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RESEARCH ARTICLE

DIFFERENCES OF RELATIONSHIPS BETWEEN IODINE AND SOME CHEMICAL ELEMENTS IN NORMAL THYROID AND THYROID BENIGN NODULES REVEALED BY SHORT-TERM NEUTRON ACTIVATION

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ABSTRACT

Thyroid benign nodules (TBN) are the most common lesions of this endocrine gland. The etiology of TBN is not clear. The aim of this exploratory study was to examine differences in the content of of bromine (Br), calcium (Ca), chlorine (Cl), iodine (I), potassium (K), magnesium (Mg), manganese (Mn), and sodium (Na), as well as I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, and I/Na content ratios in tissues of normal thyroid and TBN. Thyroid tissue levels of eight chemical elements (ChEs) were prospectively evaluated in 105 apparently healthy persons and in 79 patients with TBN. Measurements were performed using non-destructive instrumental neutron activation analysis with high resolution spectrometry of gamma-radiations from activated short-lived radionuclides. Tissue samples were divided into two portions. One was used for morphological study while the other was intended for ChEs analysis. It was observed that in TBN the Br, Cl, Mn, and Na mass fraction, as well as the I/Br, I/Cl, I/Mn, and I/Na mass fraction ratios were higher whereas mass fractions of Ca and I and also, I/K mass fraction ratio were lower than in normal thyroid. These changes can potentially be used as TBN markers. Furthermore, it was found that the levels of Br, Ca, Cl, K, Mg, Mn, and Na contents in the normal and affected thyroid gland were interconnected and depend on the content of I in thyroid tissue. Because I plays a decisive role in the function of the thyroid gland, the data obtained allow us to conclude that, along with I, such ChEs as Br, Ca, Cl, K, Mg, Mn, and Na, if not directly, then indirectly, are involved in the process of thyroid hormone synthesis.

KEYWORDS: Thyroid; Thyroid Benign Nodules; Chemical Elements; Energy-Dispersive Short-Term Neutron Activation Analysis.

1. INTRODUCTION

Thyroid benign nodules (TBN) are found in two-thirds of the population, which is a serious clinical and social problem worldwide [1]. TBN includes non-neoplastic lesions (various types of thyroid goiter, thyroiditis, and cysts) and neoplastic lesions such as thyroid adenoma. Among TBN, the most common diseases are colloid goiter, thyroiditis, and thyroid adenoma [2-4]. Throughout the 20th century, the prevailing view was that iodine deficiency was the main cause of TBN. However, numerous studies have shown that TBN is a common disease in those countries and regions where the population has never experienced iodine deficiency [4]. Moreover, an excess intake of iodine has also been found to contribute to the occurrence of TBN [5-8]. It also turned out that, along with iodine deficiency and excess, many other dietary, environmental and occupational factors play a role in the etiology of TBN [9-11]. Among these factors, the disruption of the evolutionarily stable intake of many chemical elements (ChEs) into the human body associated with the industrial revolution is a significant importance [12].

In addition to iodine, which is part of thyroid hormones, and selenium, which is involved in thyroid function, other ChEs also perform important physiological functions, such as maintaining and regulating cell function, regulating genes, activating or inhibiting enzymatic reactions, and regulating membrane function [13]. The properties of ChEs can be essential or toxic (goitrogenic, mutagenic, carcinogenic) depending on specific tissue needs or tolerance, respectively [13]. Excessive accumulation or imbalance of ChEs causes dysfunction of cells and leads to cell degeneration, death, benign or malignant transformation [13-15].

For in vivo and in vitro studies of the content of iodine and other ChEs in the normal and pathological thyroid gland, we have developed a set of nuclear analytical and related methods [16–22]. Using this set of methods, the influence of age, gender, and some non-endocrine diseases on the level of iodine in the normal human thyroid gland was studied [23,24]. In addition to iodine, the content of many other thyroidal ChEs of apparently healthy men and women was determined. As the results of these studies the age [25-35] and gender dependence of some ChEs was revealed [36-41]. In addition, it was found that the content of some ChEs of the thyroid gland with colloid goiter, thyroiditis and adenoma differs significantly from the levels of these ChEs in the normal thyroid gland [42-45].

