance document for determining an acceptable tolerance range for vitamins and minerals used in dietary supplements, still “these guidelines cannot be regarded as official interpretation of the legislation" (74). For minerals, including iodine, the lower tolerance limit is -20% of labelled, and the upper tolerance limit is +45% of labelled. This tolerance range includes measurement uncertainty and overages to compensate for losses during shelf life. It is also stated that if a maximum limit is established for the nutrient, the upper tolerance limit should not exceed this value. This does not apply to iodine, as no maximum limit has been established. An acceptable tolerance range for a labelled iodine content of 150 µg would be from 120 to 220 µg/recommended dose according to these

guidelines. The Norwegian Food Safety Authority can conduct case-by-case evaluation of dietary supplements based on ULs and intake from other dietary sources to ensure consumer safety (75). However, inspections of dietary supplements are usually done for products that has raised suspicion and mostly focus on labelling, marketing and content of harmful ingredients and to less degree the nutrient content.

Studies from the United States have found that iodine content of dietary supplements varies greatly from labelled (76, 77). There are no similar studies conducted in Norway, therefore little is known of the iodine content of iodine supplements on the Norwegian market. High variability in iodine content and difference from labelled iodine content in dietary supplements may pose a risk for both insufficient and excess iodine intake (2, 8).

1.8 Aims of this thesis

The overall aim of this thesis was to analyse iodine content in dietary supplements available on the Norwegian market and compare the results with the labelled iodine content.

Specific aims

1. Survey the Norwegian market in attempt to identify all iodine containing dietary supplements available in the given time period
2. Analyse the iodine content of the collected dietary supplements
3. Compare labelled iodine content to results obtained from analytical analysis
4. Consider safety of iodine supplementation for consumers based on our results

2. Materials

2.1 Collection of dietary supplements

Collection of dietary supplements was performed between August 2020 and October 2020. To identify iodine containing dietary supplements on the Norwegian market,
general search terms in Norwegian, «jodtilskudd », "kostilskudd" and "multivitamin mineral tilskudd" was searched for in the Google search engine. In addition, websites of pharmacies, health food stores, grocery stores and fitness stores were surveyed. Following identification of products in the online search, the products were purchased from physical stores. We did not have access to sales figures for dietary supplements and aimed to purchase all iodine containing dietary supplements available in physical stores in Bergen, the second largest city of Norway. Still, not all products identified in the online search were available for purchase in physical stores. To account for this, all iodine containing dietary supplements was purchased from two of the largest online fitness stores in Norway, Gymgrossisten.no (78) and tights.no (79). Products with algae and fungi as iodine source, in addition to protein powders fortified with iodine was not included in this study. The following information for the collected dietary supplements was recorded: target group, retail category, type of supplement, supplement matrix and recommended daily dose. In addition, marketing and misleading claims for some of the collected dietary supplements was noticed and recorded.

Three products of each identified dietary supplement were purchased, preferably with three individual batch-numbers. If individual batch-numbers were not available, I aimed to find products with two individual batch numbers. Three products with identical batch numbers were purchased from online fitness stores, as the retailers could not provide individual batch-numbers. Two subsamples were collected from each individual batch and homogenised separately. From each of the homogenisation samples, two subsamples were collected and prepared separately before determination of iodine content by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). Hence, twelve samples from each product were analysed. Sampling procedure is illustrated in **Figure 3.**

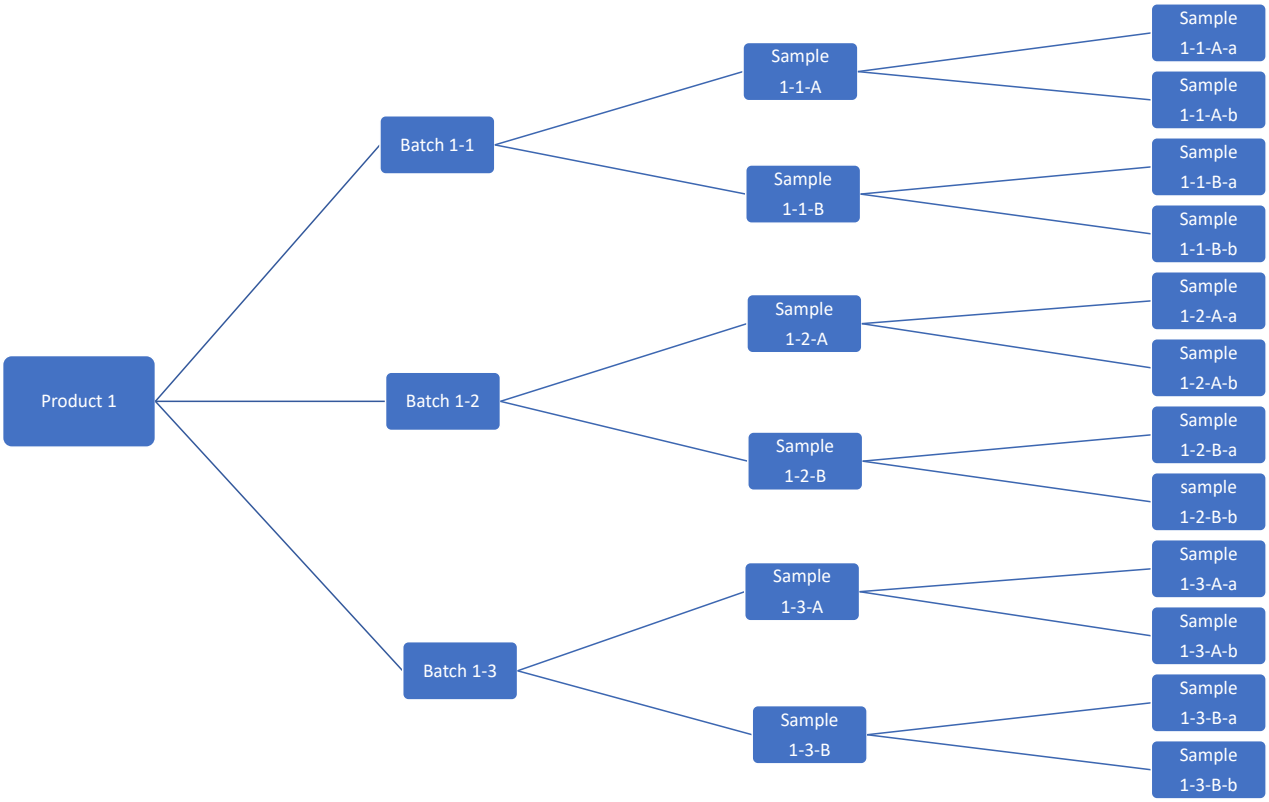

Figure 3. Sampling of iodine containing dietary supplements yield twelve samples of each product for analysis.

2.2 Homogenisation

The collected products were stored at room temperature prior to homogenisation. From each batch two samples were homogenised separately, yielding six homogenised samples from each product.

A cryogenic grinder (Spex Sample Prep 6875D Freezer/mill Dual Chamber Cryogenic Grinder, SPEX, New Jersey, USA) was used for homogenisation of products. The samples were placed in sealed cryogenic grinding vials, along with a magnet and immersed in liquid nitrogen. The sample was then ground by the magnetically moving impactor, resulting in a fine powder sample. The cryogenic grinding vials came in a large and a small size. The large vials were used for gummy and oil capsules, and the small vials for the other products. The grinding protocol for our samples was three 2-minute cycles at rate 12. Cool time between cycles was two minutes.

The pulverised samples were transferred into plastic containers using single-use plastic spatulas to avoid cross sample contamination. The grinding vials were cleaned in hot water and dish soap between each run. After homogenisation the samples were refrigerated at 4 °C. Product 38 produced heat in storing, likely due to containing reactive n-3 fatty acids. A new sample was thus homogenised and stored at -80 °C to avoid exothermic reaction. Liquid dietary supplements were not homogenised but shaken before sample preparation to ensure even distribution.

