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Relationships between Iodine and Some Chemical Elements in Normal Thyroid of Females Investigated by Neutron Activation and Inductively Coupled Plasma Atomic Emission Spectrometry

Vladimir Zaichick*
Radionuclide Diagnostics Department, Medical Radiological Research Centre, Korolyev St.- 4, Obninsk 249036, Kaluga Region, Russia

***Corresponding author:** Vladimir Zaichick, Radionuclide Diagnostics Department, Medical Radiological Research Centre, Korolyev St.- 4, Obninsk 249036, Kaluga Region, Russia

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Abstract

Thyroid diseases rank second among endocrine disorders, and prevalence of the diseases is higher in the elderly as compared to the younger population. An excess or deficiency of chemical element contents in thyroid play important role ingoitro- and carcinogenesis of gland. The correlations with age of the twenty chemical element (ChE), including I, and I/ChE content ratios, as well as inter-thyroidal relationships between ChE contents and I/ChE content ratios in normal thyroid of 33 females (age range 3.5-87 years) was investigated by two methods: instrumental neutron activation analysis and inductively coupled plasma atomic emission spectrometry. Our data reveal that the Al, Ca, Cu, P, S, and Zn contents increase, while Cl content, as well as I/Ba, I/Cu, I/Li, I/P, I/S, and I/Zn content ratios decrease in the normal thyroid of female during a lifespan. Therefore, a goitrogenic and tumorogenic effect of excessive Al, Ca, Cu, P, S, and Zn level and inadequate Cl level in the thyroid of old fmales, as well as a disturbance in intrathyroidal I/Ba, I/Cu, I/Li, I/P, I/S, and I/Zn relationships with increasing age may be assumed. Furthermore, it was found that the levels of Al, B, Ba, Br, Ca, Cl, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn in the thyroid gland are interconnected and depend on the content of I in it. 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 ChE as Al, B, Ba, Br, Ca, Cl, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn, if not directly, then indirectly, are involved in the process of thyroid hormone synthesis.

Keywords

Thyroid; Chemical elements; Age-related changes; Intrathyroidal chemical elements relationships; Neutron activation analysis; Inductively coupled plasma atomic emission spectrometry

Introduction

According to the World Health Organization (WHO), thyroid diseases rank second among endocrine disorders after diabetes mellitus. More than 665 million people in the world have endemic goiter or suffer from other thyroid pathologies. Women are affected by thyroid diseases almost ten times more often than men. At the same time, according to the same statistics, the increase in the number of thyroid diseases in the world is 5% per year [1]. It has been suggested that risk factors for the development of thyroid disorders may be numerous factors, including genetics, radiation, autoimmune diseases, as well as adverse environmental factors, such as an increase in the content of various chemicals in the environment [2].

Chemical elements (ChE) are among these various chemicals, because their levels in the environment have increased significantly over the past hundred years as a result of the industrial revolution and the tremendous technological changes that have taken place in metallurgy, chemical production, electronics, agriculture, food processing and storage, cosmetics, pharmaceuticals and medicine. In connection with these changes, the levels and ratio of ChE entering the human body from the outside have been significantly disturbed, compared with the conditions in which human societies have lived for many millennia.

More than 50 years ago, we formulated the postulate about the somatic ChE homeostasis, which is now generally recognized [3]. According to this postulate, under evolutionary environmental conditions, the mechanisms of homeostasis of organisms maintain the levels and ratios of ChE in tissues and organs within certain limits. If the content of ChE in the environment changes significantly, the mechanisms of somatic homeostasis may respond inadequately. Inadequate response of homeostasis mechanisms leads to changes in ChE levels in tissues and organs, which, in turn, can affect their function and lead to the development of pathological conditions. The correctness of this conclusion was illustrated by us earlier on the example of the study of the role of ChE in the normal and pathophysiology of the prostate [4-24]. It was shown, in particular, that a special role in the development of pathological transformations of the prostate is played by disturbances in the relationship between ChE in the tissue and gland secretion. Moreover, it was found that changes in the relationship between ChE can be used as highly informative markers of various prostate diseases, including malignant tumors [25-39]. These findings stimulated our investigations of ChE relationships in thyroid tissue in normal and pathological conditions.