In studies of the relationship of ChEs in the normal thyroid gland, it was shown that the iodine content almost does not correlate with the content of other ChEs. However, the situation changes significantly if, in studies of ChEs relationships, not the absolute values of the ChEs content are used, but the relative values of iodine/ChEs ratios [46,47].

It is generally accepted that the pathogenesis of TBN is multifactorial. The present study was conducted to elucidate the role of ChEs relationship disorders in the pathogenesis of TBN. With this in mind, our aim was to evaluate the content of bromine (Br), calcium (Ca), chlorine (Cl), iodine (I), potassium (K), magnesium (Mg), manganese (Mn), and sodium (Na) in TBN tissue using non-destructive instrumental neutron activation analysis with high resolution spectrometry of gamma-radiations from activated short-lived radionuclides (INAA-SLR) and calculate individual values of I/ChEs ratios. Another aim was to compare the levels of these I/ChEs ratios in TBN with those in the normal thyroid. Finally, differences in intrathyroidal relationships of I/ChEs ratios in normal thyroid and TBN was determined.

2. MATERIAL AND METHODS

The group of patients suffering from TBN (n=79) included persons with colloid nodular goiter (n=46), thyroid adenoma (n=19) and thyroiditis (n=14). All patients with colloid nodular goiter (mean age M±SD was 48±12 years, range 30-64 years), thyroid adenoma (mean age M±SD was 41±11 years, range 22-55 years), and thyroiditis (mean age M±SD was 39±9 years, range 34-50 years) were hospitalized in the Head and Neck Department of the Medical Radiological Research Center. The group of patients with thyroiditis included 8 persons with Hashimoto's thyroiditis and 6 persons with Riedel's Struma. Each patient underwent a thick-needle puncture biopsy of thyroid nodules for morphological examination and determination of the ChEs content in the obtained material. For all patients the diagnosis was confirmed by clinical and morphological/histological results obtained during studies of biopsy and resected materials.

Normal thyroids for the control group samples were removed at necropsy from 105 deceased (mean age 44±21 years, range 2-87), who had died suddenly. Most of the deaths were caused by trauma incompatible with life. A histological examination in the control group was used to control the age norm conformity, as well as to confirm the absence of micro-nodules and latent cancer.

All studies were approved by the Ethical Committees of the Medical Radiological Research Centre (MRRC), Obninsk. All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or with comparable ethical standards.

All samples under study were divided into two portions with a titanium scalpel [48]. One was used for morphological study and the other for ChEs analysis. Samples intended for ChEs analysis were weighed, lyophilized, and homogenized [49]. The mass fraction of ChEs was calculated by the relative way of comparing between intensities of corresponding gamma-lines induced by neutrons of nuclear reactor in tissue samples and standards. Aliquots of commercial, chemically pure compounds and synthetic standard materials were used as standards [50]. Ten sub-samples of certified reference material (CRM) of International Atomic Energy Agency IAEA H-4 (animal muscle) was analyzed to evaluate the precision and accuracy of the results. The CRM subsamples were prepared in the same manner as dry homogenized thyroid tissue samples.

Details of sample preparation, activation by neutrons of nuclear reactor, gamma-spectrometry, and quality insurance using CRM IAEA H-4 (animal muscle) were presented in our earlier publications concerning the INAA-SLR of ChEs contents in human thyroid [18,27,28].

The tissue samples were prepared in duplicate and the average values of the ChEs contents were used in the final calculations. Using Microsoft Office Excel software, the main statistical parameters were calculated, including the arithmetic mean, standard deviation, standard error of the mean, minimum and maximum values, median, percentiles with levels of 0.025 and 0.975 for the content of ChEs and I/ ChEs ratios in normal and TBN. The difference in results between normal and TBN was assessed using the parametric Student's t-test and the non-parametric Wilcoxon-Mann-Whitney U-test. Pearson's correlation coefficient was used in Microsoft Office Excel to calculate the relationship between different ChEs contents and between different I/ ChEs content ratios in normal thyroid and TBN.

3. RESULTS

Table 1 depicts comparison of our data for eight ChEs in ten sub-samples of CRM IAEA H-4 (animal muscle) with the corresponding certified values of ChEs contents in this material.

