



Nutrition

The effect of intake of sausages fortified with β -CD-I₂ complex on iodine status and thyroid function: A preliminary studyMaksym Polumbryk^{a,*}, Victor Kravchenko^b, Vasyl Pasichnyi^a, Chrystyna Omelchenko^a, Irina Pachitskaya^c^a National university of food technologies, Problem research laboratory, Volodymyrska St. 68, Kyiv, Ukraine^b Institute of endocrinology and metabolism, Department of epidemiology of endocrine diseases, Vyshgorodska St. 69, Kyiv, Ukraine^c Scientific-practical center for foodstuffs of the National Academy of Sciences of Belarus, Republican control-testing complex of foodstuffs quality and safety, Kozlova St. 29, Minsk, Belarus

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ABSTRACT

The present study evaluated influence of boiled sausages consumption fortified with β -CD-I₂ on the urinary iodine excretion (UIE) level of volunteers. Median urinary UIE level was increased from 58.02 (24.0–175.4) μ g/L to 110.6 (20.5–231.6) μ g/L during 10 days. Thyroid stimulating hormone (TSH) and free thyroxine (FT4) levels were determined by radio immunoassay analysis. As it was expected, intake of sausages fortified with β -CD-I₂ resulted in rise of FT4 level from 1.1 (0.95–1.25) to 1.23 (1.07–1.63) ng/dL, whereas TSH level decreased from 1.53 (0.47–3.37) mIU/L to 1.1 (0.51–3.17) mIU/L. A dynamic gastrointestinal model *in vitro* was used in order to determine possibility of 3,5-diiodotyrosine (DIT) formation during consumption of the fortified sausages. The DIT concentration was determined by HPLC–MS method and was found to be 0.38 ng/mL in sausage dialyzate. These findings indicate that β -CD-I₂ introduction as an iodine carrier in boiled sausages may help to improve iodine status and to control organic iodine species concentration.

1. Introduction

Iodine deficiency is a one of the major nutritional problem which affects about 2 billion people worldwide [1]. Several disorders caused by deficiency of this trace element have been prevented by iodized salt consumption [2,3]. Unfortunately, mandatory iodination of salt may cause an adverse effect in some countries and specific groups of people [4]. Moreover, the iodized food additives, such as potassium iodide and iodate, which are the main compounds of iodized salt, can be lost during food processing [5], especially boiling under high pressure [6]. Therefore, it is necessary to develop the new iodine containing food additives able to improve the iodine status. Therefore, demand for this essential trace element can be satisfied by prolonged consumption of functional foods containing these additives.

Iodine plays an important role in breast cancer physiology and has a protective role in breast cancer [7,8]. Supplementation with iodine in its molecular form causes apoptotic effect on animal and cancer cells [9]. Several mechanisms are suggested for the cancer-inhibiting effect of molecular iodine action including antioxidant effect, mainly due to 3,5-diiodotyrosine (DIT) formation [10]. It has been found that high dosage of DIT consumption by Wistar rats has a protective effect by

balancing the antioxidant system [10].

Molecular iodine cannot be directly introduced in the diet due to its high toxicity. This disadvantage can be solved by iodine encapsulation with β -cyclodextrin, which is widely used as a food encapsulating agent [11]. Encapsulation of active compounds is commonly utilized in pharmacy, chemistry, and food technology, in order to improve their stability during prolonged storage [11–13].

Boiled sausages were chosen as the vehicle for iodine fortification because they are consumed by wide range of individuals. Another reason for the choice of boiled sausages is a high amount of L-tyrosine residues. Here we suggest that consumption of the fortified sausages would result in the DIT formation due to direct reaction between I₂ and L-tyrosine, preceded by digestion of protein matrix of the sausages in gastrointestinal tract.

The purpose of this study is to investigate the effectiveness of boiled sausages fortification with the iodine-cyclodextrin complex on iodine excretion in a population studied both before and after the fortified sausages intake was introduced. Also, we have used dynamic *in vitro* gastrointestinal model in order to examine possibility of 3,5-diiodotyrosine formation during digestion of the boiled sausages.

* Corresponding author.

E-mail address: polumbr@nuft.edu.ua (M. Polumbryk).

2. Materials and methods

2.1. Materials

I₂, 3,5-diiodotyrosine, β-cyclodextrin (β-CD), DMF, HNO₃, and HCl were purchased from Sigma-Aldrich. All the chemicals were analytical reagent grade. Acetonitrile, formic acid and methanol were purchased from Merck (Germany) for HPLC purposes.