2.3 Iodine determination - Inductively coupled plasma mass spectrometry

Iodine was determined by Inductively Coupled Plasma Mass Spectrometry (ICP-MS) at the Institute of Marine Research (IMR). The IMR is accredited for this method according to ISO 17025 from 2017, in compliance with the International Organisation for Standardisation (80).

2.3.1 Sample preparation

Two subsamples of approximately 0.2g were weighed (Ohaus, EX224 model, New jersey, USA) from each homogenised sample, yielding twelve samples from each product. Samples were prepared by adding 5ml deionised water (Merck, Milli-Q advantage, Darmstadt, Germany) and 0.1ml α-amylase enzyme (Bacillus Iichemiformis from Sigma) prior to water bath at 90 °C ± 3 °C for 30 min. α-amylase was added to all samples in order to hydrolyse starch. Then 1mL ultrapure tetramethylammonium hydroxide (TMAH) was added before extraction at 90 °C ± 3 °C for 3h. After extraction the samples were diluted to 25ml with deionised water, and then centrifuged to sediment solid particles. Sample solution was collected using 10ml syringes and then filtered through a 0.45 µm disposable filter.

Samples from the liquid dietary supplements were collected in volumes determined by their declared iodine concentration and this volume was weighed (Ohaus, EX224 model, New jersey, USA). Water was then added to produce a total volume of 5ml prior to further sample preparation. The reason for this is for the samples to have concentrations within the target area for the ICP-MS instrument. Otherwise, the sample preparation was the same as described above.

2.3.2 Analysis

Trained laboratory technicians performed the analysis (Agilent 7900 ICP-MS, Agilent technologies, California, USA) according to internal IMR protocols. Blank samples and internal standards were included for quality control. ICP-MS is a type of mass spectrometry that utilises an inductively coupled plasma to ionise the sample before detection (81). The prepared sample is passed through a nebuliser to produce an aerosol, and the smaller droplets are swept into the high temperature argon plasma where they are dried, atomised and ionised. The positively charged ions that are produced in the plasma are extracted into the vacuum system where they are detected, creating a mass spectrum. The magnitude of each peak is directly proportional to the concentration of an element in the sample. Quantitative results are produced by comparing the signal intensities to those generated by calibration standards (81).

The limit of quantification (LOQ) for the method was calculated as 10 times the standard deviation (SD) from 20 blank samples analysed on the same day. The limit of detection (LOD) was calculated as three times the SD from 20 blank samples analysed on the same day. The calculated LOQ and LOD for this method are is 0.32 (µg/L) and 0-0.1 (µg/L), respectively. Measurement uncertainty is obtained from analysing standard reference materials with known concentrations. Analysis values from performing the method and standard reference material are shown in **Table 4.** Iodine concentration of the samples affect measurement uncertainty as presented in **Table 5.**

Table 4. Analysed and certified iodine concentration of standard reference material

Reference material	Analysed mean value (mg/kg)	Certified value (mg/kg)	Measured mean value (mg/kg)	RSD %
Fish Muscle (ERM-BB 422)	1.28 ± 0.3	1.4 ± 0.4	1.26 ± 0.20 2RSD = 15.9% (n=589)	89[a] 98[b]

Values are presented as means ± standard deviation.
Abbreviations: RSD, Relative Standard Deviation.
[a] Measured laboratory
[b] Analysed

Table 5. Measurement uncertainty and measurement range

	MU (%)	MU (%)	Measurement range (mg/kg dw)
	LOQ-10xLOQ	>10xLOQ	
Iodine	40	20	0.04 - 8000

Abbreviations: MU, measuring uncertainty; LOQ, limit of quantification

2.3.3 Data processing

Data was obtained from the laboratory information management system (LIMS) at the IMR. Calculations was performed in Microsoft Excel for Mac version 16. Analysed iodine concentration was given in mg/kg. Tablets, capsules and gummy product were weighed, and the analysed values were converted to µg per daily recommended dose. The weight and volume collected from each liquid supplement were used to calculate the analysed iodine concentration in µg/ml, and then the iodine content per daily recommended dose. For supplements with a range of recommended daily doses, the maximum recommended dose was selected.

Product 48 did not specify the volume of one drop thus this was calculated from the labelled bottle volume and number of daily doses. The attained drops volume from these calculations was also confirmed by contacting the manufacturer of the product. The calculated iodine content per daily dose was 5 times greater than labelled when using this volume for recommended daily dose. For reassurance, the drop volume was measured to be lower and provided more reliable results when calculating iodine content in recommended daily dose.

2.4 Representation of data

Descriptive statistics was performed in the statistical software IBM SPSS version 25.

Analysed iodine content is presented as µg/recommended dose. First, minimum, maximum, mean, SD and RSD are presented for each product batch. The relative standard deviation (RSD) gives a measure of whether the SD is small or large compared to the mean. Therefore, it was possible to compare variation of analytical values between products. For comparison to recommended daily dose, the mean analysed value of 12 samples for each product was used.

In this thesis, accordance is defined as the analysed iodine content as a percentage of the labelled iodine content. This was used to compare analysed and labelled iodine content per daily dose. If labelled and analysed iodine content is identical the accordance is 100%. Accordance exceeding 100% represent higher analysed iodine content than labelled, and accordance below 100% represent lower analysed iodine content than labelled. Since few products were expected to meet complete accordance of 100%, products within a range of ±10% was defined as in accordance with labelled iodine content.

Welch ANOVA was used to compare mean analysed values and accordance with labelled for product categories. This statistical test was used since our data violated the assumption of homogeneity of variances. Games-Howell test was used to identify the group differences. To compare mean accordance for groups with complete accordance, data points for 100% was used. Groups were defined as statistically different when $p\text{-value} < 0.05$.

3. Results

3.1 Description of collected dietary supplements

A variety of iodine containing dietary supplements was identified, and characteristic are presented in **Table 6.** All 52 supplements were categorised by iodine source, supplement type, matrix, retail category and target group. Further information of the collected supplements is given in **Appendix 1.**

Table 6. Characteristics of collected dietary supplements

Category		**n**	**% of collected**
Iodine source	Potassium iodide	51	98.1
	Other[1]	1	1.9
Supplement type	Multi[2]	46	88.5
	Single[3]	6	11.5
Matrix	Pressed tablets	29	55.8
	Powder capsule	10	19.2
	Gummy	5	9.6
	Oil capsule	4	7.7
	Liquid supplement	4	7.7
Retail category	Pharmacy	18	34.6
	Health food store	13	25
	Online fitness store	17	32.7
	Grocery store	4	7.7
Target group	Pregnant	4	7.7
	Breastfeeding	2	3.8
	Children	3	5.8
	Women	5	9.6
	Men	4	7.7
	Vegans/vegetarians	3	5.8
	Hair growth	4	7.7
	Not specified	27	51.9

[1] Elemental iodine in ethyl alcohol
[2] Single supplements are defined as those containing ≤ 2 micronutrients
[3] Multi supplements are defined as those containing > 2 micronutrients

3.2 Analysed iodine content

Analysed iodine content per daily recommended dose is presented in **Table 7.** The mean iodine content of all collected products was 150 ± 60 µg/recommended dose, with minimum and maximum values of 32 µg/recommended dose and 421 µg/recommended dose, respectively. None of the products were below the minimum allowed iodine content of 23 µg/recommended dose. The mean value of four products (8%) exceeded the previous maximum dose of 225 µg/recommended dose. The relative standard deviation (RSD) of analytical values within products ranged from 1 - 80%, with a mean of 16%. In nearly half of the products (46%, n=24) RSD was under 10%. In 38.5% (n=20) of products the RSD was 10-29%, whereas 13.5% (n=7) had RSD of 30-50%. Product 40 had RSD of 80%. Further assessment of the dietary supplements in this thesis is based on the mean iodine content per daily recommended dose.

