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RESEARCH ARTICLE

Development of a new inversion-voltammetric technique in determining inorganic iodine in *Laminariae thalli* L. for the quality control of raw materials in factory laboratories

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Abstract

Objectives. To develop and validate a methodology for determining inorganic iodine in *Laminariae thalli* L., corresponding to the norms of the State Pharmacopoeia of the Russian Federation, 15th edition (SPh 15). The methodology needs to be valid and suitable for the quality control of pharmaceutical raw materials in factory laboratories.

Methods. Cathode inversion voltammetry was used as an instrumental method for determining inorganic iodine using a graphite electrode capable of sorbing electroactive ion associates of surfactant–iodine.

Results. When compared with the titrimetric technique recommended by SPh 15, the proposed technique is more selective, sensitive and less time-consuming. The efficiency and metrological characteristics of the technique were confirmed by validation in accordance with the requirements of SPh 15.

Conclusion. The paper presents a new method for determining the gross content of inorganic iodine in *Laminariae thalli* L. This technique can be used not only in scientific research, but also in the routine quality control of medicinal plant raw materials in control and analytical laboratories engaged in pharmaceutical quality control.

Keywords

Laminariae thalli L., gross iodine content, inversion voltammetry

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НАУЧНАЯ СТАТЬЯ

Разработка новой инверсионно-вольтамперометрической методики определения неорганического йода в слоевищах ламинарии (*Laminariae thalli* L.) для контроля качества сырья в условиях заводских лабораторий

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Аннотация

Цели. Разработка и валидация методики определения неорганического йода в талломе ламинарии (*Laminariae thalli* L.), соответствующей нормам Государственной Фармакопеи Российской Федерации XV издания (ГФ РФ XV). Методика должна быть валидной и пригодной для контроля качества фармацевтического сырья в условиях заводских лабораторий.

Методы. В качестве инструментального метода определения неорганического йода была применена катодная инверсионная вольтамперометрия с использованием графитового электрода, способного сорбировать электроактивные ионные ассоциаты поверхностно-активного вещества (ПАВ)–йода.

Результаты. По сравнению с титриметрической методикой, рекомендуемой ГФ РФ XV, предлагаемая методика более селективна, чувствительна и менее трудоемка. Работоспособность и метрологические характеристики методики были подтверждены валидацией согласно требованиям ГФ РФ XV.

Выводы. В работе представлена новая методика определения валового содержания неорганического йода в слоевищах ламинарии (*Laminariae thalli* L.). Данная методика может быть использована не только в научных исследованиях, но и в рутинном контроле качества лекарственного растительного сырья в контрольно-аналитических лабораториях, занимающихся фармацевтическим контролем качества.

Ключевые слова

слоевища ламинарии, валовое содержание йода, инверсионная вольтамперометрия

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INTRODUCTION

Iodine is a trace element essential for human health [1–2]. In particular, iodine is necessary for the synthesis of thyroid hormones—thyroxine and triiodothyronine which play a major role in ensuring normal metabolism [3–4]. Insufficient iodine intake has significant effects on the functioning of muscles, heart, liver, kidneys and brain [5]. It can also cause a wide range of endocrine and neurological diseases [3, 6–10]. To this day, iodine deficiency remains a persistent medical problem, despite international efforts to eliminate it.

Herbal medicines deserve special attention in the treatment of iodine deficiency conditions due to their low toxicity and mild action [11]. The highest concentration of iodine is known to be found in seaweed [12]. Iodine content and its chemical form in these plants vary among species, but the largest amount of this element is to be found in brown algae, in particular in various types of laminaria [13]. For this reason, *Laminariae thalli* L. is considered one of the best sources of iodine. This type of medicinal plant raw materials is included in the State Pharmacopoeia of the Russian Federation, 15th edition (SPh 15)[1], the European[2] and British[3] Pharmacopoeia. The most bioavailable are believed to be inorganic forms of iodine, which, according to literature, are represented by iodides and iodates [14–15], which account for approximately 80 to 90% of the total iodine content [16].

Various chemical and physicochemical methods were used, in order to determine iodine in *Laminariae thalli* L. Thus, for the purpose of quality control of medicinal plant raw materials according to the Iodine indicator, SPh 15 and foreign pharmacopoeias recommend the use of insufficiently selective iodometric titration. At the same time, sample preparation used for the purposes of determination (burning in an open flame or using the Schöniger method) is time-consuming and can lead to significant losses of the analyte.

For the purposes of scientific research, iodine determination is most often performed by inductively coupled plasma mass spectrometry (ICP-MS) [17–20], and the fairly sensitive Sandell–Kolthoff kinetic method [21–26]. The ICP-MS method is expensive, extremely sensitive to the presence of organic components in the analyzed solutions, and insufficiently selective due to significant isobaric influences from the matrix components [27]. The isobaric influences are most often corrected by introducing an isotopic tracer—a radioactive isotope of iodine, ^{129}I, which is hazardous to health [19–20, 28–29]. The kinetic method is labor-intensive and not selective enough [25–26], requiring the use of special sample preparation procedures. The listed disadvantages of the Sandell–Kolthoff and ICP-MS methods prevent their use in routine quality control of medicinal plant raw materials in pharmaceutical enterprises. A more accessible and simpler alternative is to use electrochemical methods. The most modern version, in particular, is inverse voltammetry (IVA)[4] [30]. This method is characterized by a high level of sensitivity and does not require the use of expensive equipment.