TABLE 1- INAA-SLR Data of Chemical Element Contents in The IAEA H-4 (Animal Muscle) Reference Material Compared to Certified Values (Mg/Kg, Dry Mass Basis)

Element	Certified values			This work results
	Mean	95% confidence interval	Type	Mean±SD
Br	4.1	3.5 – 4.7	N	5.0±0.9
Ca	188	163 – 213	N	238±59
Cl	1890	1810 – 1970	N	1950±230
I	0.08	-	N	<1.0
K	15800	15300 – 16400	C	16200±3800
Mg	1050	990 – 1110	C	1100±190
Mn	0.52	0.48 – 0.55	C	0.55±0.11
Na	2060	1930 – 2180	C	2190±140

Mean - arithmetical mean, SD - standard deviation, C - certified values, N - non-certified values.

Table 2 represents certain statistical parameters (arithmetic mean, standard deviation, standard error of mean, minimal and maximal values, median, percentiles with 0.025 and 0.975 levels) of the Br, Ca, Cl, I, K, Mg, Mn, and Na mass fractions, as well as I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, and I/Na mass fraction ratios in normal thyroid and TBN.

TABLE 2- Some Statistical Parameters of Br, Ca, Cl, I, K, Mg, Mn, And Na Mass Fraction (Mg/Kg, Dry Mass Basis) As Well As I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, And I/Na Mass Fraction Ratios in Normal Thyroid (NT) And Thyroid Benign Nodules (TBN)

Tissue	Element	Mean	SD	SEM	Min	Max	Median	P 0.025	P 0.975
NT n=105	Br	16.3	11.6	1.3	1.90	66.9	13.6	2.57	51.0
	Ca	1692	1022	109	414	6230	1451	460	3805
	Cl	3400	1452	174	1030	6000	3470	1244	5869
	I	1841	1027	107	114	5061	1695	230	4232
	K	6071	2773	306	1740	14300	5477	2541	13285
	Mg	285	139	16.5	66.0	930	271	81.6	541
	Mn	1.35	0.58	0.07	0.510	4.18	1.32	0.537	2.23
	Na	6702	1764	178	3050	13453	6690	3855	10709
	I/Br	164	128	14	7.08	576	131	10.4	466
	I/Ca	1.43	1.32	0.15	0.136	7.45	1.03	0.151	5.01
	I/Cl	0.714	0.540	0.065	0.027	2.74	0.590	0.174	2.35
	I/K	0.397	0.334	0.039	0.0209	1.51	0.285	0.0267	1.23

	I/Mg	8.53	7.73	0.98	0.551	42.2	6.35	0.756	27.5
	I/Mn	1552	1256	161	98.3	7102	1334	209	4672
	I/Na	0.288	0.167	0.018	0.026	0.728	0.252	0.0309	0.650
TBN n=79	Br	412	662	98	3.20	2628	64.5	8.35	2336
	Ca	1237	902	138	52.0	4333	1108	116	3536
	Cl	8231	3702	772	1757	16786	8326	2543	15157
	I	992	901	103	29.0	3906	695	84.8	3629
	K	6190	2360	352	797	12222	6185	1438	10297
	Mg	331	180	26	13.0	844	311	15.0	745
	Mn	1.80	1.38	0.21	0.100	5.54	1.45	0.367	5.48
	Na	10207	3786	558	2319	22381	9802	3689	16969
	I/Br	29.3	66.3	9.6	0.180	374	5.82	0.281	243
	I/Ca	1.83	2.72	0.43	0.0976	12.2	0.792	0.121	9.23
	I/Cl	0.141	0.159	0.034	0.0161	0.623	0.068	0.0191	0.511
	I/K	0.207	0.191	0.029	0.0129	0.793	0.157	0.0159	0.754
	I/Mg	12.0	39.9	6.0	0.173	260	2.79	0.224	52.8
	I/Mn	1075	1343	207	33.1	5011	563	48.4	4368
	I/Na	0.109	0.095	0.014	0.0134	0.418	0.076	0.0163	0.362

M – arithmetic mean, SD – standard deviation, SEM – standard error of mean, Min – minimum value, Max – maximum value, P 0.025 – percentile with 0.025 level, P 0.975 – percentile with 0.975 level.

The comparison of our results with published data for the Br, Ca, Cl, I, K, Mg, Mn, and Na contents in the human thyroid and TBN is shown in Table 3.