There are many studies regarding ChE content in human thyroid, using chemical techniques and instrumental methods [40-60]. However, among the published data, no works on the relationship of ChE in the normal human thyroid were found. This work had three aims. The primary purpose of this study was to determine reliable values for the Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions in the normal thyroid of subjects ranging from children to elderly females using instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides (INAA-SLR) combined in consecutive order with destructive inductively coupled plasma atomic emission spectrometry (ICP-AES)and calculate individual values of I/Al, I/B, I/Ba, I/Br, I/Ca, I/Cl, I/Cu, I/Fe, I/K, I/Li, I/Mg, I/Mn, I/Na, I/P, I/S, I/Si, I/Sr, I/V, and I/Zn. The second aim was to compare the twenty ChEmass fractions in thyroid gland obtained in the study with published data. The final aim was to estimate the inter-thyroidal correlations between ChE contents and between I/ChE content ratios in normal thyroid of females and changes of these parameters with age.

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

Materials and Methods

Randomly selected tissue samples of the thyroid gland were obtained from autopsies of 33 practically healthy residents (European-Caucasian nationality) of the Obninskcity, who died suddenly. The age of the deceased women ranged from 3.5 to 87 years. The main causes of sudden death were injuries in car accidents. Several women have died from suicide, alcohol poisoning, stroke, acute heart failure, and pulmonary embolism. Autopsies were carried out in the forensic medical examination department of the city hospital. In the anamnesis of the deceased women there were no chronic diseases, as well as medications or nutritional supplements that affect the development and function of the thyroid gland. Thyroid tissue samples were taken from the right lobe of the gland using a titanium scalpel [61] and divided into two parts. One part was subjected to histological examination in order to confirm compliance with the age norm, as well as to exclude the presence of microadenomas and latent cancer. The second part was intended to determine the content of ChE in it.

Thyroid tissue samples were delivered frozen to the Medical Radiological Research Center, where they were weighed and stored at -20°C. Subsequently, all samples were lyophilized and homogenized [62]. To determine the contents of the ChE by comparison with a known standard, aliquots of commercial, chemically pure compounds were used [63]. Ten subsamples of the Certified Reference Material (CRM) IAEA H-4 (animal muscle), as well as Polish CRM INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2Mixed Polish Herbs were analyzed to estimate the precision and accuracy of results. The CRM subsamples were prepared in the same way as the samples of dry homogenized thyroid tissue.

A horizontal channel equipped with the pneumatic rabbit system of the WWR-C research nuclear reactor was applied to determine the mass fraction of Br, Ca, I, K, Mg, Mn, and Na by INAA-SLR. The neutron flux in the channel was 1.7 × 10^{13}n cm^{-2} s^{-1}. Method ICP-AES were used to determine the Al, B, Ba, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractionsusing the Spectrometer ICAP-61 (Thermo Jarrell Ash, USA). The determination of the ChE content in aqueous solutions was made by the quantitative method using calibration solutions (High Purity Standards, USA) of 0.5 and 10 mg/L of each element. The calculations of the tChE contents in the probe were carried out using software of a spectrometer (ThermoSPEC, version 4.1). Information detailing with the NAA-SLR and ICP-AES methods used, and other details of the analysis was presented in our previous studies on ChE contents in hair and prostate [64-70].

A dedicated computer program for INAA-SLR mode optimization was used [71]. All thyroid samples were prepared in duplicate, and mean values of ChE contents were used in final calculation. The main statistical characteristics of the ChEcontent and the I/ChEcontent ratio of. such as the arithmetic mean, standard deviation, standard error of the mean, minimum and maximum values, median, percentiles with levels of 0.025 and 0.975 were found using Microsoft Office Excel.Pearson's correlation coefficient was used in Microsoft Office Excel to calculate the relationship "age – ChEmass fraction" and "age – I/ChEmass fraction", as well as to identify inter-thyroidal relationships between different ChEcontents and between different ChEcontent ratios.