For the purposes of the routine determination of iodine (most often in the form of iodates) by means of the IVA method[5], silver or mercury film electrodes (MFE's) are predominantly used (GOST 31660-2012[6]) [31, 32]. Despite the fact that RPEs make it possible to obtain a stable signal, their use in flow analysis is severely limited by the toxicity of mercury salts used to obtain a mercury film on the electrode surface. Silver electrodes are safe to use, make it easier to provide a renewed surface and have a higher detection sensitivity when compared to MFE's. However, they are not sufficiently resistant to complex matrices of natural samples. There are works in which electrodes covalently modified with commercially difficult to obtain organic reagents were used to increase the determination selectivity and sensitivity[7] [33, 34]. The process of obtaining this type of electrodes is labor-intensive and multi-stage. This significantly limits their use in flow analysis in factory quality control laboratories. Standardized commercially available graphite electrodes are more promising from this point of view. They are capable of sorbing organic reagent–analyte element complexes on their surface. Surfactants can be proposed as available organic reagents. In the work by D.M. Fedulov[8] research was conducted on the influence of the nature and structure of surfactants on the deposition of surfactant–iodine complexes on the surface of a graphite electrode. Based on the research conducted, the authors have proposed methodological guidelines for the determination of iodine in food products, food raw materials, food

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[1] State Pharmacopoeia of the Russian Federation. 15th ed. Moscow: Ministry of Health of the Russian Federation, 2018;4:6181–6187. https://pharmacopoeia.regmed.ru/pharmacopoeia/izdanie-15/. Accessed May 11, 2024.

[2] European Pharmacopoeia. 6th ed. Strasburg: EDQM, 2008;2:2213–2214. https://archive.org/details/europeanpharmaco2008unse. Accessed May 11, 2024.

[3] British Pharmacopoeia. Herbal drugs and herbal drug preparations. Kelp. London: Medicines and healthcare products regulatory agency, 2009(3):1–2. https://archive.org/details/britishpharmacop0003unse. Accessed May 11, 2024.

[4] *Opredelenie massovoi kontsentratsii ioda v pishchevykh produktakh, prodovol'stvennom syr'e, pishchevykh i biologicheski aktivnykh dobavkakh vol'tamperometricheskim metodom: Metodicheskie ukazaniya* (*Determination of the Mass Concentration of Iodine in Food Products, Food Raw Materials, Food and Biologically Active Additives by Volamperometric Method: Guidelines*). Moscow: Federal'nyi tsentr gossanepidnadzora Minzdrava Rossii; 2003.42 p. (in Russ.).

[5] Noskova G.N. *Determination of various forms of iodine-containing compounds in waters by voltammetric methods*. Diss. Cand. Sci. (Chem.). Tomsk: 2004. 177 p.

[6] GOST 31660-2012. Interstate Standard. Foods. Anodic stripping voltametric method of iodine mass concentration determination. Moscow: Standartinform; 2012. https://docs.cntd.ru/document/1200095486?ysclid=lvxs4018b2463460075. Accessed May 11, 2024.

[7] Pham K.N. *Voltammetric behavior of iodine, selenium and nickel on organo-modified electrodes*. Diss. Cand. Sci. (Chem.). Tomsk: 2012. 160 p.

[8] Fedulov D.M. *Determination of iodine, lead and selenium in environmental objects in the presence of organic compounds by inversion voltammetry*. Diss. Cand. Sci. (Chem.). Moscow: 2004. 162 p.

additives and biologically active additives. This approach is convenient in that it does not require the complex preparation of the electrode for measurements (there is no impregnation stage). However, the authors consider this procedure to have two significant drawbacks. The first drawback is the influence of matrix components, which they propose to be removed by "dry" mineralization of samples (analyte loss). The second drawback is the need to select conditions for converting all forms of iodine into the iodide form. This form provides the highest level of sensitivity in determining the element. Unfortunately, the authors do not prescribe methods for sample preparation and transfer of the element into an analyzed form. Moreover, metrological certification of the method using water as an example show that, despite the ease of performing measurements using the additive method[9], it is not possible to obtain validation characteristics which meet the requirements of the SPh 15, even for such a simple object. Accordingly, the procedure described in the guidelines is not applicable for complex natural samples. Therefore, in order to determine the gross content of inorganic iodine in a pharmaceutical sample—the *Laminariae thalli* L.—it is necessary not only to reproduce the determination conditions, but to develop and validate a new method compliant with the standards of the SPh 15. In this case, the technique should include labor-intensive sample preparation, which to the maximum extent possible eliminates the loss of the element being determined. It should also include a simple method of converting the element into a single analyzed form, as well as an effective combination of the above stages with the stage of IVA determination using a surfactant.