The chicken thigh meat was obtained from “Havrylivski kurchata” (Ukraine). The thigh meat was deboned and skinned before being stored under vacuum at –20 °C and was used within a 10 days of storage. Dry beef isolate “Bilkozine” was obtained from Bilkozine Co. (Ukraine). All the other hydrocolloids, namely, xanthan gum, guar gum, soybean isolate, Carboxymethylcellulose (CMC), whey protein isolate, soybean isolate, salt, sodium nitrite were obtained from Roeper (Germany). Silicagel A300 was sourced from Shandong Silica Gel (China). Aromatizer “Frankfurter’s sausages” was obtained from a local supermarket chain Auchan.

Crystalline pepsin and trypsin were purchased from Biopharma (Ukraine).

2.2. Study population

Thirty one patients (14 women and 17 men) participated in a case control clinical study at Institute of endocrinology and metabolism (Kyiv, Ukraine). The participants didn't differ significantly in age, sex or BMI. Exclusion criteria were history of thyroid diseases, treatment with iodine containing drugs, or supplements and food additives including iodinated salt. Two weeks prior to the start of experiment, patients stopped consumption of any iodine containing drugs and food products fortified with iodine. The individuals were observed by a trained doctor in order to exclude somatic and endocrine pathology before the start of experiments. Thyroid glands were examined by manual palpation according to the procedure, recommended by World Health Organization [1]. The patients gave their consent in a written form, and the study was approved by ethics committee of the Institute.

All participants consumed equal portion (150 g) of boiled sausages every day for the duration of 10 days, independently on age, sex or body weight. Patients were asked to collect urine samples on days 0 and 10 of sausages consumption and 10 days after sausages consumption was terminated. None of the patients took drugs containing iodine and food products fortified with iodine.

2.3. Ultrasound

Thyroid ultrasound measurements were performed using a real-time ultrasonographic portable scanner Terason 2000 with linear sensor and the frequency of 10 MHz. The thyroid sizes were determined according to the recommendations of J. Brunn et al. [14].

2.4. Instrumentation and sample preparation

Urinary iodine excretion (UIE) levels were measured in a laboratory of epidemiology department of V. P. Komissarenko Institute of endocrinology and metabolism (Kyiv, Ukraine) using a modification of the classical Sandall-Kolthoff reaction after digestion with hydrochloric acid, as described by Dunn et al. [15]. Spot urine samples were obtained from the volunteers on the day before the sausages administration was started and, on the day after the consumption of sausages was terminated, and on the tenth day after end of the sausages consumption. The limit of qualitative determination of iodine concentration was 5 µg/mL. In addition to applying internal quality control, the laboratory participated in the external quality control for urinary iodine of EQUIP (Ensuring the Quality of Urinary Iodine Procedures) standardization program of the CDC (Centers for Disease Control and Prevention, Atlanta, USA).

Sample preparation was performed according to the procedure used for iodine determination in food [16]. A sample of boiled sausages (200 mg) was placed in a quartz flask, and 5 mL of concentrated HNO₃ was added. The microwave heating program was (1) 1400 W for 60 min (ramp of 10 min) and (2) 0 W for 10 min (cooling step). After cooling, the digests were diluted in a polypropylene vessel with 30 mL of water. Iodine content was determined by a luminescence spectrophotometer (JenWay 6300, USA), using an external calibration curve. The measurements were done at the emission wavelength of 481 nm.

Non-fasting blood samples were obtained from each volunteer via venipuncture by a trained phlebotomist. The laboratory measurements of the total FT4 (free thyroxine) and TSH (Thyreo stimulating hormone) levels were performed by radio immunoassay analysis using a reagent pack (Amersham, U.K.). The reference ranges for TSH and FT4 levels were 0.4–4.6 mIU/mL, and 0.89–1.76 ng/dL, respectively.

2.5. Synthesis of β-cyclodextrin-I₂ complex

Synthesis of the β-CD/I₂ complex was done according to the synthesis procedure described by Wang et al. [17]. 3.8 g of KI and 0.38 g of I₂ (1.5 mM) were dissolved in 15 mL of distilled water during 10 min resulting in KI₃ formation. Then, this solution was dropped into 10 mL β-cyclodextrin solution (223 mg, 0.5 mM) contained in a 50 mL conical flask. The mixture was stirred for 5 h at 25 °C and then retained 10 h at 4 °C, in order to fully encapsulate iodine in β-CD. After that, brown crystals of β-CD/I₂ were filtered, washed by KI solution, in order to remove I₂ molecules from the filter cake, and rinsed by distilled water to get rid from both KI and β-CD. The final product was dried in vacuum for 4 h at 40 °C.