Results

Table 1 depicts the similarity of the means of the Ca, K, Mg, Mn, and Na mass fractions in the normal thyroid of female determined by both NAA-SLR and ICP-AES methods.

Element	NAA-SLR M_1	ICP-AES M_2	Δ, %
Ca	1662±198	1598±245	3.9
K	5395±726	5815±776	-7.8
Mg	212±24	247±35	-16.5
Mn	1.50±0.22	1.14±0.24	24.0
Na	6421±320	6645±290	-3.5

Table 1: Comparison of the mean values (M±SEM) of the chemical element mass fractions (mg/kg, on dry-mass basis)in the normal thyroid of females obtained by both NAA-SLR and ICP-AES methods.

Table 2 represents the main statistical characteristics of the Al, B,Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions, as well as I/Al, I/B, I/Ba, I/Br, I/Ca, I/Cl, I/Cu, I/Fe, I/K, I/Li, I/Mg, I/Mn, I/Na, I/P, I/S, I/Si, I/Sr, I/V, and I/Zn mass fraction ratios in normal thyroid of females.

Gender	Element	M	SD	SEM	Min	Max	Median	P 0.025	P 0.975
Females	Al	7.43	4.49	1.24	2.50	17.2	5.50	2.77	16.6
n=33	B	0.418	0.257	0.074	0.200	1.00	0.315	0.200	0.890
	Ba	1.42	1.38	0.38	0.048	5.00	0.770	0.121	4.34
	Br	22.4	16.2	3.23	5.00	66.9	16.3	5.00	59.2
	Ca	1630	1071	219	461	4256	1132	539	3902
	Cl	3317	1480	290	1200	6000	3375	1388	5906
	Cu	3.40	1.41	0.35	0.500	5.90	3.35	1.10	5.79

	Fe	225	98	20	52.0	435	199	64.0	391
	I	1956	1199	219	114	5061	1562	309	4662
	K	5605	3272	732	1914	13700	5058	2360	13230
	Li	0.0153	0.0078	0.0024	0.0015	0.0251	0.0152	0.0030	0.0250
	Mg	230	105	26	66.0	426	216	73.5	403
	Mn	1.32	0.84	0.22	0.550	4.04	1.10	0.603	3.28
	Na	6533	1744	324	3686	10450	6739	4088	9924
	P	3860	2175	603	496	7368	3422	585	7337
	S	6579	2662	738	644	9921	7097	1238	9868
	Si	75.7	58.1	16.1	6.90	176	47.6	9.90	175
	Sr	3.30	2.77	0.69	0.200	10.9	2.85	0.369	9.18
	V	0.970	0.056	0.016	0.0200	0.250	0.100	0.0260	0.211
	Zn	84.5	38.9	7.63	7.10	166	83.5	23.0	156
	I/Al	290	208	60	16.3	786	252	26.4	721
	I/B	5230	3662	1057	193	14143	3887	557	12321
	I/Ba	4713	8507	2456	168	28708	1403	241	24837
	I/Br	127	111	23	7.10	441	95.4	9.00	378
	I/Ca	1.64	1.48	0.31	0.150	5.65	1.36	0.161	4.96
	I/Cl	0.689	0.543	0.109	0.0270	2.74	0.605	0.148	1.81
	I/Cu	660	665	172	54.3	2756	418	89.3	2228
	I/Fe	11.2	10.2	2.1	2.19	47.0	8.53	2.38	36.1
	I/K	0.454	0.396	0.091	0.028	1.51	0.332	0.0422	1.24
	I/Li	201732	269484	85218	12391	918667	96069	17968	774775
	I/Mg	10.0	9.9	2.6	1.33	42.2	6.96	1.77	32.7
	I/Mn	1524	878	235	161	3214	1242	182	2999
	I/Na	0.295	0.166	0.032	0.0162	0.680	0.258	0.0641	0.665
	I/P	0.675	0.745	0.215	0.125	2.78	0.431	0.130	2.35
	I/S	0.412	0.570	0.164	0.0434	2.14	0.202	0.0530	1.70
	I/Si	56.2	80.7	23.3	2.39	251	26.6	3.61	237
	I/Sr	1317	1943	502	88.0	6890	533	100	5828
	I/V	25765	26723	7714	1295	77000	13722	2720	74773
	I/Zn	36.3	45.0	9.2	5.66	222	23.4	6.28	147