TABLE 3- Median, Minimum and Maximum Value of Means Br, Ca, Cl, I, K, Mg, Mn, And Na Contents in Normal Thyroid (NT) And Thyroid Benign Nodules (TBN) According to Data from The Literature in Comparison with Our Results (Mg/Kg, Dry Mass Basis)

Tissue	**Element**	**Published data [Reference]**			**This work**
		Median of means (n)*	**Minimum of means M or M±SD, (n)****	**Maximum of means M or M±SD, (n)****	**M±SD**
NT	Br	18.1 (11)	5.12 (44) [51]	284±44 (14) [52]	16.3±11.6
	Ca	1600 (17)	840±240 (10) [53]	3800±320 (29) [53]	1692±1022
	Cl	6800 (5)	804±80 (4) [54]	8000 (-) [55]	3400±1452
	I	1888 (95)	159±8 (23) [56]	5772±2708 (50) [57]	1841±1027
	K	4400 (16)	46.4±4.8 (4) [54]	6090 (17) [58]	6071±2773
	Mg	390 (16)	3.5 (-) [59]	1520 (20) [60]	285±139
	Mn	1.62 (40)	0.076 (83) [61]	69.2±7.2 (4) [54]	1.35±0.58
	Na	8000 (9)	438 (-) [62]	10000±5000 (11) [63]	6702±1764
TBN	Br	585 (5)	20.2±11.3 (5) [64]	1277 (1) [65]	412±662
	Ca	1664 (10)	1080 (2) [64]	8010±1290 (-) [66]	1237±902
	Cl	864 (1)	864±84 (4) [67]	864±84 (4) [67]	8231±3702
	I	812 (55)	77±14 (66) [68]	2800 (4) [69]	992±901
	K	3100 (6)	72,8±7,2 (4) [67]	6030±620 (-) [66]	6190±2360
	Mg	834 (4)	588±388 (13) [70]	1616 (70) [71]	331±180
	Mn	2.36 (21)	0.40±0.22 (64) [72]	57.6±6.0 (4) [67]	1.80±1.38
	Na	3520 (1)	3520 (25) [73]	3520 (25) [73]	10207±3786

M –arithmetic mean, SD – standard deviation, (n) – number of all references, (n)** – number of samples.*

Table 4 indicates the differences between mean values of Br, Ca, Cl, I, K, Mg, Mn, and Na mass fraction, as well as between mean values of I/Br, I/Cu, I/Fe, I/Rb, I/Sr, and I/Zn mass fraction ratios in normal thyroid and TBN estimated using the parametric Student's t-test and the non-parametric Wilcoxon-Mann-Whitney U-test.

TABLE 4- Differences Between Mean Values (M□SEM) Of Br, Ca, Cl, I, K, Mg, Mn, And Na Mass Fraction (Mg/Kg, Dry Mass Basis), As Well As Between Mean Values Of I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, And I/Na Mass Fraction Ratios in Normal Thyroid (NT) And Thyroid Benign Nodules (TBN)

Ratio	**Thyroid tissue**				**Ratio**
	NT n=105	**TBN n=79**	**Student's t-test *p***	**U-test *p***	**TBN/NT**
Br	16.3±1.3	412±98	<0.0002*	<0.01*	25.3
Ca	1692±109	1237±138	<0.008*	<0.05*	0.73
Cl	3400±174	8231±772	<0.000003*	<0.01*	2.42
I	1841±107	992±103	<0.00000005*	<0.01*	0.54
K	6071±306	6190±352	0.797	>0.05	1.02
Mg	285±17	331±26	0.140	>0.05	1.16
Mn	1.35±0.07	1.80±0.21	0.048*	<0.01*	1.33
Na	6702±1785	10207±558	<0.0000002*	<0.01*	1.52
I/Br	164±14	29.3±9.6	<0.00001*	<0.01*	0.18
I/Ca	1.43±0.15	1.83±0.43	0.388	>0.05	1.28
I/Cl	0.714±0.065	0.141±0.034	<0.00001*	<0.01*	0.20
I/K	0.397±0.039	0.207±0.029	0.00018*	<0.01*	0.52
I/Mg	8.53±0.98	12.0±6.0	0.574	>0.05	1.41
I/Mn	1552±161	1075±207	0.073	<0.05*	0.69
I/Na	0.288±0.018	0.109±0.014	<0.00001*	<0.01*	0.38

*M – arithmetic mean, SEM – standard error of mean, * Significant values.*

The data of inter-thyroidal correlations (values of *r* – Pearson's coefficient of correlation) between all ChEs and between I/ChEs ratios identified by us in normal thyroid and TBN are presented in Table 5.