Thus, the purpose of this work is to develop and validate a simple, reproducible, selective, highly sensitive, combined IVA method for determining the total iodine content in a new type of pharmaceutical object for IVA analysis—*Laminariae thalli* L. containing inorganic iodine mainly in the form of iodides and iodates easily soluble in water[10] [35, 36]. At the same time, the methodology must comply with the capabilities of the control and analytical laboratories of pharmaceutical enterprises and the requirements of the SPh 15.

MATERIALS AND METHODS

Sample preparation was carried out using a WiseVen drying cabinet (*Wisd*, South Korea) and a laboratory centrifuge SM-6M (*Elmi*, Latvia). Inorganic iodine determination was performed using a voltammetric analyzer Ekotest-VA (*Ekoniks-Expert*, Russia) by means of a three-electrode cell consisting of a working impregnated graphite electrode (IGE) (*Ekoniks-Expert*, Russia), a silver-silver chloride reference electrode ESr-10107 (*Izmeritelnaya Tekhnika* (*Measuring Equipment*), Russia), a platinum auxiliary electrode EPL-02 (*Gomel Plant of Measuring Equipment*, Belarus), and a magnetic stirrer (*Elmi*, Latvia).

The following reagents were used in the work: purified water (conductivity <4.3 μS/cm at 20°C), concentrated sulfuric acid (chemically pure, *Lenreaktiv*, Russia), potassium iodide (chemically pure, *Chemical Line*, Russia), potassium bromide (reagent grade, *Lenreaktiv*, Russia), cetyltrimethylammonium bromide (*Sisco Research Laboratories*, India), and zinc dust 95% (*Clearsynth*, India).

Solutions of 1 M H_2SO_4 and 10% potassium bromide were prepared in accordance with SPh 15. Samples of *Laminariae thalli* L. which meet the requirements of SPh 15 were purchased from a pharmacy chain in Moscow.

0.1 M solution of potassium bromide

12.0 mL of 10% potassium bromide solution were placed into a 100-mL volumetric flask. The volume of the solution was brought to the mark with water, and the mixture was stirred.

Cetyltrimethylammonium bromide solution

An exactly weighed portion of cetyltrimethylammonium bromide weighing 0.1850 g was placed into a 250-mL volumetric flask. The volume of the solution was adjusted to the mark with water, and the mixture was stirred.

Standard solution

An exactly weighed portion of 1.3081 g of potassium iodide was placed in a 1000-mL volumetric flask. 700 mL of water was added, and the mixture was stirred until the sample was completely dissolved. The solution volume was adjusted to the mark with the same solvent, and the mixture was stirred (iodine concentration 1.0 mg/mL, solution A).

Solution A of 5.0 mL was added to a 50-mL volumetric flask. The volume of the solution was adjusted to the mark with water, and the mixture was stirred (iodine concentration 100.0 μg/mL, solution B).

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[9] The additive method is one of the standard quantitative methods in analytical chemistry, in which a precisely known amount of the substance being determined is introduced into the test sample, and the content of this substance in the sample (test sample) is calculated from the change in the analytical signal.

[10] Savchuk I.A. *Investigation of pharmacological properties and chemical composition of dry Japanese kelp extract*. Diss. Cand. Sci. (Biol.). Smolensk: 2012. 122 p.

Solution B of 10.0 mL was placed into a 100-mL volumetric flask, the volume of the solution was adjusted to the mark with water, and the mixture was stirred (iodine concentration 10.0 µg/mL, solution C).

Solutions for studying the method linearity (calibration solutions)

Solution C of 0.05–0.75 mL, 0.50 mL of the cetyltrimethylammonium bromide solution, 2.5 mL of 1 M H_2SO_4, and 1.0 mL of 0.1 M potassium bromide solution were added to a 25-mL volumetric flask. The volume of the solution was adjusted to the mark with water, and the mixture was stirred (iodine concentration was 20–300 µg/L).

Test solution

A sample of the raw material passed through a sieve with a hole size of 2 mm, weighing 0.5 g (exactly weighed), was placed into a 100-mL conical flask, and 40 mL of water were added. The mixture was kept at 90°C for 15 min and centrifuged for 15 min at a speed of 2000 rpm. The supernatant was transferred to a 250-mL volumetric flask. The precipitate was filtered off, and the filtrate was transferred into the same volumetric flask through cheesecloth. The solution volume was adjusted to the mark with water, and the mixture was stirred.

The resulting solution of 5.0 mL, 10.0 mL of 1 M H_2SO_4, and 0.5 g of zinc dust were placed into a 100-mL volumetric flask. The mixture was kept at 80°C for 30 min and cooled. The solution volume was brought to the mark with water. The mixture was stirred and filtered through a paper filter from the *Sinyaya Lenta* (*Blue Ribbon*) brand (Russia).

Reference solution

Cetyltrimethylammonium bromide solution of 0.5 mL, 2.5 mL of 1 M H_2SO_4, and 1.0 mL of 0.1 M potassium bromide solution were placed into to a 25.0 mL volumetric flask. The solution volume was adjusted to the mark with water, and the mixture was stirred.