Table 2: Some statistical parameters of Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction (mg/kg, dry mass basis) as well as of I/Al, I/B, I/Ba, I/Br, I/Ca, I/Cl, I/Cu, I/Fe, I/K, I/Li, I/Mg, I/Mn, I/Na, I/P, I/S, I/Si, I/Sr, I/V, and I/Zn mass fraction ratios in the normal thyroid of female.

The comparison of our results with published data for contents of all ChE in the human thyroid determined in the present study is shown in Table 3.

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
Al	33.6 (12)	0.33 (-) [40]	420 (25) [41]	7.43±4.49
B	0.151 (2)	0.084 (3) [42]	0.46 (3) [42]	0.418±0.257
Ba	0.67 (7)	0.0084 (83) [43]	≤5.0 (16) [44]	1.42±1.38
Br	18.1 (11)	5.12 (44) [45]	284±44 (14) [46]	22.4±16.2
Ca	1600 (17)	840±240 (10) [47]	3800±320 (29) [47]	1630±1071
Cl	6800 (5)	804±80 (4) [48]	8000 (-) [49]	3317±1480
Cu	6.1 (57)	1.42 (120) [50]	220±22 (10) [48]	3.40±1.41
Fe	252 (21)	56 (120) [50]	2444±700 (14) [46]	225±98
I	1888 (95)	159±8 (23) [51]	5772±2708 (50) [52]	1956±1199
K	4400 (17)	46.4±4.8 (4) [48]	6090 (17) [44]	5605±3272
Li	6.3 (2)	0.092 (-) [53]	12.6 (180) [54]	0.0153±0.0078
Mg	390 (16)	3.5 (-) [40]	840±400 (14) [55]	230±105
Mn	1.82 (36)	0.44±11 (12) [56]	69.2±7.2 (4) [48]	1.32±0.84
Na	8000 (9)	438 (-) [57]	10000±5000 (11) [55]	6533±1744
P	3200 (10)	16 (7) [58]	7520 (60) [45]	3860±2175
S	11000 (3)	4000 (-) [49]	11800 (44) [45]	6579±2662
Si	16.0 (3)	0.97 (-) [40]	143±6 (40) [59]	75.7±58.1
Sr	0.73 (9)	0.55±0.26 (21) [42]	46.8±4.8(4) [48]	3.30±2.77
V	0.042 (6)	0.012 (2) [60]	18±2 (4) [48]	0.9700.056
Zn	118 (51)	32(120) [50]	820±204 (14) [46]	84.5±38.9

Table 3: Median, minimum and maximum value of means Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V and Zn contents in the normal thyroid according to data from the literature in comparison with our results (mg/kg, dry mass basis).

To estimate the effect of age on the ChE contents and I/ ChE content ratios Pearson's correlation coefficient was used (Table 4). The data of inter-thyroidal correlation (values of *r* – Pearson's coefficient of correlation) including all ChEand I/ChEcontent ratios identified by us are presented in Tables 5 and 6, respectively.

Element	**Al**	**B**	**Ba**	**Br**	**Ca**	**Cl**	**Cu**	**Fe**	**I**	**K**
r	0.46[a]	0.26	0.45	0.18	0.38[a]	-0.43[a]	0.50[a]	0.26	0.08	0.01
Element	Li	Mg	Mn	Na	P	S	Si	Sr	V	Zn
r	0.45	-0.11	0.16	0.20	0.61[a]	0.68[b]	0.48	0.22	0.31	0.66[c]
Ratio	I/Al	I/B	I/Ba	I/Br	I/Ca	I/Cl	I/Cu	I/Fe	I/K	I/Li
r	-0.39	-0.24	-0.73[b]	-0.38	-0.02	0.20	-0.60[a]	0.21	0.32	-0.73[a]
Ratio	I/Mg	I/Mn	I/Na	I/P	I/S	I/Si	I/Sr	I/V	I/Zn	
r	0.44	0.27	-0.04	-0.70[b]	-0.71[b]	-0.55	-0.54	-0.42	-0.59[b]	

Table 4: Correlations between age (years) and chemical element content (mg/kg, dry tissue), as well as between age and I/chemical element mass fraction ratiosin the normal female thyroid (*r* – coefficient of correlation).