Iodine content in the complex was determined by iodimetric titration procedure, described by Wang et al. (2009a).

The iodine content in the complex was calculated to be 16.9 ± 0.1%, indicating that the ratio between β-CD and I₂ in the complex was 1:1. Also, we did morphological assay and X-ray analysis of the synthesized complex [18]. Iodine content was found to be 16.82 ± 0.4% [18] what is in agreement with the data obtained by Wang et al. [17].

2.6. Boiled sausages manufacture

The chicken sausage formulation is shown in Table 1. The chicken thigh meat had been minced in a cutter of 100 kg capacity for 2 min. In order to improve sensory features of the final product, a dry mixture of hydrocolloids, containing dry beef isolate “Belkozine”, whey protein isolate, CMC, guar and xanthan gum was mixed with 3 L of β-CD/I₂ aqueous solution. Dissolution of β-CD/I₂ in water serves to assure uniform distribution of β-CD/I₂ in the food matrix. Further, the rest of dry ingredients and water were added into the cutter.

The batter was stuffed into a natural sheep casing, and the obtained

Table 1
Raw chicken sausage product formulation.

Ingredient	Content, kg
Dark meat	17.5
Water	12.3
Soybean isolate	3.75
Dry beef isolate “Belkozine”	2.25
Whey protein isolate	0.75
Carboxymethylcellulose	0.187
Guar gum	0.375
Xanthan gum	0.188
Sodium nitrite	0.002
Salt	0.52
Silicagel A300	0.15
Aromatizer “Frankfurter’s sausages”	0.25
CD/I ₂ complex	0.00011

sausages were hand linked at about 15 cm intervals. The sausages were placed on PET trays and wrapped with PA films before being cooked at 90 °C during 30 min. The cooked sausages were retained at 70 °C for 90 min and cooled at room temperature for 2 h. Finally, these sausages were placed in cardboard wrapper and stored at 4 °C before being taken by volunteers.

2.7. Set-up of the *in vitro* digestion experiments

The experiments were performed in a dynamic gastrointestinal model with compartments simulating the stomach and small intestine, according to the procedure described in literature [19]. For dialysis of the digested products and for water absorption, a cartridge with semi-permeable membranes (Sophadex., cut-off of 5–7 kDa) was connected to the compartments, which were retained at 37 ± 0.5 °C during experiments. The samples of boiled sausages were cut into cubes of about 0.5 cm of size, followed by addition of these samples containing 6 g of proteins into the inner gastric compartment. These samples were mixed with 50 mL of 0.2 M HCl and 300 mg of crystalline pepsin. Additional experiment was performed with 11.3 mg of β -CD- I_2 addition into the mixture in order to compare effect of DIT formation in digested fortified sausages (sample 2). The samples were incubated with pepsin for 2 h. After that, the protein slurry in the compartments was adjusted to pH 8.2 and 300 mg of trypsin were added. This enzyme favors proteins and peptides digestion in the small intestine. Finally, the enzymatic reaction was interrupted after 2 h of digestion and samples were taken from external compartments [19]. Each was repeated 3 times.

2.8. HPLC–MS spectrometry analysis and solid phase extraction (SPE) clean-up

DIT concentration in the above samples of hydrolysate solutions was determined according to the known analytical procedure of the DIT analysis described by Wang et al. [20], which they applied for DIT determination in the hydrolysates of iodinated casein.

The SPE clean-up procedure had the following steps: SPE cartridges (AccuBond II ODS-C18 Cartridges) conditioning with 3 mL of methanol followed by 3 mL of distilled water; 2 mL of sample application to the cartridges; loading; rinsing with 3 mL of methanol; elution with 2 mL of a methanol–water–formic acid solution (25:24:1, v/v) followed by filtration through a membrane filter and complete collection of the eluent into an HPLC. The eluent was then injected and analyzed.

The HPLC–MS system consisted of liquid chromatographer Agilent 1200 equipped with mass-selective detector Agilent 6460 QQQ LC–MS. A Zorbax Eclipse Plus C18 analytical column (3.5 μ m particle size, 2.1 mm \times 150 mm) was used and run at 30 °C. Gradient elution was performed with a solution of acetonitrile and 0.1% formic acid in water (0.1%, v/v) at the flow rate of 0.2 mL/min. An injection volume of 5 μ L was used for all sample solutions. The analysis has controlled by Mass Hunter Workstation software.