Procedure

The test solution of 4.0 mL was placed in a 25-mL volumetric flask, then 0.5 mL of cetyltrimethylammonium bromide solution, 2.5 mL of 1 M H_2SO_4, and 1.0 mL of 0.1 M potassium bromide solution were added. The solution volume was adjusted to the mark with water, and the mixture was stirred. The determination was carried out using the calibration curve method.

The voltammograms of the test solution and of the reference solution were recorded in the potential range from −200 to 800 mV.

The amount of inorganic iodine (X, %) in the raw material was calculated using the following formula:

$$X = \frac{(C - C_0) \times 250 \times 100 \times 25 \times 100 \times 10^{-9} \times P}{4 \times 5 \times a \times 100 \times (100 - W)} \times 100 = \frac{(C - C_0) \times 3.12 \times 10^{-3} \times P}{a \times (100 - W)},$$

where a is the mass of a sample of plant raw materials, g; C is the concentration of inorganic iodine in the test solution determined from the calibration curve, µg/L; C_0 is iodine concentration in the reference solution, µg/L; P is the main substance content in the standard sample of potassium iodide, %; W is raw material moisture, %.

RESULTS AND DISCUSSION

The IVA determination of iodine was based on the electrochemical oxidation of iodide ions to molecular iodine [34]. At the accumulation step, in the presence of bromide ions and a quaternary ammonium base (cetyltrimethylammonium bromide), the resulting iodine is adsorbed onto the surface of the working IGE in the form of a poorly soluble ionic associate. When the potential is deployed to the cathode region, electrochemical dissolution of the precipitate occurs, and a peak of electrochemical reduction of iodine appears on the voltammogram. This process can be roughly represented as follows:

$$2I^- - 2e^- \rightarrow I_2,$$

$$I_2 + Br^- \rightarrow I_2Br^-,$$

$$I_2Br^- + R \rightarrow R\left[I_2Br^-\right]\downarrow,$$

$$R\left[I_2Br^-\right] + 2e^- \rightarrow R + 2I^- + Br^-,$$

wherein R is the quaternary ammonium base. The precipitate dissolution is accompanied by the flow of a cathodic current, the magnitude of which is an analytical signal.

At the first stage of the study, we succeeded in showing that the greatest recovery of inorganic forms of iodine is achieved when extracting analytes with water under the following conditions: raw material particle size—less than 2 mm; extractant volume—40 mL; extraction temperature—90°C; extraction time—15 min; and extraction multiplicity is 1. It was also found that the simplest version of the method described in [34] is not suitable for the bulk determination of iodine inorganic form. This is due to the extreme complexity of the matrix composition of the natural analyzed sample, as well as the simultaneous presence of the analyte in several forms. For this reason, the work explored the possibility of converting various inorganic forms of iodine (iodides and iodates) into a single form (iodides).

Iodates can be converted to iodides under the action of hydrogen, easily obtained by the reaction of zinc dust with acid. Therefore, mixing sulfuric acid and zinc dust with the resulting extract and additional heating to speed up the reaction allowed us to obtain the required result. The reactions carried out can be roughly represented as follows:

$$Zn + H_2SO_4 = ZnSO_4 + H_2\uparrow,$$

$$KIO_3 + 3H_2 = KI + 3H_2O,$$

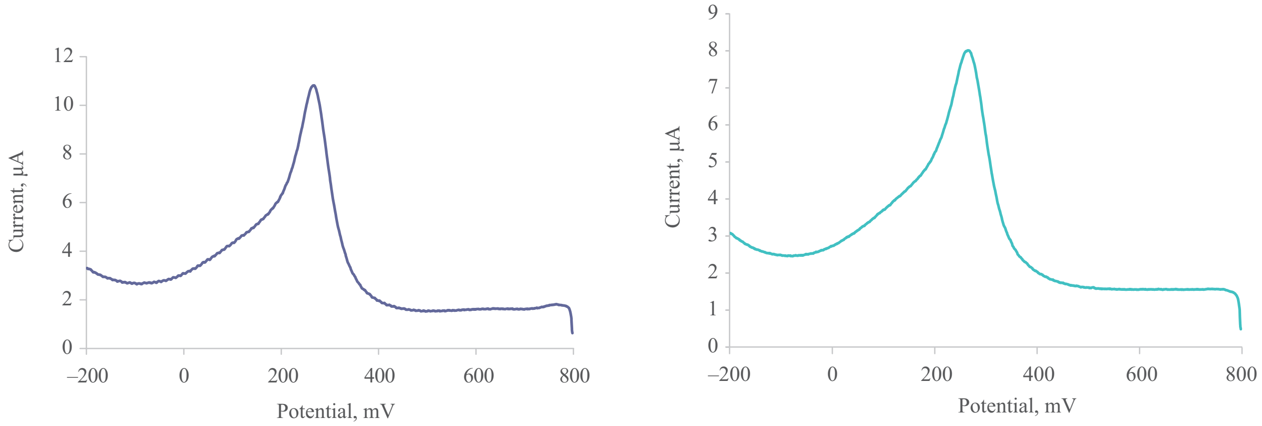
or in general:

$$KIO_3 + 3Zn + 3H_2SO_4 = KI + 3ZnSO_4 + 3H_2O.$$

The influence of temperature, reaction time, mass of zinc dust, and concentration of sulfuric acid solution on the completeness of the reaction was studied using a model solution of potassium iodate (iodine concentration was 202 µg/L). The assessment was carried out on the basis of the resulting iodides content using ionometry. As a result of the complete reaction, the concentration of iodide ions should be about 202 ng/mL, corresponding to the most complete transition of iodate to iodide. The results of the experiments are presented in Table 1.