El	**Al**	**B**	**Ba**	**Br**	**Ca**	**Cl**	**Cu**	**Fe**	**I**	**K**
Al	**1.00**	0.82[c]	0.68[b]	0.51[a]	0.60[a]	-0.44	0.57[a]	0.44	0.15	0.01
B	0.82[c]	**1.00**	0.85[c]	-0.01	0.66[a]	0.01	0.23	0.26	0.25	-0.31
Ba	0.68[b]	0.85[c]	**1.00**	0.10	0.77[b]	-0.71[b]	0.24	0.37	0.32	0.02
Br	0.51[a]	-0.01	0.10	**1.00**	0.20	0.07	0.46[a]	0.26	-0.05	0.46[a]
Ca	0.60[a]	0.66[a]	0.77[b]	0.20	**1.00**	-0.64[c]	0.08	0.09	0.18	0.14
Cl	-0.44	0.01	-0.71[b]	0.07	-0.64[c]	**1.00**	0.20	0.19	0.16	-0.34
Cu	0.57[a]	0.23	0.24	0.46[a]	0.08	0.20	**1.00**	0.74[c]	0.11	0.54[a]
Fe	0.44	0.26	0.37	0.26	0.09	0.19	0.74[c]	**1.00**	-0.09	0.40[a]
I	0.15	0.25	0.32	-0.05	0.18	0.16	0.11	-0.09	**1.00**	-0.27
K	0.01	-0.31	0.02	0.46[a]	0.14	-0.34	0.54[a]	0.40[a]	-0.27	**1.00**
Li	0.25	0.19	0.33	0.13	0.44	0.17	0.59[a]	0.31	0.15	0.56[a]
Mg	-0.07	-0.16	0.11	-0.19	0.14	0.54[a]	0.53[a]	0.38	0.17	0.84[c]
Mn	0.74[b]	0.31	0.14	0.81[c]	0.19	-0.10	0.54[a]	0.32	-0.03	0.14
Na	-0.20	-0.27	-0.26	0.21	-0.20	0.42	0.44[a]	0.09	0.41[a]	-0.21
P	0.01	-0.06	0.02	0.56[a]	-0.02	0.40	0.87[c]	0.52[a]	0.16	0.80[b]
S	-0.04	-0.26	0.05	0.31	0.12	0.31	0.59[a]	0.29	0.16	0.72[b]
Si	0.85[c]	0.85[c]	0.76[b]	0.11	0.53[a]	-0.48[a]	0.58[a]	0.60[a]	0.22	0.11
Sr	0.22	0.01	0.03	0.10	0.22	-0.57[a]	0.11	-0.05	-0.12	0.70[b]
V	0.24	0.08	-0.16	0.03	-0.16	0.16	0.57[a]	0.30	-0.09	-0.24
Zn	0.49	0.38	0.58[a]	0.21	0.61[b]	-0.34[a]	0.54[a]	0.26	0.25	0.20
El	Li	Mg	Mn	Na	P	S	Si	Sr	V	Zn
Al	0.25	-0.07	0.74[b]	-0.20	0.01	-0.04	0.85[c]	0.22	0.24	0.49
B	0.19	-0.16	0.31	-0.27	-0.06	-0.26	0.85[c]	0.01	0.08	0.38
Ba	0.33	0.11	0.14	-0.26	0.02	0.05	0.76[b]	0.03	-0.16	0.58[a]
Br	0.13	-0.19	0.81[c]	0.21	0.56[a]	0.31	0.11	0.10	0.03	0.21
Ca	0.44	0.14	0.19	-0.20	-0.02	0.12	0.53[a]	0.22	-0.16	0.61[b]
Cl	0.17	0.54[a]	-0.10	0.42	0.40	0.31	-0.48[a]	-0.57[a]	0.16	-0.34
Cu	0.59[a]	0.53[a]	0.54[a]	0.44[a]	0.87[c]	0.59[a]	0.58[a]	0.11	0.57[a]	0.54[a]
Fe	0.31	0.38	0.32	0.09	0.52[a]	0.29	0.60[a]	-0.05	0.30	0.26
I	0.15	0.17	-0.03	0.41[a]	0.16	0.16	0.22	-0.12	-0.09	0.25
K	0.56[a]	0.84[c]	0.14	-0.21	0.80[b]	0.72[b]	0.11	0.67[b]	-0.24	0.20
Li	**1.00**	0.77[b]	0.05	0.21	0.55[a]	0.57[a]	0.32	0.53[a]	0.12	0.81[b]
Mg	0.77[b]	**1.00**	-0.11	0.16	0.63[a]	0.68[a]	0.12	0.28	0.16	0.46
Mn	0.05	-0.11	**1.00**	-0.17	0.58[a]	-0.01	0.42	0.24	0.28	0.21
Na	0.21	0.16	-0.17	**1.00**	0.48[a]	0.66[a]	-0.16	-0.14	0.37	0.35
P	0.55[a]	0.63[a]	0.58[a]	0.48[a]	**1.00**	0.65[a]	0.26	0.29	0.42	0.59[a]
S	0.57[a]	0.68[a]	-0.01	0.66[a]	0.65[a]	**1.00**	0.04	0.52[a]	0.38	0.63[a]
Si	0.32	0.12	0.42	-0.16	0.26	0.04	**1.00**	0.17	0.41	0.63[a]
Sr	0.53[a]	0.28	0.24	-0.14	0.29	0.52[a]	0.17	**1.00**	0.47	0.53[a]
V	0.12	0.16	0.28	0.37	0.42	0.38	0.41	0.47	**1.00**	0.29
Zn	0.81[b]	0.46	0.21	0.35	0.59[a]	0.63[a]	0.63[a]	0.53[a]	0.29	**1.00**