Table 7. Analysed iodine content (µg) in recommended daily dose of dietary supplements (n=52)

Product number	Labelled	Mean ± SD Batch 1[a]	Mean ± SD Batch 2[a]	Mean ± SD Batch 3[a]	Mean ± SD Batch 1-3[b]	Min Batch 1-3[b]	Max Batch 1-3[b]	RSD (%)
1	225	237 ± 3	215 ± 11	272 ± 15	242 ± 27	200	292	11
2	150	143 ± 47	139 ± 5	179 ± 33	154 ± 35	102	213	23
3	100	115 ± 15	126 ± 11	103 ± 18	115 ± 17	86	137	15
4	100	112 ± 47	102 ± 8	95 ± 6	103 ± 26	70	153	25
5	150	140 ± 4	143 ± 8	99 ± 4	127 ± 22	95	153	17
6	150	235 ± 6	131 ± 58	184 ± 14	184 ± 62	81	289	34
7	100	87 ± 14	106 ± 19	121 ± 16	105 ± 21	76	137	20
8	150	150 ± 3	146 ± 7	147 ± 6	147 ± 6	138	153	4
9	200	187 ± 5	184 ± 6	182 ± 7	184 ± 6	175	192	3
10	175	158 ± 5	166 ± 2	161 ± 9	162 ± 7	147	169	4
11	150	138 ± 5	140 ± 5	134 ± 2	138 ± 5	133	146	3
12	150	179 ± 26	154 ± 24	118 ± 36	150 ± 37	86	203	25
13	150	135 ± 5	138 ± 8	137 ± 2	136 ± 5	130	149	4
14	175	154 ± 11	192 ± 31	155 ± 64	167 ± 42	99	222	25
15	225	226 ± 30	198 ± 3	199 ± 3	208 ± 21	194	254	10
16	200	194 ± 8	189 ± 2	205 ± 51	196 ± 28	159	258	14

17	150	186 ± 8	139 ± 35	154 ± 33	160 ± 32	107	196	20
18	150	152 ± 49	140 ± 2	150 ± 67	148 ± 46	92	224	31
19	150	179 ± 68	163 ± 5	189 ± 46	177 ± 44	120	240	25
20	150	143 ± 9	125 ± 5	144 ± 4	137 ± 11	118	156	8
21	100	71 ± 30	108 ± 58	104 ± 29	94 ± 41	49	174	44
22	150	129 ± 35	81 ± 16	108 ± 23	106 ± 31	66	163	30
23	100	134 ± 59	142 ± 34	152 ± 17	143 ± 37	85	212	26
24	68	89 ± 15	68 ± 5	96 ± 40	84 ± 26	60	134	30
25	160	137 ± 13	140 ± 4	144 ± 4	140 ± 8	118	147	6
26	200	191 ± 39	206 ± 30	198 ± 20	198 ± 28	167	249	14
27	160	138 ± 4	137 ± 2	137 ± 2	137 ± 3	133	141	2
28	70	66 ± 1	64 ± 5	66 ± 1	66 ± 3	56	68	5
29	120	88 ± 10	100 ± 4	109 ± 2	99 ± 11	77	112	11
30	75	72 ± 5	69 ± 3	75 ± 6	72 ± 5	64	83	7
31	150	144 ± 28	107 ± 4	145 ± 6	132 ± 23	105	169	18
32	150	138 ± 15	141 ± 10	134 ± 1	137 ± 10	124	152	7
33	150	121 ± 57	170 ± 11	139 ± 1	143 ± 37	71	180	26
34	150	159 ± 8	156 ± 1	143 ± 10	153 ± 10	133	170	7

35	150	138 ± 5	152 ± 1	154 ± 7	148 ± 9	131	160	6
36	150	141 ± 3	180 ± 7	169 ± 3	163 ± 18	137	186	11
37	150	145 ± 7	136 ± 3	137 ± 4	139 ± 6	133	150	4
38	150	131 ± 8	138 ± 4	126 ± 10	132 ± 9	114	142	7
39	150	140 ± 3	145 ± 13	136 ± 4	140 ± 8	127	158	6
40	225	57 ± 28	41 ± 9	204 ± 41	101 ± 81	32	241	80
41	150	119 ± 49	174 ± 6	135 ± 18	143 ± 37	75	183	26
42	150	226 ± 110	179 ± 27	120 ± 20	175 ± 75	102	328	43
43	150	145 ± 9	144 ± 18	160 ± 8	150 ± 14	125	167	9
44	150	173 ± 4	173 ± 2	171 ± 4	172 ± 3	165	178	2
45	75	91 ± 1	91 ± 1	92 ± 1	92 ± 1	90	94	1
46	42	62 ± 0	62 ± 1	61 ± 2	62 ± 1	60	64	2
47	80	112 ± 2	116 ± 9	115 ± 2	114 ± 5	109	129	4
48	200	393 ± 24	249 ± 15	273 ± 26	305 ± 69	235	421	23
49	300	331 ± 18	340 ± 6	331 ± 11	334 ± 12	307	348	4
50	150	184 ± 2	183 ± 4	165 ± 1	177 ± 10	164	189	5
51	300	285 ± 10	308 ± 14	282 ± 11	291 ± 16	270	321	5
52	72	127 ± 33	86 ± 22	63 ± 12	92 ± 35	53	156	38

Abbreviations: SD, Standard Deviation; min, minimum; max, maximum; RSD, Relative Standard Deviation

[a] Values calculated from the four samples of that batch
[b] Values calculated from all three batches for that product, hence all 12 samples.

3.3 Accordance with labelled iodine content

The agreement between labelled and analysed iodine content for all products is presented in **Figure 4**. Most of the products (58%) were within ±10% accordance of labelled. The accordance of iodine content was higher than 10% in 27% (n=14) of products, and under -10% in 15% (n=8) of products. Thus, 42% of products were not in accordance with labelled iodine content. Mean difference from labelled for all products was 2.5%. Four products were not within tolerance range as presented in **Figure 5.** Products 22 and 40 (4 %) were below lower tolerance limit, and products 46 and 48 (4 %) exceeded upper tolerance limit. The four products all had three identical batch numbers, as individual batch numbers were not attainable. Product 48 was a liquid dietary supplement purchased from health food store, and the three other products were purchased from online fitness stores. Product 46 was a gummy supplement targeted for use in children, whereas the three other products were aimed at adults.