Table 1. Influence of different parameters on the completeness of iodates to iodides conversion (the volume of the test solution is 5 mL, the volume of sulfuric acid is 10 mL)

Reaction temperature, °C	Sulfuric acid concentration, M	Zinc powder mass, g	Reaction time, min	Mass concentration *C*(I), mcg/L
Reaction temperature				
25	0.1	0.5	30	196.2
40	0.1	0.5	30	198.5
80	0.1	0.5	30	207.1
100	0.1	0.5	30	200.2
Sulfuric acid concentration				
80	0.1	0.5	30	205.2
80	0.5	0.5	30	199.1
80	1.0	0.5	30	195.0
80	2.0	0.5	30	184.7
Zinc mass				
80	0.1	0.5	30	205.2
80	0.1	0.75	30	178.4
80	0.1	1.0	30	179.4
80	0.1	2.0	30	182.4
Reaction time				
80	0.1	0.5	10	181.7
80	0.1	0.5	20	175.7
80	0.1	0.5	30	201.9
80	0.1	0.5	60	172.0



(a) (b)

Fig. 1. Voltammograms of: (a) the standard solution with the iodine concentration of 200 μg/L, (b) the test solution

The data presented in Table 1 indicates that the most complete conversion of iodates into iodides is achieved at a temperature of 80°C, a reaction time of 30 min, a concentration of sulfuric acid of 0.1 M, and a mass of zinc dust of 0.5 g. The results obtained are quite easy to explain. Thus, as the temperature increases, the reaction rate increases. The increase in the concentration of the sulfuric acid solution leads to a decrease in the content of the element being determined in the solution due to the formation of volatile iodine (reaction between KIO_3 and KI). Iodine leaves the reaction sphere during the reaction mixture heating. An increase in the mass of zinc dust prevents hydrogen bubbles from moving freely in the solution, also complicating the reaction of iodides formation.

Since laminaria is a typical representative of the brown seaweed family, it tends to accumulate elements contained in seawater in the largest quantities. These elements include sodium, potassium, calcium, and magnesium. Therefore, we studied the matrix influence of these elements upon the analytical signal of the element being determined. As a result of the experiments, it was found that sodium, potassium, calcium and magnesium with a thousandfold excess in the test solution do not interfere with the analytical signal. Thus, as a result of the research, a new voltammetric method was proposed for the quantitative determination of the gross content of inorganic iodine in the *Laminariae thalli* L. The study of metrological characteristics was carried out in accordance with the requirements of the SPh 15.

Figure 1 shows voltammograms of one of the standard solutions used to plot the calibration curve (Fig. 1a) and of the test solution (Fig. 1b) recorded in the range from −200 to 800 mV.

Figure 1 indicates that the local maximum is achieved at a potential of 233 ± 10 mV both in the voltammogram of the standard and in the voltammogram of the test solutions. No maxima were found in the reference solution voltammogram. The results obtained indicate a fairly high specificity of the proposed method in relation to the analyte.

Figure 2 shows the effect of iodine concentration on the analytical signal of the element being determined.

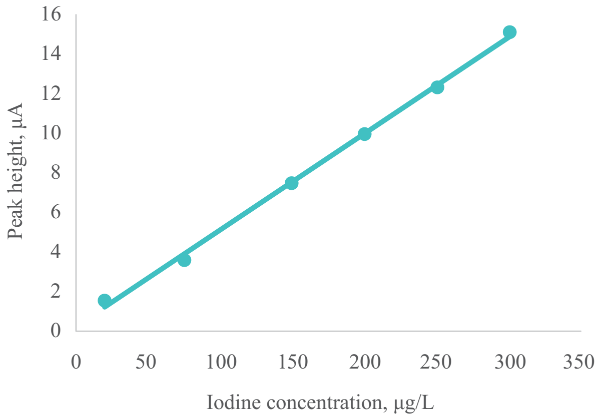


Fig. 2. Dependence of the cathode current value on the iodine concentration

Analysis of the graph presented in Fig. 2 showed that the relationship between the iodine content in the analyzed solution and the cathode current is linear in the concentration range of the element being determined from 20 to 300 μg/L ($R^2 = 0.9993$).

The addition method was used to study the correctness. It consisted in adding the exact amount of a standard sample of potassium iodide (in terms of iodine) to extracts diluted to a half concentration (for working in the linear region of the technique). Discoverability was calculated as the ratio of the experimentally found amount of an element to its theoretical content. The results are shown in Table 2.