Table 5: Intercorrelations of the chemical element mass fractions in the normal female thyroid(*r* – coefficient of correlation).

Ratio	I/Al	I/B	I/Ba	I/Br	I/Ca	I/Cl	I/Cu	I/Fe	I/K	I/Li
I/Al	**1.00**	0.910[c]	0.729[b]	0.520	0.830[c]	0.308	0.693[a]	0.795[b]	0.607[a]	0.617
I/B	0.910[c]	**1.00**	0.520	0.367	0.725[b]	0.194	0.430	0.780[b]	0.498	0.371
I/Ba	0.729[b]	0.520	**1.00**	0.385	0.499	-0.078	0.920[c]	0.376	0.317	0.924[c]
I/Br	0.520	0.367	0.385	**1.00**	0.477[a]	0.269	0.497	0.411	0.529[a]	0.583
I/Ca	0.830[c]	0.725[b]	0.499	0.477[a]	**1.00**	0.168	0.535[a]	0.741[c]	0.726[c]	0.457
I/Cl	0.308	0.194	-0.078	0.269	0.168	**1.00**	0.172	0.538[b]	0.612[b]	0.061
I/Cu	0.693[a]	0.430	0.920[c]	0.497	0.535[a]	0.172	**1.00**	0.408	0.531[a]	0.964[c]
I/Fe	0.795[b]	0.780[b]	0.376	0.411	0.741[c]	0.538[b]	0.408	**1.00**	0.895[c]	0.232
I/K	0.607[a]	0.498	0.317	0.529[a]	0.726[c]	0.612[b]	0.531[a]	0.895[c]	**1.00**	0.344
I/Li	0.617	0.371	0.924[c]	0.583	0.457	0.061	0.964[c]	0.232	0.344	**1.00**
I/Mg	0.622[a]	0.502	0.321	0.127	0.352	0.507	0.537[a]	0.735[b]	0.741[b]	0.426
I/Mn	0.774[b]	0.708[b]	0.249	0.524	0.729[b]	0.767[b]	0.394	0.763[c]	0.818[c]	0.249
I/Na	0.486	0.355	0.289	0.644[c]	0.531[b]	0.745[c]	0.549[a]	0.690[c]	0.818[c]	0.368
I/P	0.545	0.271	0.854[c]	0.450	0.359	0.261	0.975[c]	0.262	0.499	0.943[c]
I/S	0.543	0.269	0.920[c]	0.421	0.365	0.082	0.969[c]	0.194	0.358	0.971[c]
I/Si	0.917[c]	0.793[b]	0.873[c]	0.433	0.697[a]	0.089	0.756[b]	0.717[b]	0.497	0.692[a]
I/Sr	0.750[b]	0.460	0.889[c]	0.474	0.676[b]	0.096	0.933[c]	0.449	0.517[a]	0.938[c]
I/V	0.623[a]	0.442	0.649[a]	0.543	0.422	0.568	0.789[b]	0.557	0.809[b]	0.621