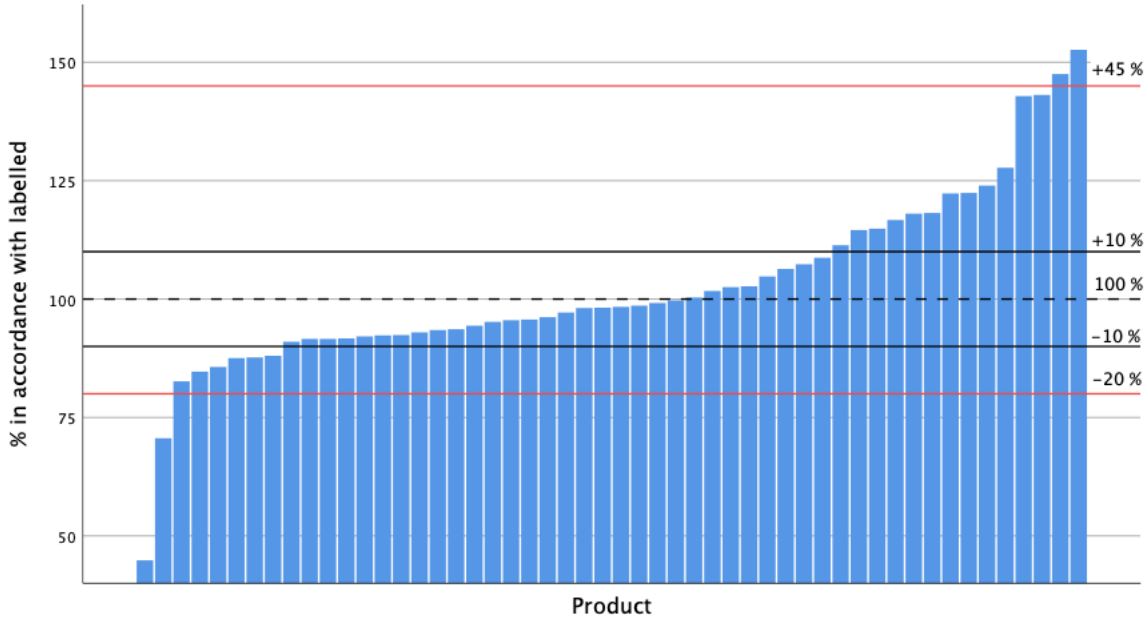

Figure 4. Accordance of iodine content in recommended dose of dietary supplements. Bars illustrate % accordance of analysed iodine content with labelled iodine content. Values below 100% indicate lower analysed values than labelled, whereas values over 100% indicate higher analysed values than labelled. The dashed reference line illustrates 100% in accordance with labelled. The black reference lines illustrate ±10% of accordance with labelled iodine content. The red reference lines illustrate tolerance range of lower tolerance limit (-20% of labelled), and upper tolerance limit (+45% of labelled), according to the European Commission (71).

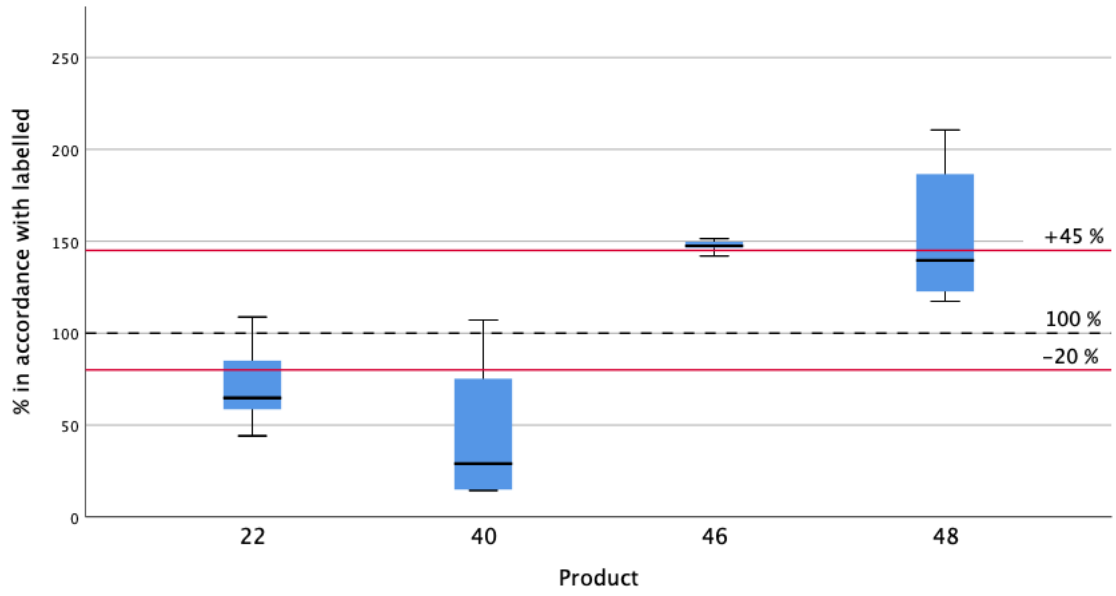

Figure 5. Accordance of iodine content in recommended dose of dietary supplements not within tolerance range. Values below 100% indicate lower analysed values than labelled, whereas values over 100% indicate higher analysed values than labelled. The dashed reference line illustrates 100% in accordance with labelled. The red reference lines illustrate tolerance range of lower tolerance limit (-20% of labelled), and upper tolerance limit (+45% of labelled), according to the European Commission (71). The blue boxes represent interquartile range between 25th percentile and 75th percentile. The black middle line of the boxes represents the median (50th percentile). End of whiskers indicate 1,5 times interquartile range.

When looking at retail category, grocery stores had lower analysed values than labelled (p <.001) and health food stores had higher analysed values than labelled (p=.002). The mean analysed values for pharmacies (p=.964) and online fitness stores (p=.226) did not differ from labelled iodine content. Products for hair growth had higher analysed values than labelled (p=.001). The mean analysed iodine content was higher than labelled for products aimed at vegans/vegetarians (p=.148), and lower than labelled for products for use during pregnancy (p=.118), breastfeeding (p=.359) and in men (p=.811), although the differences were not significant. There was no difference in accordance with labelled between single and multi supplements (p= .415). Accordance with labelled for the different matrices is presented in **Figure 5.** Liquid (p <.001) and gummy supplements (p <.001) had higher analysed values than labelled, whereas oil capsules (p <.001) had lower analysed values than labelled. Although powder capsules had lower mean analysed iodine content than labelled iodine content, this difference was not significant (p=.233). The mean analysed iodine content of pressed tablets did not differ from labelled iodine content (p=.999).

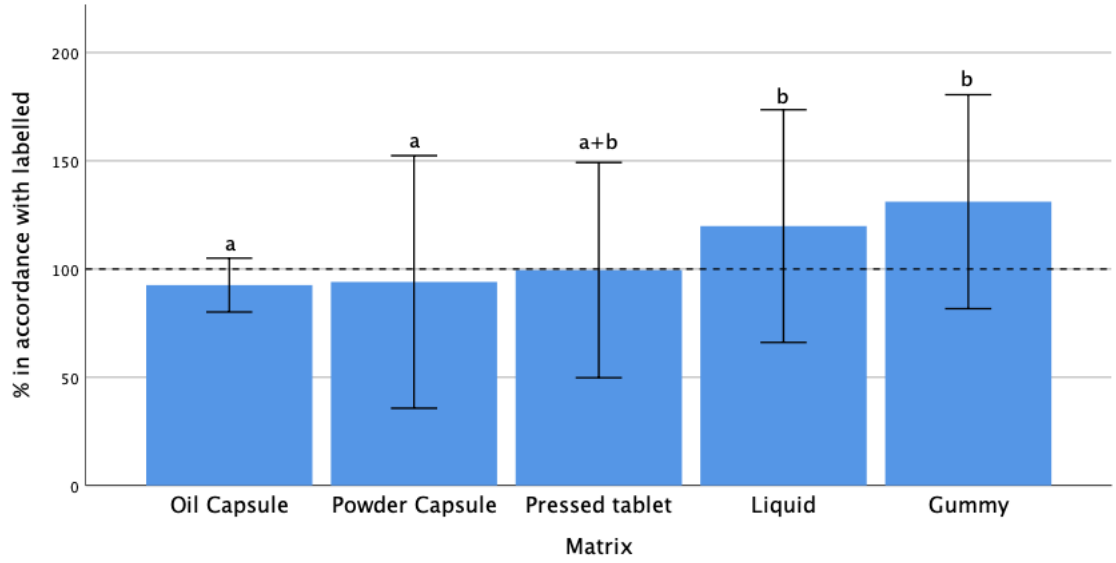

Figure 6. Accordance of analysed iodine content categorised by supplement matrix. Bars illustrate % accordance with labelled iodine content. Error bars illustrate 2SD. Values below 100% indicate lower analysed values than labelled, whereas values over 100% indicate higher analysed values than labelled. The dotted reference line represents 100% accordance with labelled. Different letters indicate significant difference between groups ($p > .05$)

3.4Analysed iodine content and recommended intake

Collected products not targeted for use during pregnancy, breastfeeding or in children were defined as targeted for use in adults. The mean analytical values for these products are presented in **Figure 6**. Of the dietary supplements targeted for use in adults 35% (n=15) exceeded and 60% (n=26) were below RI of 150 µg/day (NNR). Only 5% (n=2) was in line with RI of 150 µg/day. The mean analytical values of products targeted for use during pregnancy and breastfeeding is presented in **Figure 7**. All products for use during pregnancy and breastfeeding were below the RI of 175 µg/day and 200 µg/day, respectively. The mean analytical values of products targeted for use in children is presented in **Figure 8.** Two products were below and one product exceeded RI of 90 µg/day for children 2-5 years old. In total 31% (n=16) of all products exceeded, 65% (n=34) were below, and 4% (n=2) met RI for their target group.