4. DISCUSSION

4.1. Precision and Accuracy of Results

Previously found good agreement of the Br, Ca, Cl, I, K, Mg, Mn, and Na contents analyzed by INAA-SLR with the certified data of CRM IAEA H-4 [18,27,28] (Table 1) indicates an acceptable accuracy of the results obtained in the present study of ChE in the thyroid samples presented in Tables 2–5.

The content of ChEs was determined in all or most of the examined samples, which made it possible to calculate the main statistical parameters: the mean value of the mass fraction (M), standard deviation (SD), standard error of the mean (SEM), minimum (Min), maximum (Max), median (Med), and percentiles with levels of 0.025 (P 0.025) and 0.975 (P 0.975), of the Br, Ca, Cl, I, K, Mg, Mn, and Na mass fractions, as well as I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, and I/Na mass fraction ratios in normal thyroid and TBN (Table 2). The values of M, SD, and SEM can be used to compare data for normal thyroid and TBN only under the condition of a normal distribution of the results of determining the content of ChEs in the samples under study. Statistically reliable identification of the law of distribution of results requires large sample sizes, usually several hundred samples, and therefore is rarely used in biomedical research. In the conducted study, we could not prove or disprove the "normality" of the distribution of the results obtained due to the insufficient number of samples studied. Therefore, in addition to the M, SD, and SEM values, such statistical characteristics as Median, range (Min-Max) and percentiles P 0.025 and P 0.975 were calculated, which are valid for any law of distribution of the results of ChEs content in normal and pathological thyroid tissue.

4.2. Comparison with Published Data

The obtained means for Br, Ca, Cl, I, K, Mg, Mn, and Na mass fraction, as shown in Table 3, agree well with the medians of mean values cited by other researches for the human thyroid [51-63]. In TBN tissues (Table 3) our results were comparable with published data for Br, Ca, I, and Mn contents [64-73]. Our mean of K content was outside the range of published means, but close to the upper limit of this range, while the mean of Mg content was slightly below the minimum value of the reported range of means. The obtained means for Cl and Na were 9.5 and 2.9 times higher, respectively, than the only reported result. No published data referring Cl contents of goitrous thyroid tissue were found. Some values for means of ChEs mass fractions reported were not expressed on a dry mass basis. Because of this we recalculated these values using published data for water (75%) [74] and ash (4.16% on dry mass basis) [75] contents in thyroid of adults. No published data referring of I/Br, I/Cu, I/Fe, I/Rb, I/Sr, I/Zn in the normal thyroid gland and TBN were found

The results shown in Table 3 for the normal thyroid also includes samples from patients who died from various non-endocrine diseases. In our previous study, it was shown that some non-endocrine diseases can affect the content of ChEs in the thyroid gland [24]. Moreover, in many studies, "normal" thyroid refers to visually unaffected tissue adjacent to benign or malignant thyroid nodules. However, it was previously found that the tissue adjacent to benign or malignant thyroid nodules is not identical in its elemental composition to healthy thyroid tissue [76-81].

The range of means of Br, Ca, Cl, I, K, Mg, Mn, and Na reported in the literature for normal thyroid and TBN vary widely (Table 3). This can be explained by the dependence of the ChEs content on many factors, including the “normality” of the thyroid samples (see above), the region of the thyroid gland from which the sample was taken, age, gender, ethnicity, gland mass, and goiter stage. Not all these factors were strictly controlled in the cited studies. However, in our opinion, the main reasons for the variability in published data may be related to the accuracy of analytical methods, sample preparation methods, and the impossibility of taking homogeneous samples from affected tissues. It was insufficient quality control of results in these studies. In many scientific investigations, tissue samples were incinerated or dried at high temperature for many hours. In other cases, thyroid samples were treated with solvents (distilled water, ethanol, formalin, etc.). There is evidence that during ashing, drying and digestion at high temperature, significant amounts of some ChEs are lost as a result of such processing. This applies not only to such volatile halogens as Br and I, but also to other ChEs studied in the present work [82-84].