2.9. Statistical analysis

Microsoft Office Excel 2009 software was used for data summarizing and calculations, SPSS 11.0 and MedStat software was subsequently used for statistical analysis. Data were expressed as mean \pm standard deviation (mean \pm SD) and median (range). Normality of distribution was calculated using a Kolmogorov–Smirnov test, and a Mann–Whitney *U* test was used to compare means. All the experiments were considered statistically significant when $P < 0.05$.

3. Results

The iodine intake by adults should not be less than 100 μ g per day, according to WHO recommendations [1]. Therefore, β -CD- I_2 content in the boiled sausages formulation was estimated to provide 100 μ g of

iodine in a serving size (150 g) of the final product portion. Obviously, the iodine concentration can be decreased throughout food production and further storage. It should be noted, that high retention and uniform distribution are the basic requirements for biologically active additive, which have been utilized in food products. Thus, these parameters of β -CD- I_2 were examined.

The effectiveness of food fortification with iodine depends on its retention during food processing. It was found, that the most uniform distribution of iodine was observed in the sausages prepared with preliminary stabilization of proteins. This was done during meat comminution stage. We have examined iodine content in the 3 different samples of sausages. It was determined that iodine content in the 150 g of sausages varies from 91.7 to 96.9 μ g, which corresponds to the mean iodine retention of 94.3%. Thus, there was no need to adjust serving size, taking into account additional sources of iodine in volunteer's diet.

In the ideal case, temperature of food processing should not exceed melting point of the iodine containing additive. It has been reported, that β -CD- I_2 complex melted at 72 °C and decomposed at 185 °C on the further heating [17]. Therefore, boiled sausages were chosen as the object of fortification, since their manufacturing needs mild thermal treatment.

We have studied the influence of the boiled sausages consumption on iodine status of humans. Our results provide data related to the changes in urine iodine excretion during 10 days of fortified boiled sausages ingestion by 31 volunteers. All the data are given in Fig. 1.

The values of median urinary iodine excretion before and after consumption of the boiled sausages had no significant difference between males and females, old and young volunteers. In the group of mild iodine deficiency median UIE was 35.26 μ g/L (27.72–43.74, $p = 0.008$) prior to start of the sausages consumption and was increased among these individuals to 147.26 μ g/L (73.53–174.6, $p = 0.008$) after 10 days of iodinated sausages consumption. Also, median UIE was increased in the group of mild iodine deficiency from 69.61 μ g/L (57.85–82.01, $p = 0.01$) to 111.39 μ g/L (78.13–132.73, $p = 0.01$) during this period of time. Thus, intake of iodine containing sausages had beneficial effect on iodine status of the volunteers during the experiments

Changes in TSH and FT4 were examined for all subjects before and after ingestion of the fortified sausages. The participants did not show a significant difference of FT4 or TSH level before and after consumption of sausages fortified with iodine. Decreased serum TSH level among individuals after sausages consumption was linked with normalization of iodine status. Nevertheless, levels of thyroid hormones were within the normal range during the experiments. Changes in volume of thyroid glands were not detected during our experiments. The volume of thyroid glands of the volunteers before and after 10 days of the fortified sausages intake was analyzed. These ultrasonic measurements were indicated presence of increased thyroid lobe for one person only,

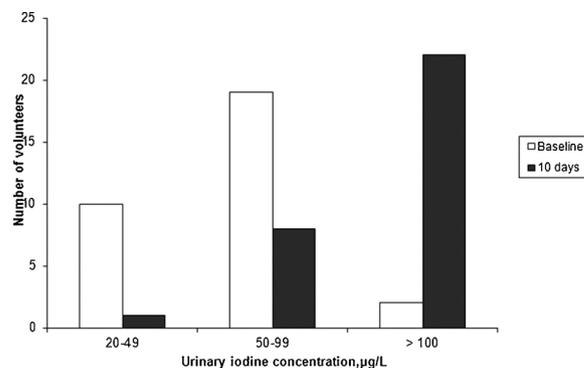


Fig. 1. UIE levels of the volunteers before (baseline) and after (10 days) consumption of sausages, fortified with β -CD- I_2 complex Table 1. Raw chicken sausage product formulation.

Table 2
Urinary iodine excretion and thyroid status of the volunteers.