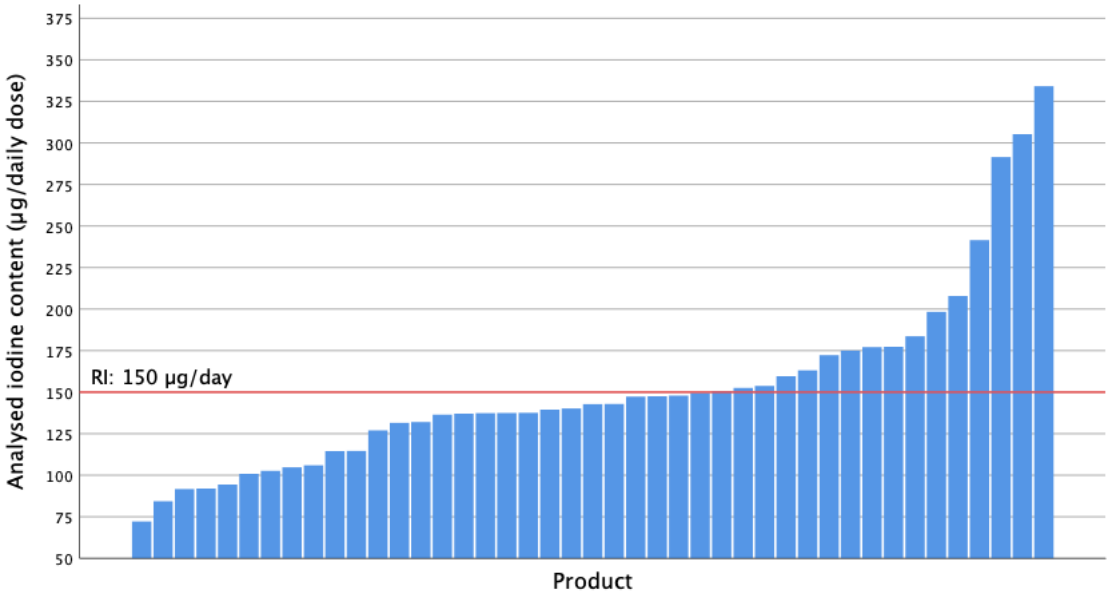

Figure 7. Iodine content in recommended daily dose of dietary supplements. Products marketed for use in pregnancy, breastfeeding and in children are not shown. Bars illustrate mean iodine content (µg/recommended dose) of 12 samples for each product. The red reference line illustrates the recommended iodine intake (RI) in adults (150 µg/day), according to the Nordic Nutrition Recommendations (NNR, 2012).

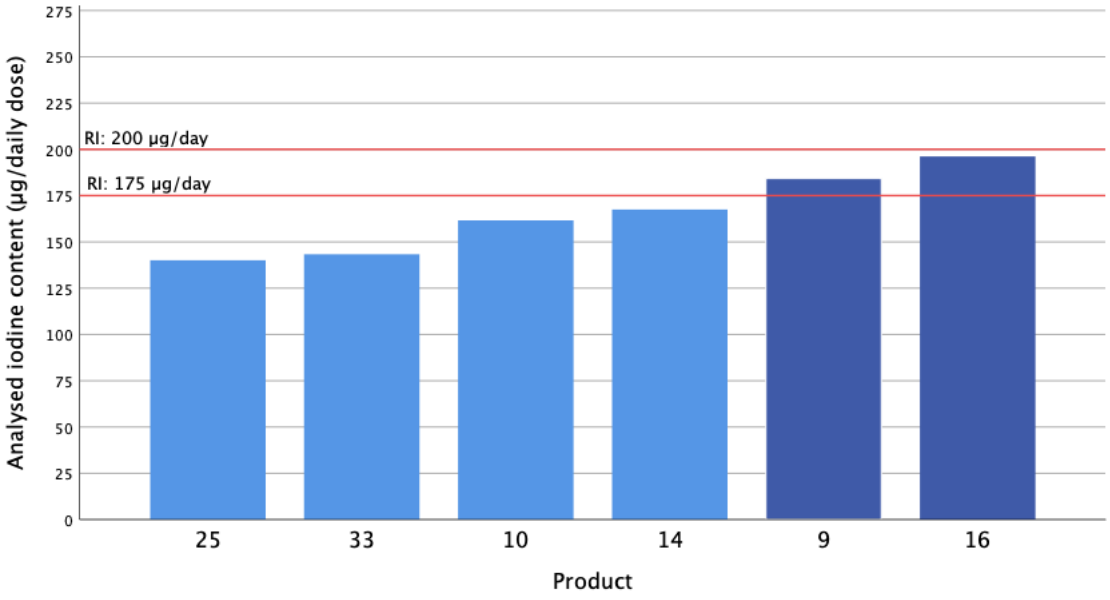

Figure 8. Iodine content in recommended daily dose of dietary supplements marketed for use in pregnancy and breastfeeding. Bars illustrate mean iodine content (µg/ recommended dose) of 12 samples for each product. Light blue bars illustrate products marketed for use during pregnancy and dark blue bars illustrate products marketed for use during breastfeeding. The red reference lines illustrate the recommended iodine intake (RI) in pregnancy (150 µg /day) and during breastfeeding (175 µg /day), according to the Nordic Nutrition Recommendations (NNR, 2012).

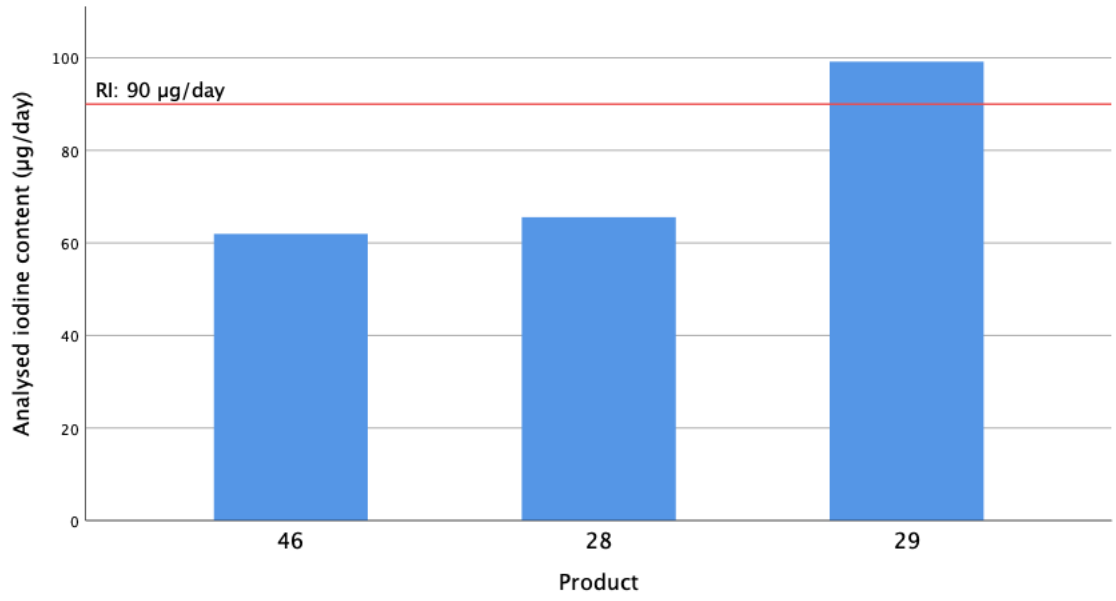

Figure 9. Iodine content in recommended dose of dietary supplements marketed for use in children. Bars illustrate mean iodine content (µg/ recommended dose) of 12 samples for each product. The red reference line illustrates the recommended iodine intake (RI) in children 2-5 years old (90 µg /day), according to the Nordic Nutrition Recommendations (NNR, 2012)