Table 2. Evaluation of the discoverability of the iodine content in the sample (h^{*} = 3.26 µg, m^{**}_{test} = 2.21 µg)

Added (m), µg	h_{add}	$m + m_{\text{test}}$, µg	h_{theor}	Found, µg	h_{exp}	Discoverability, %
0.60	1.07	2.81	4.33	2.91	4.23	103.5
0.60	1.02	2.81	4.28	2.91	4.23	103.5
0.60	1.04	2.81	4.30	2.90	4.22	103.3
1.50	2.31	3.71	5.57	3.82	5.49	103.1
1.50	2.27	3.71	5.53	3.83	5.50	103.3
1.50	2.28	3.71	5.54	3.82	5.49	103.1
2.70	3.91	4.91	7.17	5.07	7.20	103.2
2.70	3.93	4.91	7.19	5.07	7.21	103.3
2.70	3.88	4.91	7.14	5.08	7.22	103.5

$^{*}h$ is an analytical signal (peak height) of the solution diluted to half concentration.

$^{**}m_{\text{test}}$ is the content of the determined component in the test solution diluted to half concentration.

On the basis of the data obtained, it was concluded that the method enables correct determination of the analyte in the analyzed solution obtained at sample preparation stage. The accuracy ranges from 100 to 105%, and the coefficient of variation (with the number of parallel measurements $n = 9$) was 0.2%.

The study of repeatability consisted in calculating the variability index and confidence interval on the basis of the results of quantitative determination of inorganic iodine gross content in *Laminariae thalli* L. in several replicates. The results are presented in Table 3.

Table 3. Evaluation of the reproducibility of the technique of inorganic iodine determination (the number of parallel measurements $n = 6$, confidence level $p = 0.95$), the content of the main substance in the standard sample of potassium iodide $P = 99.9\%$, raw material humidity $W = 8.80\%$

Parameter	Measurements					
	1	2	3	4	5	6
h_1	6.11	6.10	6.06	6.12	6.18	6.22
h_2	6.12	6.16	6.09	6.13	6.16	6.25
h_3	6.15	6.14	6.10	6.17	6.15	6.20
Average h	6.13	6.13	6.08	6.14	6.16	6.20
X, %	1.15	1.15	1.14	1.15	1.16	1.16
X_{ave}, %	1.15					
Standard deviation, S	0.01					
Standard deviation of the average result, $S_{\tilde{o}}$	0.003					
Coefficient of variation, $S_{\tilde{o}}$, %	0.90					
Confidence interval, %	1.14–1.16					
Analysis result, %	1.15 ± 0.01					

Table 4. Assessment of intralaboratory precision of the IVA method for determining the gross content of inorganic iodine ($n = 6$, $p = 0.95$), $P = 99.9\%$, $W = 8.80\%$

Parameter	Measurements					
	1	2	3	4	5	6
h_1	5.98	6.02	6.10	6.06	6.20	6.17
h_2	5.97	5.98	6.12	6.10	6.15	6.15
h_3	6.00	5.97	6.16	6.09	6.19	6.11
Average h	5.98	5.99	6.13	6.08	6.18	6.14
X, %	1.12	1.12	1.15	1.14	1.16	1.15
X_{ave}, %	1.14					
Standard deviation, S	0.02					
Standard deviation of the average result, $S_{\tilde{o}}$	0.007					
Coefficient of variation, $S_{\tilde{o}}$, %	1.80					
Confidence interval, %	1.12–1.16					
Analysis result, %	1.14 ± 0.02					

The results presented in Table 3 show that the coefficient of variation of the results of inorganic iodine quantitative determination ($n = 6$) was 0.9%, and the confidence interval was in the range of ±0.01%.

Intralaboratory precision was studied by means of quantifying the element in six replicates on a different day by a different analytical chemist. The data is shown in Table 4.

The data shown in Tables 3 and 4 allows a comparison of the variances of the average results of the two samples using the Fisher and Student tests. The calculated values of Fisher $F_{\text{exp}} = 4.700$ and Student $t_{\text{exp}} = 0.141$ criteria were lower than the tabulated ones ($F_{\text{table}} = 5.050$; $t_{\text{table}} = 2.571$). This confirms that the two samples belong to the general population. The results of inorganic iodine quantitative determination using the method developed herein are reproducible and showed satisfactory intralaboratory precision.

CONCLUSIONS

As a result of the study, a new highly sensitive, selective, combined IVA method for determining inorganic iodine in *Laminariae thalli* L. was developed. Unlike the most commonly used pharmacopoeial methods, the proposed method involves extremely simple sample preparation. This method consists of extraction of the inorganic analyte with water and subsequent conversion of the iodate and iodide forms of iodine (the most common in the *Laminariae thalli* L.) into a single analytical form by processing the extract with zinc dust in acidic environment. The validation results demonstrated that the new method provides a satisfactory level of metrological characteristics (specificity, linearity, discoverability, repeatability, intralaboratory precision). The method also complies with the requirements of the SPh 15 and can be recommended for use in control and analytical laboratories involved in pharmaceutical quality control.