Characteristics	Values			
	Before sausages consumption		After sausages consumption	
	Mean \pm s.d.	Median (range)	Mean \pm s.d.	Median (range)
Urinary iodine ($\mu\text{g/L}$)	*60.1 \pm 11	*58.02 (24.0–175.4)	*110 \pm 15	*110.6 (20.5–231.6)
Serum TSH (mIU/L)	1.88 \pm 0.02	1.53 (0.47–3.37)	1.1 \pm 0.02	1.1 (0.51–3.17)
Serum FT4, (ng/dL)	1.11 \pm 0.8	1.1 (0.95–1.25)	1.34 \pm 0.07	1.23 (1.07–1.63)

* $p < 0.05$.

whereas the existence of goiter has not been found among all the subjects, except this person who had a first class goitre. All the UIE, TSH and T4 data before and after sausages consumption are given in Table 2.

Different *in vitro* digestion procedures have been used to assess bioavailability of proteins [19,21]. The optimized enzymatic digestion and HPLC-MS analytical procedure were used to analyze DIT concentration in the samples of enzymatically treated boiled sausages fortified with β -CD- I_2 . This enzymatic digestion method has been widely used in the determination of proteins quality, which reflected by essential amino acids content. The results of DIT formation in enzymatically digested boiled sausages, fortified with β -CD- I_2 are given in Table 3.

The data given in Table 3 revealed that, the average DIT content in the enzymatically digested sausages (Sample 1) was detected at very low level (0.38 ± 0.1 ng/mL). We have studied DIT accumulation in the sample 2, where 10 mL of 0.2M HCl were substituted for the equivalent volume of 3,5-diiodotyrosine solution. For this purpose, 11.3 mg of β -CD- I_2 were dissolved in 10 mL 0.2 M HCl and added to the appropriated compartment prior to the pepsin treatment. As expected, significant increase of DIT concentration (2.8 ± 0.2 ng/mL) was observed in the sample of sausage dialyzate with external β -CD- I_2 addition (Sample 2). In other words, the amount of bio-available DIT as well as total iodine level can be increased by direct β -CD- I_2 incorporation into the diet as a supplement.

4. Discussion

Recommended iodine daily intake at minimal level corresponds to a spot urinary iodine concentration approximately $100 \mu\text{g/L}$ [1]. Most of the volunteers were in the range of mild and moderate iodine deficiency prior to participation in the clinical trials. Our study, comprised individuals who has this range with individual UIE from $24.0 \mu\text{g/L}$ to $175.4 \mu\text{g/L}$, and thus provides valid data. Duration of sausages intake was limited to 10 days taking to account the possibility of short term changes of UIE values after administration of iodine containing compounds [22]. The problems of consumers encountered with necessity of day-to-day sausages consumption was another reason for time restriction of sausages administration

UIE is considered to be the most valid biomarker of the iodine status. The measurements of iodine content in the collected spots of urine are recommended for the monitoring of iodine nutrition. Iodine

Table 3
Analytical results of DIT formation in hydrolysates of boiled sausages.

Sample ID	DIT concentration, ng/mL
Sample 1	0.38 ± 0.1
Sample 2	2.8 ± 0.2

status is classified as severe, mild, and moderate for the UIE values below $20 \mu\text{g/L}$, between $20 \mu\text{g/L}$ and $50 \mu\text{g/L}$, and above $50 \mu\text{g/L}$, respectively. Out of all the participants, only 2 person had a UIE level $> 100 \mu\text{g/L}$ before sausage ingestion, while after 10 days of the sausages consumption, 22 volunteers had a UIE level $> 100 \mu\text{g/L}$ (Fig. 1). Interesting, that 22 out of 31 participants had normal UIE ($> 100 \mu\text{g/L}$) after 10 days of the sausages consumption, whereas only one person still was in the group of moderate iodine deficiency after the sausages intake was terminated. We did not observe cases of severe iodine deficiency during the experiments.

The present study indicates that, for majority of volunteers, the iodine deficiency was absent after sausages consumption, even though it was present prior to the experiment. The above was supported by the mean UIE ($60 \pm 11 \mu\text{g/L}$) prior to sausages consumption (Day 0), and UIE was increased to the adequate level of $110 \pm 15 \mu\text{g/L}$ within 10 days of the experiment. At the same time, 25% ($n = 8$) and 3.2% ($n = 1$) of cases were detected having moderate and mild iodine deficiency, respectively. It is interesting to note that 10 days after the consumption of sausages was terminated, the value of mean UIE was $65 \pm 13 \mu\text{g/L}$ which was closed to the UIE level prior to the start sausages consumption.