The mean analysed iodine content of products purchased from pharmacies was higher than products purchased from online fitness stores and grocery stores ($p < .001$) and $p = .001$ respectively, and lower than products purchased from health food stores ($p < .001$). The analysed iodine content of products purchased from health food stores was also higher than products purchased from online fitness stores and grocery stores ($p < .001$ and $p < .001$ respectively). There was no difference in analysed iodine content between products purchased from online fitness stores and grocery stores ($p = .335$). Single iodine supplements had higher mean iodine content than multi supplements ($p < .001$). The mean analysed iodine content in liquid products was higher than the mean analysed iodine content from all other matrices ($p < .001$) as presented in **Figure 9.**

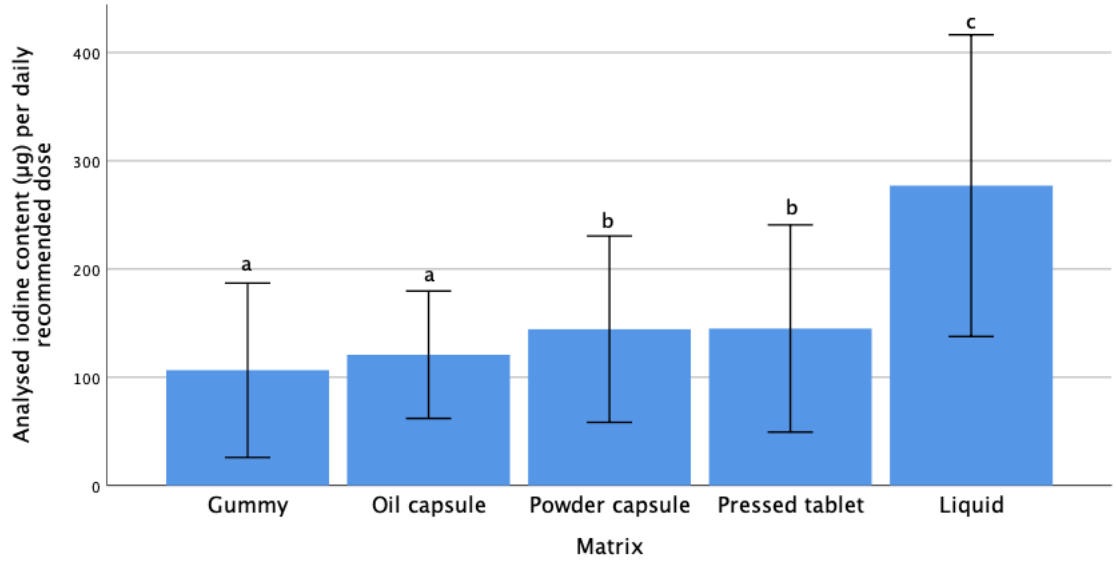

Figure 10. Analysed iodine content categorised by supplement matrix. Bars illustrate mean of analysed iodine content (µg/recommended dose) and error bars illustrate 2SD. Different letters indicate significant difference between groups ($p > .05$).

4. Discussion

The aim of this thesis was to analyse iodine content in dietary supplements available on the Norwegian market, and further compare the results with the labelled iodine content. The main finding of this thesis is that the majority of dietary supplements were in accordance with labelled iodine content, and the mean difference between analysed and labelled iodine content was small. However, some products were not in accordance with labelled iodine content, and four products were not within the tolerance range recommended by the EC. The following chapter will begin with a discussion of the main findings and further their implications, before a methodological discussion.

4.1 Discussion of main findings

4.1.1 Accordance with labelled

Of the collected supplements in this study, 58% was within ±10% of complete accordance with labelled iodine content. The mean difference between analysed and labelled iodine content for all collected supplements was 2.5%. Since deviation from labelled iodine content is expected, the European Commission has established guidelines for how much analysed iodine content may differ from labelled (71). A lower tolerance limit of -20 %, and an upper tolerance limit of +45 % is recommended for minerals, including iodine (71).

Of the collected supplements that was not in accordance with labelled, 34% were within the tolerance range defined by the EC. Since these tolerances are defined as percentages of the labelled iodine content, the range is affected by the labelled iodine content. For example, a supplement with a labelled iodine content of 50 µg/ recommended dose would have a tolerance range from 40 to 73 µg/recommended dose. Further, a supplement with a labelled iodine content of 300 µg/recommended dose, would have a tolerance range from 240 to 435 µg/recommended dose. Thus, even for products within tolerance range the iodine content can deviate greatly from labelled. This may have consequences for consumers as the optimal range of iodine intake is small. A narrower tolerance range could provide consumers more safe and accurate information of iodine content in supplements. Four of the collected products in our study was not within the tolerance range from EC. This is not considered break of regulations as the tolerance limits are merely guidelines. However, manufacturers are responsible for producing supplements that are

safe for consumers. Deviation from the labelled iodine content may mislead consumers and pose a risk of both insufficient and excess iodine intake (74). Iodine supplementation is recommended in individuals with low iodine intake from food (4), and a lower iodine content in dietary supplements than labelled could lead to continued insufficient intake. On the other hand, higher iodine content of dietary supplements than labelled may pose a risk of excess intake, particularly in individuals with high iodine intake from food. Although some products deviated from labelled, the iodine content was below the UL of 600 µg/day for adults and can be considered safe (38). Supplements targeted for use during pregnancy and breastfeeding had lower mean analytical values than labelled, although the difference from labelled was not significant (*P*=.118 and p=.359, respectively). Mild-to-moderate iodine deficiency during pregnancy has been associated with impaired child neurodevelopment (17-22, 67). Pregnant and breastfeeding women are at risk of iodine deficiency and iodine supplementation is intended to provide adequate iodine status for both mother and child. A lower iodine content than labelled may result in continued insufficient iodine intake. When assessing iodine content in research (for example when calculating iodine intake from an FFQ), the labelled iodine content of supplements may be used. If the iodine content differs greatly from labelled, this could affect the estimated iodine intake. Since the mean difference from labelled iodine content was low in our study it is unlikely that using labelled iodine content for dietary assessment would cause inaccurate estimation of iodine intake in research studies conducted in Norway.

To my knowledge there few studies that have investigated iodine content in dietary supplements Thus, this study contributes to increased knowledge of iodine content in dietary supplements. One study from the US, have investigated adult multivitamineral supplements available in the US marked. Here, they found that iodine had the highest mean percentage difference from labelled (25.9 %) and the highest variability, of all the micronutrients analysed (77). Another study from the US found that iodine content of prenatal multivitamins available in the US considerably differed from labelled for both potassium iodine and kelp supplements (76). However, the US study (76) did not provide methodological explanations for sampling or analysis, therefore the results should be evaluated with caution. Thus, the few available results from previous studies are not in line with our results. One possible explanation for the conflicting results is different methods for analysing iodine content. In addition, the US dietary supplement market may not be comparable to the Norwegian supplement market due to different legislations.

4.1.2 Iodine content of dietary supplements and recommended intake

The minimum limit for iodine content in dietary supplements is 23 µg/recommended dose(72). While the EC are working on establishing joint maximum limits for iodine in dietary supplements, the previous Norwegian limit of 225 µg/recommended dose was retracted in 2017 (73). None of the products in the current study had analysed iodine content below the minimum limit, whereas four products exceeded the previous maximum limit of 225 µg/recommend dose. Also, none of the products collected in this study exceeded upper tolerable intake level for their intended target group. Thus, all the products collected in this study can be considered safe for consumers.