Authors' contributions

A.V. Nikulin—planning and conducting the experiments, writing and editing the main section of the article, data processing, and discussion of the results.

L.Yu. Martynov—planning and conducting the experiments related to inversion voltammetry, data processing, and discussion of the results.

R.S. Gabaeva—writing the main section of the article, conducting the experiments, preparing figures and tables, and discussion of the results.

M.A. Lazov—conducting the experimental work related to obtaining the total amount of iodine, and editing and formatting the article.

The authors declare no conflicts of interest.

REFERENCES

1. Ahad F., Ganie S.A. Iodine, Iodine metabolism and Iodine deficiency disorders revisited. *Indian J. Endocrinol. Metab*. 2010;14(1):13–17. https://pubmed.ncbi.nlm.nih.gov/21448409
2. Swanson C.A., Pearce E.N. Iodine insufficiency: a global health problem? *Adv. Nutr.* 2013;4(5):533–535. https://doi.org/10.3945/an.113.004192
3. Haldimann M., Alt A., Blanc A., Blondeau K. Iodine content of food groups. *J. Food Compos. Anal.* 2005;18(6):461–471. https://doi.org/10.1016/j.jfca.2004.06.003
4. Eftychia G.K., Roupas N.D., Markou K.B. Effect of excess iodine intake on thyroid on human health. *Minerva Med.* 2017;108(2):136–146. https://doi.org/10.23736/s0026-4806.17.04923-0
5. Kapil U. Health consequences of iodine deficiency. *Sultan Qaboos Univ. Med. J.* 2007;7(3):267–272. https://pubmed.ncbi.nlm.nih.gov/21748117/
6. Thilly C.H., Vanderpas J.B., Bebe N., Ntambue K., Contempre B., Swennen B., Moreno-Reyes R., Bourdoux P., Delange F. Iodine deficiency, other trace elements, and goitrogenic factors in the etiopathogeny of iodine deficiency disorders (IDD). *Biol. Trace Elem. Res.* 1992;32:229–243. https://doi.org/10.1007/bf02784606
7. Delange F. The role of iodine in brain development. *Proc. Nutr. Soc.* 2000;59(1):75–79. https://doi.org/10.1017/s0029665100000094
8. Morreale de Escobar G., Obregón M.J., Escobar del Rey F. Role of thyroid hormone during early brain development. *Eur. J. Endocrinol.* 2004;151(3):U25–U37. https://doi.org/10.1530/eje.0.151u025
9. Zimmermann M.B. Iodine deficiency. *Endocrin. Rev.* 2009;30(4):376–408. https://doi.org/10.1210/er.2009-0011
10. Lazarus J.H. The importance of iodine in public health. *Environ. Geochem. Health.* 2015;37:605–618. https://doi.org/10.1007/s10653-015-9681-4
11. Nerhus I., Odland M., Kjellevold M., Midtbø L.K., Markhus M.W., Graff I.E., Lie Ø., Kvestad I., Frøyland L., Dahl L., Øyen J. Iodine status in Norwegian preschool children and associations with dietary iodine sources: the FINS-KIDS study. *Eur. J. Nutr.* 2019;58:2219–2227. https://doi.org/10.1007/s00394-018-1768-0
12. Müssig K. Iodine-induced toxic effects due to seaweed consumption. *Comprehensive handbook of iodine*. 2009:897–908. https://doi.org/10.1016/B978-0-12-374135-6.00093-5
13. Smyth P.P.A. Iodine, seaweed, and the thyroid. *Eur. Thyroid J.* 2021;10(2):101–108. https://doi.org/10.1159/000512971
14. Martinelango P.K., Tian K., Dasgupta P.K. Perchlorate in seawater: bioconcentration of iodide and perchlorate by various seaweed species. *Anal. Chim. Acta.* 2006;567(1):100–107. https://doi.org/10.1016/j.aca.2006.02.015
15. Yang M., Her N., Ryu J., Yoon Y. Determination of perchlorate and iodide concentrations in edible seaweeds. *Int. J. Environ. Sci. Technol.* 2014;11:565–570. https://doi.org/10.1007/s13762-013-0263-7
16. Leblanc C., Colin C., Cosse A., Delage L., La Barre S., Morin P., Fiévet B., Voiseux C., Ambroise Y., Verhaeghe E., Amouroux D., Donard O., Tessier E., Potine P. Iodine transfers in the coastal marine environment: the key role of brown algae and of their vanadium-dependent haloperoxidases. *Biochimie.* 2006;88(11):1773–1785. https://doi.org/10.1016/j.biochi.2006.09.001
17. Tinggi U., Schoendorfer N., Davies P.S., Scheelings P., Olszowy H. Determination of iodine in selected foods and diets by inductively coupled plasma-mass spectrometry. *Pure Appl. Chem.* 2011;84(2):291–299. https://doi.org/10.1351/PAC-CON-11-08-03
18. Pröfrock D., Prange A. Inductively coupled plasma–mass spectrometry (ICP-MS) for quantitative analysis in environmental and life sciences: a review of challenges, solutions, and trends. *Appl. Spectrosc.* 2012;66(8):843–868. https://doi.org/10.1366/12-06681
19. Dyke J.V., Dasgupta P.K., Kirk A.B. Trace iodine quantitation in biological samples by mass spectrometric methods: the optimum internal standard. *Talanta.* 2009;79(2):235–242. https://doi.org/10.1016/j.talanta.2009.03.038
20. Haldimann M., Zimmerli B., Als C., Gerber H. Direct determination of urinary iodine by inductively coupled plasma mass spectrometry using isotope dilution with iodine-129. *Clin. Chem.* 1998;44(4):817–824. https://doi.org/10.1093/clinchem/44.4.817
21. Shelor C.P., Dasgupta P.K. Review of analytical methods for the quantification of iodine in complex matrices. *Anal. Chim. Acta.* 2011;702(1):16–36. https://doi.org/10.1016/j.aca.2011.05.039
22. Bellanger J.R., Tressol J.C., Piel H.P. A semi-automated method for the determination of iodine in plants. *Ann. Rech. Vet.* 1979;10(1):113–118. https://pubmed.ncbi.nlm.nih.gov/539772/
23. Fischer P.W., L'abbé M.R. Acid digestion determination of iodine in foods. *J. Assoc. Off. Anal. Chem.* 1981;64(1):71–74. https://doi.org/10.1093/jaoac/64.1.71
24. Fischer P.W., L'Abbé M.R., Giroux A. Colorimetric determination of total iodine in foods by iodide-catalyzed reduction of Ce^{+4}. *J. Assoc. Off. Anal. Chem.* 1986;69(4):687–689. https://doi.org/10.1093/jaoac/69.4.687
25. Sandell E.B., Kolthoff I.M. Micro determination of iodine by a catalytic method. *Microchim. Acta.* 1937;1:9–25. https://doi.org/10.1007/BF01476194
26. May W., Wu D., Eastman C., Bourdoux P., Maberly G. Evaluation of automated urinary iodine methods: problems of interfering substances identified. *Clin. Chem.* 1990;36(6):865–869. https://doi.org/10.1093/clinchem/36.6.865
27. Pupyshev A.A., Surikov V.T. *Mass-spektrometriya s induktivno svyazannoi plazmoi. Obrazovanie ionov* (*Inductively Coupled Plasma Mass Spectrometry: Formation of Ions*). Yekaterinburg: Ural Otd. Ross. Akad. Nauk; 2006. 237 p. (in Russ.).
28. Poluzzi V., Cavalchi B., Mazzoli A., Alberini G., Lutman A., Coan P., Ciani I., Trentini P., Ascanelli M., Davoli V. Comparison of two different inductively coupled plasma mass spectrometric procedures and high-performance liquid chromatography with electrochemical detection in the determination of iodine in urine. *J. Anal. At. Spectrom.* 1996;11(9):731–734. https://doi.org/10.1039/JA9961100731
29. Santamaria-Fernandez R., Evans P., Wolff-Briche C.S., Hearn R. A high accuracy primary ratio method for the determination of iodine in complex matrices by double isotope dilution using MC-ICPMS and ^{129}I spike. *J. Anal. At. Spectrom.* 2006;21(4):413–421. https://doi.org/10.1039/B516767A
30. Vydra F., Shtulik K., Yulakova E. *Inversionnaya vol'tamperometriya* (*Inversion Voltammetry*). Moscow: Mir; 1980. 278 p. (in Russ.).