I/Zn	0.676[a]	0.426	0.969[c]	0.456[a]	0.454	-0.040	0.961[c]	0.206	0.255	0.984[c]
Ratio	I/Mg	I/Mn	I/Na	I/P	I/S	I/Si	I/Sr	I/V	I/Zn	
I/Al	0.622[a]	0.774[b]	0.486	0.545	0.543	0.917[c]	0.750[b]	0.623[a]	0.676[a]	
I/B	0.502	0.708[b]	0.355	0.271	0.269	0.793[b]	0.460	0.442	0.426	
I/Ba	0.321	0.249	0.289	0.854[c]	0.920[c]	0.873[c]	0.889[c]	0.649[a]	0.969[c]	
I/Br	0.127	0.524	0.644[c]	0.450	0.421	0.433	0.474	0.543	0.456[a]	
I/Ca	0.352	0.729[b]	0.531[b]	0.359	0.365	0.697[a]	0.676[b]	0.422	0.454	
I/Cl	0.507	0.767[b]	0.745[c]	0.261	0.082	0.089	0.096	0.568	-0.040	
I/Cu	0.537[a]	0.394	0.549[a]	0.975[c]	0.969[c]	0.756[b]	0.933[c]	0.789[b]	0.961[c]	
I/Fe	0.735[b]	0.763[c]	0.690[c]	0.262	0.194	0.717[b]	0.449	0.557	0.206	
I/K	0.741[b]	0.818[c]	0.818[c]	0.499	0.358	0.497	0.517[a]	0.809[b]	0.255	
I/Li	0.426	0.249	0.368	0.943[c]	0.971[c]	0.692[a]	0.938[c]	0.621	0.984[c]	
I/Mg	**1.00**	0.475	0.428	0.470	0.353	0.473	0.582[a]	0.619[a]	0.417	
I/Mn	0.475	**1.00**	0.718[b]	0.303	0.188	0.534[a]	0.456	0.593[a]	0.269	
I/Na	0.428	0.718[b]	**1.00**	0.559	0.420	0.370	0.461	0.835[c]	0.322	
I/P	0.470	0.303	0.559	**1.00**	0.973[c]	0.619[a]	0.877[c]	0.791[b]	0.931[c]	
I/S	0.353	0.188	0.420	0.973[c]	**1.00**	0.662[a]	0.895[c]	0.709[b]	0.966[c]	
I/Si	0.473	0.534[a]	0.370	0.619[a]	0.662[a]	**1.00**	0.783[b]	0.660[a]	0.784[b]	
I/Sr	0.582[a]	0.456	0.461	0.877[c]	0.895[c]	0.783[b]	**1.00**	0.679[a]	0.946[c]	
I/V	0.619[a]	0.593[a]	0.835[c]	0.791[b]	0.709[b]	0.660[a]	0.679[a]	**1.00**	0,665[a]	
I/Zn	0.417	0.269	0.322	0.931[c]	0.966[c]	0.784[b]	0.946[c]	0,665[a]	**1.00**	

Table 6: Intercorrelations of the I/chemical element mass fraction ratios in the normal female thyroid(*r* – coefficient of correlation).