Since certain groups of the Norwegian population is at risk of iodine deficiency, supplementation is an important strategy to ensure sufficient iodine intake (2, 4). The analysed iodine content of the majority of collected products in our study was below the recommended intake (RI) for their intended target group. Still, it is likely that consumers reach sufficient intake when using supplements with iodine content below recommended intake, as most individuals get some iodine through food (50). Of the collected dietary supplements, 31% had iodine content higher than recommended intake for their intended target group. Supplementation of iodine is not recommended in individuals that have a sufficient iodine intake from food. Still, it is possible that supplements are used even if not necessary. Thus, dietary supplements with high iodine content are a potential risk of excess intake in individuals with high iodine intake from food (2, 28). High doses of iodine from dietary supplements are unnecessary, as it does not provide any additional health benefits, and can potentially be harmful (23, 28). Both hypo- and hyperthyroidism has been reported from excessive intake of iodine in vulnerable individuals, such as those with autoimmune thyroiditis and those that have previously been exposed to iodine deficiency (23). Impaired thyroid function has also been reported in infants of mothers taking high doses of iodine from dietary supplements (26, 28). It is reassuring that none of the dietary supplements in our study exceeded the upper tolerable intake level, but official legislation preventing high doses of iodine in dietary supplements is lacking. Therefore, there is a need for new maximum limits for iodine content in dietary supplements, to ensure consumer safety. The Norwegian Food Safety Authority has assigned The Norwegian Scientific Committee for Food and Environment to conduct an independent risk assessment for consequences of establishing new national maximum limits (73).

We found that single iodine supplements had higher iodine content compared to multi supplements ($p < .001$). The recommended daily dose for iodine supplementation in individuals at risk of insufficient intake is 100-150 µg/day (4). Of the collected supplements in this study, only multi supplements was in line with this recommendation. This may be the reason that the Norwegian Directorate of Health specify to choose multi supplements in their recommendations (4). However, consumers may not want to use multi supplements, and instead chose a single supplement with high iodine content. Only one of the single iodine supplements (Product 22) in our study had labelled iodine content close to the recommended intake. This product was purchased from an online fitness store and is therefore less available for many consumers. Hence, there is a need for single iodine supplements with lower iodine content more available on the market.

Liquid iodine supplements had high concentrations of iodine and had higher analysed values than labelled ($p < .001$). The instructions for one of the liquid supplements included in this study, suggested to drop the product directly on the tongue (product 49). It may be difficult to measure the correct dose, when ingested in this way. Thus, there is a potential for exceeding the daily recommended dose, especially if the iodine content is higher than labelled. Dietary supplements with a pre-measured daily dose, such as tablets, capsules and gummy matrices reduce the risk of user mistake and may be safer for consumers. One benefit of liquid dietary supplements is the possibility to reduce the daily dose, and consequently iodine intake. This could be appealing for consumers that want to follow the recommended iodine intake from supplements, without using multi supplements. Labelling information for another liquid iodine supplement (Product 48) recommended to drop into a glass of water before intake. This may be a safer strategy for consumers that want to use liquid dietary supplements.

4.1.3 Marketing of iodine containing supplements

The dietary supplement market is large and complex, with new products emerging rapidly. Dietary supplements are not approved by the Norwegian Food Safety Authority before introduction on the market and the manufacturer itself is responsible to follow legislation (72) (82). The Norwegian Food Safety Authority can monitor supplements on the market, but this is usually done for products that has raised suspicion, not routine controls of all dietary supplements on the market. These inspections mostly focus on labelling, marketing and content of harmful ingredients and less degree to the content of nutrients. Controls in other European countries, found that most break of regulations was tied to misleading marketing (82).

Misleading marketing and labelling can contribute to unnecessary use of supplements, and consumption of harmful amounts of nutrients (82). During collection of products, we noted information on websites, from retailers and on product packaging that may be considered misleading. Product 48 was a liquid dietary supplement purchased from health food stores. The recommended daily dose of this supplement for individuals over 10 years old was 100-400 µg, higher than the established UL of 300 µg/day for children under 11 years old. Children in Norway generally have a sufficient iodine (60), and addition of high doses from supplementation may pose a risk of excess intake. On the website of this product, it is also suggested that potassium iodine used in other supplements is harmful (83). This may cause consumers to avoid other iodine supplements with lower iodine content, and instead consume high doses of iodine from this supplement. Product 22 also had misleading labelling. The daily recommended dose for this supplement was ambiguous and could potentially lead consumers to ingest twice the recommended daily dose.

It is not allowed to market dietary supplements for the purpose of relieving or cure diseases (72). Still, a report from the Norwegian Food Safety Authority on dietary supplements in Norway, found that many consumers report using dietary supplements to prevent or heal disease, and some used supplements to improve hair and skin health (82). Of the collected supplements our study, four was marketed to promote hair growth. The target group of this marketing is mainly young women. This is a group at risk of insufficient iodine intake and use of supplements is unlikely to be harmful. It is however concerning that supplements are used with the intention of following a trend or to improve physical appearance.

4.2 Methodological discussion

4.2.1 Collection of dietary supplements

Aspects related to collection and sampling of dietary supplement products could have effects on the within product variation in analysis results. Sales figures for dietary supplements were not available, therefore we did not have the opportunity to collect supplement products based on consumer popularity. Instead, all available iodine containing supplements available from physical stores in Norway were collected. It is however challenging to collect all iodine containing dietary supplements available to Norwegian consumers, as the online market is complex. Dietary supplements from two online fitness stores were included in this study. The strength of including online stores in the collection of products is that the characteristics of products and customer base of online stores may differ from the physical stores. A report from the Norwegian Food Safety Authority, found that physical stores represent the largest shares in the dietary supplement market (82). Thus, we believe to have collected a representable sample of the Norwegian supplement market, despite not collecting all iodine containing supplement available to Norwegian consumers. The dietary supplement market is dynamic, with new products emerging rapidly. The included products in this thesis represent the available dietary supplements at the restricted collection period of August - October 2020.

A strength of our sampling is that we aimed to collect three individual batch numbers from each product to consider variation in iodine content in the supplement products. Between batch variation can be a result of differences in production and degradation of nutrients during transportation and storage. Dietary supplements typically have long shelf life and finding individual batch numbers proved to be challenging. Less popular stores often had older batch numbers, possibly due to lower turnover rate. Additional batch numbers were also searched for in other cities, including Haugesund and Oslo. Still, three individual batch numbers were not identified for every product, and all products from online fitness stores had identical batch numbers. This is a limitation since variation between batches could not be identified for these products, however it is unlikely to have affected our results.

Four samples were collected from each batch during homogenisation and sample preparation, providing a total of twelve samples for each product **(Figure 3).** Inclusion of more samples may contribute to within product variation in analysis results. Still, it is a strength of our study that

twelve samples were used, as variation caused by methodological limitations is possible to identify.

4.2.2 Iodine determination

To compare the variation in analysed iodine content between products the relative standard deviation (RSD) for each product was calculated. The RSD of analytical values within products ranged from 1 to 80 %, which suggests methodological limitations. Aspects related to homogenisation, sample preparation and analysis may have contributed to the within product variation in analysis results. During homogenisation there is a risk of between sample contamination that could explain variations in analysed iodine content within products. Measures to reduce this risk included the use of single-use plastic spatulas and thorough cleaning of homogenisation vials with hot water and dish soap. Thus, it is unlikely that between sample contamination could explain the great within product variation for some products, though it could have minor effects. Within product variations in analysed iodine content could also be explained by variations in iodine content in a product batch. Since two samples from each batch were homogenised separately, this could result in different iodine concentration for each homogenised sample. Aspects related to storage and transportation of samples could affect iodine concentration. However, samples were stored in closed containers at 4 °C following homogenisation to reduce this risk. Aspects related to sample preparation may have contributed to the within product variations in analysed iodine content. Some of the samples did not solve completely during sample preparation, and a lower iodine content would be expected from these samples. This could explain the high variability and low mean values for products 22 and 40. The ICP-MS method has a high selectivity and sensitivity, making it the preferred method for iodine determination and the IMR is accredited for this method (84). Results may have been affected by the uncertainty of the ICP-MS method, although the analysed and measured values from reference material with known iodine concentration were in agreement with the certified values.