31. Deryabina V.I., Slepchenko G.B., Fam K.N., Kirillova M.E. *Method for quantitative determination of iodine through stripping voltammetry*: RF Pat. 2459199. Publ. 20.08.2012 (in Russ.).
32. Espada-Bellido E., Bi Z., Salaün P., van den Berg C.M.G. Determination of iodide and total iodine in estuarine waters by cathodic stripping voltammetry using a vibrating silver amalgam microwire electrode. *Talanta*. 2017;174:165–170. https://doi.org/10.1016/j.talanta.2017.06.004
33. Bibi S., Zaman M.I., Niaz A., Tariq M., Khan S.Z., Zulfiqar A., Rahim A., Jan S. Electrocatalytic response of chitosan modified multiwall carbon nanotube paste electrode toward iodode: A facile voltametric method for determination of iodide in biological sample. *Mater. Chem. Phys*. 2023;294:126984. https://doi.org/10.1016/j.matchemphys.2022.126984
34. Cunha-Silva H., Arcos-Martinez M.J. Cathodic stripping voltametric determination of iodide using disposable sensors. *Talanta.* 2019;199:262–269. https://doi.org/10.1016/j.talanta.2019.02.061
35. Elupov V.Yu., Denisov V.L. *Method for production of laminaria extract with increased iodine content*: RF Pat. 2311043. Publ. 27.11.2007 (in Russ.).
36. Podkorytova A.V. *Marine algae – macrophytes and herbs.* Moscow: VNIRO; 2005. 174 p. (in Russ.).

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