Adequate iodine intake is a key factor at synthesis of thyroid hormones in thyroid gland. Our results indicated the FT4 and TSH levels in all participants were normal, suggesting no lack of iodine, which is required for the thyroid hormones synthesis in thyroid gland. We demonstrated that there were no significant differences in the TSH and FT4 levels in individuals with normal UIE. Similar findings were observed in ultrasound examination of thyroid glands. We found the increase thyroid lobe for one person only, whereas the existence of goiter had not detected among all the subjects. The latter is rather affiliated to volunteers' attribute than to experimental data, due to a very small duration of experiment.

The correlation between thyroid function or iodine intake and incidences of breast cancer has been established a long time ago [7]. The low number of breast cancer incidences in Japan has associated with high intake of marine algae enriched with iodine. Molecular iodine is more effective in breast cancer therapy than I^- [9]. Moreover, molecular iodine causes a 10- and 50-fold greater antioxidant effect than does ascorbic acid and potassium iodide, respectively [23]. We have encapsulated molecular iodine by β -CD in order to provide a controlled release of iodine during digestion of food in gastrointestinal tract.

We proposed, that the interactions between molecular iodine and tyrosine residues give rise to the 3,5-diiodotyrosine formation. Romaris-Horitas et al. performed comparative investigations of bioavailability of iodine species of edible seaweeds [24]. They found that DIT content in the dialyzates of seaweeds vary from 2.1 ng per gram of algae in NIES 09 Sargass to 487 ng/g in Kombu [24]. These data can be explained by the extremely high total amount of iodine ($1075 \mu\text{g/g}$) in the dialysate of Kombu algae. It should be noted that DIT presence was not detected in the Nori and Walkami seaweeds, which are considered to be very popular in the diet of Japanese people. At the same time, the small amount of 3-monoiodotyrosine (MIT) was found in these species [24]. Similar findings have been reported for methanolic extract of seaweed [21]. The total MIT and DIT concentration in Nori red seaweed extract was found to be 0.815 and 0.376 ppm, respectively [21]. Thus, DIT or/and MIT analysis in the dialyzates requires instrumentation with extremely low limit of detection (LOD). It was found that, for the 3,5-diiodotyrosine, the LOD was 0.1 ng/mL.

We used triple quadrupole LC-MS which can be attributed to superior sensitivity. The average concentration of DIT in the dialyzates of boiled sausages fortified with β -CD- I_2 was found to be 0.38 ng/mL . This corresponds to the 7.6 ng of DIT per gram of boiled sausages. The level of DIT in dialyzate can be easily changed by both formulation adjusting and β -CD- I_2 incorporation into the diet as a supplement. It was found, that addition of 11.3 mg of β -CD- I_2 into the compartments prior to *in vitro* digestion resulted in the increase of DIT level in the dialyzate up to

2.8 ng/mL, which corresponds to the 56 ng of DIT per gram of boiled sausages. Surprisingly, an essential rise of iodine content from 4 µg up to 2000 µg in the inner compartment prior to digestion procedure was resulted in increase of DIT concentration in the dialyzate to about 7-fold only. In our opinion, such food products as boiled sausages are the better carriers of β-CD-I₂ than this additive itself, in the terms of DIT formation. Also, these results can be explained by the predominant 3-moniodotyrosine formation during dialysis. However, these assumptions have to be confirmed during the future investigations.

It must be noted, that excessive amount of thyroid hormones in a diet may result in the thyrotoxicosis [25]. Thus, the amount of thyroid hormones as well as hormones precursors, especially DIT and MIT content must be strongly controlled. Nevertheless, DIT is considered to be a promising antioxidant [10]. It causes less damage effect to thyroid follicular cells than KI when exposed to physiologically excessive level [10].

5. Conclusions

In conclusion, this study proved that β-CD-I₂ is a promising additive which is able to restore iodine status in a short period of time. The boiled sausages fortified with this additive exert noticeable increase of the UIE level during 10 of consumption by 31 individuals without any unwanted side effects. The host-guest complex of iodine and β-CD, as well as boiled sausages fortified with this additive may have a positive impact on decrease of breast cancer incidence rate. We suggest that β-CD-I₂ utilization as a food additive will result in decrease of low UIE level occurrences among population and will lead to reduction of iodine related diseases. Moreover, the implementation of mandatory salt iodination in Ukraine will lead to lower cancer risks among Ukrainians; we strongly urge the Ukrainian government to pass all the necessary legislation in a timely manner.

Conflict of interest

The authors declare that they have no conflict of interest.

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