Although some products had great within product variation, the mean RSD was 16% and the RSD was under 10% in nearly half (46%) of the products. Great within product variation is a limitation of this study, although including twelve samples of each products allowed for identification of this limitation. The results of dietary supplements with little within product variation are likely to reflect the iodine content. Products 22 and 40 were below the lower

tolerance limit of -20% of labelled recommended by the European Commission (74). There was however great within product variation in analysed iodine content, and the difference from labelled could explained by the methodological limitations described above. Mean analytical values for product 46 exceeded the upper tolerance limit of +45% recommended by the European Commission, and are likely to reflect the iodine content, as there was little variation in analysis results. Product 48 was a very concentrated liquid supplement, and even small measuring mistakes during sample preparation and dilution could explain the variation in analytical values. Still, the analytical values were higher than labelled for all 12 samples and may reflect the iodine content of this product. When comparing product categories, few products in one group can affect the result. We found that health foods stores, liquid supplements and gummy supplements had higher mean analytical values than labelled. These results are likely to be affected by the difference from labelled in product 46 and 48.

5 Conclusion

Our findings suggests that iodine content of most dietary supplements available on the Norwegian market is in accordance with the labelling. For products with iodine content that were not in accordance with the labelling, the analysed content was found to be at levels not likely to be harmful for most consumers. However, we found that the marketing of some products could cause unnecessary use of supplements or consumption of excess iodine.

The current regulations on dietary supplements in Norway are limited and allow for deviation from labelled iodine content. Controls of nutrient composition of dietary supplements are rare. Hence, there is potential for harmful products to be available on the Norwegian market, even though none were discovered in this study. Since the dietary supplement market is dynamic, and the findings in our study are not globally representable, this type of research should be repeated to gain a better understanding of the iodine content in dietary supplements.

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7 Appendix

Appendix 1. Detailed characteristics of collected dietary supplements.

Product number	Product name	Manufacturer	Retail category	Target group	single/multi*	Supplement matrix	Labelled (µg/recommended dose)
1	Berthelsen jod	Berthelsen	health food	not specified	single	pressed tablet	225
2	Clear brain	New Nordic AS	health food	Not specified	multi	pressed tablet	150
3	Complete Kvinne	Karo Pharma	pharmacy	women	multi	pressed tablet	100
4	Complete Mann	Karo Pharma	pharmacy	men	multi	pressed tablet	100
5	Gerimax daglig energi	Orkla Health Norge	grocery	Not specified	multi	pressed tablet	150
6	Gevita multiveg	Orkla Health Norge	pharmacy	vegan/vegetarian	multi	pressed tablet	150
7	Hair Luxious	Good for me	pharmacy	hair growth	multi	pressed tablet	100
8	Collett Kostpluss multitotal	Orkla Health Norge	grocery	not specified	multi	pressed tablet	150
9	Lifeline Care ammende	Lifeline Pharma AS	pharmacy	postnatal / breastfeeding	multi	pressed tablet	200
10	Lifeline Care Gravid	Lifeline Pharma AS	pharmacy	pregnancy	multi	pressed tablet	175
11	Lifeline Care Kvinne	Lifeline Pharma AS	pharmacy	women	multi	pressed tablet	150

12	Metode Multi Vitamin & Mineral	Apotek 1 PXG Pharma Gmbh	pharmacy	not specified	multi	pressed tablet	150
13	Møllers total	Orkla Health Norge	grocery	not specified	multi	pressed tablet	150
14	Nycoplus gravid	Nycoplus Takeda AS	pharmacy	pregnancy	multi	pressed tablet	175
15	Nycoplus jod	Nycoplus Takeda AS	pharmacy	not specified	single	pressed tablet	225
16	Nycoplus mamma	Nycoplus Takeda AS	pharmacy	postnatal / breastfeeding	multi	pressed tablet	200
17	Nycoplus multi 100tab	Nycoplus Takeda AS	pharmacy	not specified	multi	pressed tablet	150
18	Nycoplus multi uten A, D og K	Nycoplus Takeda AS	pharmacy	not specified	multi	pressed tablet	150
19	Omni-vegan	Biosym AS	health food	vegan/vegetarian	multi	pressed tablet	150
20	Vitaplex vitamineral	Orkla Health Norge	grocery	not specified	multi	pressed tablet	150
21	Opti-men	Optimum Nutrition	Online fitness	men	multi	pressed tablet	100
22	Bodyfuel jod tabletter	Netthandelsgruppen AS	Online fitness	not specified	single	pressed tablet	150
23	Work like a pro! Vitaminpro daily multi	First Class Brands of Sweden	Online fitness	not specified	multi	pressed tablet	100
24	Holistic multimineral	Holistic Sweden AB	Online fitness	not specified	multi	pressed tablet	68

25	Alpha plus mamma	Alpha Plus	Online fitness	pregnancy	multi	pressed tablet	160
26	Ultimate vitamins & minerals	Star Nutrition, HSNG AB	Online fitness	not specified	multi	pressed tablet	200
27	Alpha plus kvinna	Alpha Plus	Online fitness	women	multi	pressed tablet	160
28	Alpha plus barn	Alpha Plus	Online fitness	children	multi	pressed tablet	70
29	Nycoplus Multi Barn	Nycoplus Takeda AS	pharmacy	children	multi	pressed tablet	120
30	Arcon-Tisane plus	Arcon International GmbH	health food	hair growth	multi	oil capsule	75
31	Life multi man	Life AS Norge	health food	men	multi	powder capsule	150
32	Life multi man 55+	Life AS Norge	health food	men	multi	powder capsule	150
33	Life multi pregnant	Life AS Norge	health food	pregnancy	multi	powder capsule	150
34	Life multi vegetarian	Life AS Norge	health food	vegan/vegetarian	multi	powder capsule	150
35	Life multiwoman	Life AS Norge	health food	women	multi	powder capsule	150
36	Life multiwoman 55+	Life AS Norge	health food	women	multi	powder capsule	150
37	Metode Ginseng multi	Apotek 1 PXG Pharma Gmbh	pharmacy	not specified	multi	oil capsule	150

38	Metode omega-3 multi	Apotek 1 PXG Pharma Gmbh	pharmacy	not specified	multi	oil capsule	150
39	Nycoplus omega-3 multi	Nycoplus Takeda AS	pharmacy	not specified	multi	oil capsule	150
40	Self multivitamin	Self Omninutrition	Online fitness	not specified	multi	powder capsule	225
41	Vitamins & minereals daily	Star Nutrition HSNG AB	Online fitness	not specified	multi	powder capsule	150
42	vitamins & minerals athlete	Star Nutrition HSNG AB	Online fitness	not specified	multi	powder capsule	150
43	Vita-min one	Olimp Sport Nutrition, Olimp Laboratories	Online fitness	not specified	multi	powder capsule	150
44	Beauty Bear Hair vegan vitamins	Bertheksen, Letsfaceit Nordic AS	pharmacy	hair growth	multi	gummy	150
45	Stardust beautybears	Netthandelsgruppen AS	Online fitness	hair growth	multi	gummy	75
46	Ultravit kids multivitamin	VP Laboratories	Online fitness	children	multi	gummy	42
47	Ultravit adult multivitamin	VP Laboratories	Online fitness	not specified	multi	gummy	80
48	1% høyoppløst jod	Probioform	health food	not specified	single	liquid	200
49	Flytende ionisk jod med selen	MSM Norge AS	health food	not specified	single	liquid	300
50	Mivitotal pluss	Midsona	health food	not specified	multi	liquid	150

51	Bodyfuel jod flytende	Netthandelsgruppen AS	Online fitness	not specified	single	liquid	300
52	Mivitotal kapsler	Midsona	Online fitness	not specified	multi	powder capsule	72