4.3. Differences Between the Normal Thyroid and TBN In the Content of Tes and I/Tes Relationships

From Table 4, it is observed that in TBN the mass fraction of Br, Cl, Mn, and Na were 25.3, 2.42, 1.33, and 1.52 times, respectively, higher whereas mass fractions of Ca and I were 27% and 46% , respectively, lower than in normal tissues of the thyroid. Since the changes in the content of Br, Cl, Mn, and Na, on the one hand, and I, on the other hand, in TBN were in different directions, the I/Br, I/Cl, I/Mn, and I/Na ratios in TBN also differed significantly from the norm (Table 4). Moreover, the I/K ratio in TBN was significantly below (48%) the normal level. This confirmed that the I/ChEs ratios are more sensitive parameters than the absolute values of the ChEs content in thyroid tissue.

Generally, elevated or decreased levels of ChEs observed in TBN are discussed in terms of their potential role in the pathogenesis of TBN. In other words, researchers are trying to determine the role of deficiency or excess of each ChEs in the occurrence of TBN by the low or high level of ChEs in TBN tissues. In our opinion, the abnormal levels of many ChEs in TBN could be both a cause and a consequence of thyroid transformation. Thus, based on the results of such studies, it is not possible to decide whether the measured decrease or increase in the level of ChEs in pathologically altered tissue is the cause or consequence of the disease.

4.4. Relationships Between Trace Elements in Normal Thyroid And TBN

A significant direct correlation between the mass fractions of Br and Mn, Ca and Mg, Cl and Na, K and Mg, Mg and Na, as well as an inverse correlation between the mass fractions of Ca and Cl, Cl and K, I and K, was observed in the normal thyroid gland (Table 5). The absence of correlations between I and other ChEs in the normal thyroid gland, with the exception of an inverse relationship between I and K, suggested that the content of Br, Ca, Cl, Mg, Mn, and Na in the thyroid gland does not depend on the content of iodine. However, this is not quite true. When the content of the studied ChEs was reduced to the content of I (I/ChEs ratio), it turned out that there is a direct correlation between the I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, and I/Na ratios, with the exception of correlation between I/Br and I/Cl, as well as between I/Br and I/Mg (Table 5).

In TBN, there were no correlations between Br and Mn, Ca and Mg, Mg and Na and between I and Fe, as well as an inverse correlation between the mass fractions of Cl and K, I and K, but new direct relationships between Ca and Cl and between K and Mn appeared. As regards the I/ChEs ratios in TBN, compared to the normal thyroid, some correlations disappeared (I/Mg and I/Mn), while others emerged (I/Br and I/Cl). It followed that, at least, the levels of Br, Ca, Cl, K, Mg, Mn, and Na in the normal thyroid gland and TBN are interrelated and depend on the content of I in it and that along with I these ChEs participate, if not directly, then indirectly, in the process of synthesis of thyroid hormones.

5. CONCLUSION

In this work, ChEs analyses were carried out in the tissue samples of normal thyroid and TBN using INAA-SLR. It was shown that INAA-SLR is an adequate analytical tool for the non-destructive determination of Br, Ca, Cl, I, K, Mg, Mn, and Na contents in the tissue samples of human normal and affected thyroid glands, including core needle biopsies.

Our data reveal that in TBN the Br, Cl, Mn, and Na mass fraction, as well as the I/Br, I/Cl, I/Mn, and I/Na mass fraction ratios were higher whereas mass fractions of Ca and I and also, I/K mass fraction ratio were lower than in normal thyroid. These changes can potentially be used as TBN markers. Furthermore, it was found that the levels of Br, Ca, Cl, K, Mg, Mn, and Na contents in the normal and affected thyroid gland were interconnected and depend on the content of I in thyroid tissue. Because I plays a decisive role in the function of the thyroid gland, the data obtained allow us to conclude that, along with I, such ChEs as Br, Ca, Cl, K, Mg, Mn, and Na, if not directly, then indirectly, are involved in the process of thyroid hormone synthesis. It follows that for the normal functioning of the thyroid gland, it is necessary to maintain an adequate concentration of I in its tissue, balanced with the levels of other ChEs.

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CONFLICT OF INTEREST

The author has not declared any conflict of interests.

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