Discussion

A good agreement of our results for the Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions with the certified values of CRM IAEA H-4 Animal Muscle, INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2Mixed Polish Herbs [64-70] as well as the similarity of the means of the Ca, K, Mg, Mn, and Na mass fractions in the normal thyroid of female determined by both NAA-SLR and ICP-AES methods (Table 1) demonstrates an acceptable precision and accuracy of the results obtained in the study and presented in Tables 2-6. The content of ChE 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 Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions, as well as I/Al, I/B, I/Ba, I/Br, I/Ca, I/Cl, I/Cu, I/Fe, I/K, I/Li, I/Mg, I/Mn, I/Na, I/P, I/S, I/Si, I/Sr, I/V, and I/Zn mass fraction ratios in normal thyroid of females (Table 2). The values of M, SD, and SEM can be used to compare data for different groups of samples only under the condition of a normal distribution of the results of determining the content of ChE 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 Med, 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 ChE content in thyroid tissue.

The obtained means for Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction, as shown in Table 3, agree well with the medians of mean values reported by other researches for the human thyroid, including samples received from persons who died from different non-thyroid diseases [40-60]. The obtained mean for Li is two orders of magnitude lower the median of previously reported data. Moreover, this value is beyond the previously published average values of the content of this element in the thyroid gland. In some published articles, the values of the mass fractions of ChE were presented in terms of ash or wet weight of the thyroid tissue. Therefore, we recalculated these data for dry mass basis using published values of 75% for water [72] and 4.16% for ash [73] in adult thyroids.No published data referring to I/Al, I/B, I/Ba, I/Br, I/Ca, I/Cl, I/Cu, I/Fe, I/K, I/Li, I/Mg, I/Mn, I/Na, I/P, I/S, I/Si, I/Sr, I/V, and I/Zn mass fraction ratios in human thyroid was found.

With age, the Al, Ca, Cu, P, S, and Zn contents increase, while Cl content, as well as I/Ba, I/Cu, I/Li, I/P, I/S, and I/Zn content ratios decrease (Table 4). All these characteristics can be used to estimate the "biological age" of the female thyroid gland. A significant direct correlation between the I and Na mass fractions was only seen in female thyroid (Table 5). Since no correlations were found between I and other ChE, it would appear that the content of Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, P, S, Si, Sr, V, and Zn in the thyroid gland is independent of I content. However, this is not quite so. If we bring the content of the studied ChE to the content of I (I/ ChE ratio), then there are close relationships between I/Al, I/B, I/Ba, I/Br, I/Ca, I/Cl, I/Cu, I/Fe, I/K, I/Li, I/Mg, I/Mn, I/Na, I/P, I/S, I/Si, I/Sr, I/V, and I/Zn (Table 6). From this it follows that, at least, the levels of all these ChE in the thyroid gland are interconnected and depend on the content of I in it. 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 ChE as Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn, if not directly, then indirectly, are involved in the process of thyroid hormone synthesis.

Conclusion

The combination of INAA-SLR and ICP-AES is a useful analytical tool for the determination of ChE contents in the thyroid tissue samples. This method allows determine means for Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V and Zn (twenty ChE). Our data reveal that the Al, Ca, Cu, P, S, and Zn contents increase, while Cl content, as well as I/Ba, I/Cu, I/Li, I/P, I/S, and I/Zn content ratios decrease in the normal thyroid of female during a lifespan. Therefore, a goitrogenic and tumorogenic effect of excessive Al, Ca, Cu, P, S, and Zn level and inadequate Cl level in the thyroid of old fmales, as well as a disturbance in intrathyroidal I/Ba, I/Cu, I/Li, I/P, I/S, and I/Zn relationships with increasing age may be assumed. Furthermore, it was found that the levels of Al, B, Ba, Br, Ca, Cl, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn in the thyroid gland are interconnected and depend on the content of I in it. 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 ChE as Al, B, Ba, Br, Ca, Cl, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn, if not directly, then indirectly, are involved in the process of thyroid hormone synthesis.

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