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ORIGINAL RESEARCH ARTICLE

Contents of twelve chemical elements in normal human breast determined using inductively coupled plasma atomic emission spectrometry

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ABSTRACT

Inductively coupled plasma atomic emission spectrometry (ICP-AES) has been shown to be an effective method for determining the content of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in small mass samples of breast tissue. The method is relatively simple and applicable directly in the clinic for express diagnostics. The autopsy material of 38 practically healthy women aged 16–60 years who died suddenly was studied using the developed method of ICP-AES. Mean values (M ± SD) of mass fractions (mg kg-1 of dry tissue) of chemical elements in normal breast tissue of women were: Al 3.62 ± 2.44, Ca 77.7 ± 61.8, Cu 1.03 ± 1.01, Fe 13.8 ± 12.3, K 194 ± 114, Mg 18.5 ± 9.0, Na 686 ± 516, P 201 ± 74, S 385 ± 224, Si 8.75 ± 6.22b, Sr 0.50 ± 0.24, and Zn 3.29 ± 1.65. The ability of breast tissue to absorb Al, Fe and Sr from the interstitial fluid was revealed. The selective accumulation of Al, Fe, and Sr should be taken into account in further studies of the role of chemical elements in the etiology of breast pathologies, as well as in the development of methods for the differential diagnosis of diseases, for example, benign and malignant tumors of the mammary gland.

Keywords: mammary gland of health females; chemical elements; inductively coupled plasma atomic emission spectrometry

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1. Introduction

Breast cancer (BC) is one of the most common types of malignant neoplasms and the leading cause of death from cancer among women in both developing and developed countries. According to WHO, the annual increase in the incidence of BC worldwide is approximately 2%. Between 2005 and 2020, the incidence of BC increased by 26% in developed countries, and this increase is even higher in developing countries[1].

The cause of BC is unknown and is likely related to a combination of genetic factors, such as susceptibility genes (BRCA1 and BRCA2), and adverse environmental factors[2]. Despite numerous studies, adverse environmental factors have not been clearly identified, although many candidates have been found that increase the risk of BC[3]. Since the change in the human gene pool is rather slow, it can be assumed that the alarmingly rapid increase in the incidence of BC is primarily associated with the transformations taking place in the environment. The steady development of industry, industrial chemistry and technology in agriculture, food production, pharmaceuticals, medicine, cosmetics, especially over the past 100 years, has led to global changes in the quality of the human environment[4]. These changes also apply to the amounts of chemical elements (ChE) entering the human body.

The female breast is a specialized organ whose main function is to produce milk to feed the baby. The female breast is made up of mammary glands (glandular tissue) as well as stroma (adipose tissue and ligaments, surrounding ducts and lobules, blood, and lymph vessels)[2]. The concentration of many ChE in breast milk, such as calcium (Ca), cobalt (Co), chromium (Cr), iodine (I), manganese (Mn), molybdenum (Mo), nickel (Ni), rubidium (Rb), zinc (Zn) and some others are higher than in blood serum[5]. It was found that the mammary gland is able to regulate these ChE concentrations even with a significant change in the maternal diet or with various effects on the maternal condition[6]. This conclusion is in good agreement with our position on ChE homeostasis in fluids and tissues of the human body, formulated by us about fifty years ago[4]. The ability of the glandular tissue during lactation to accumulate significant amounts of ChE for milk production suggests a special elemental composition of this tissue during the dormant period of breast as well. In addition, it is known that adipose tissue is a pool for some trace elements[7].

Our previous studies have shown that ChE homeostasis plays an important role in the normal and pathophysiology of human bones, thyroid, and prostate glands[4,8–39]. From this we can conclude that the specific physiological factors of the human breast probably play a key role not only in the normal physiology of the glandular tissue, but also in the etiology of various diseases of the breast, including BC. Despite the understanding of the important role of ChE, surprisingly little is known about the involvement of ChE in the normal and pathological physiology of the human breast.

There are few studies of ChE content in the mammary gland of women using chemical and instrumental methods[40–53]. However, in the published data for almost all breast ChE, there are large differences in the obtained mean values, which is probably due mainly to analytical difficulties.

The main objective of this study was to determine reliable values for the content of aluminum (Al), calcium (Ca), copper (Cu), iron (Fe), potassium (K), magnesium (Mg), manganese (Mn), sodium (Na), phosphorus (P), sulfur (S), silicon (Si), strontium (Sr), and zinc (Zn) in normal adult female breasts using inductively coupled plasma atomic emission spectrometry (ICP-AES). The second goal was to evaluate the quality of the results obtained. The third objective was to compare the average mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in normal breast tissue obtained in the study with data published in literature. The ultimate goal was to find differences between the results obtained for normal breast tissue and the reference data for the mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in blood serum, adipose tissue, and also tissues of the prostate and thyroid[2,5,34,54–57].

2. Material and methods

2.1. Samples

A randomized sample of normal breast tissue was obtained from autopsies of 38 women (age from 16 to 60 years, Caucasian race, Caucasian lifestyle) who died suddenly. Autopsies were carried out in the forensic medical examination department of the Obninsk city hospital during the first day after sudden death. Typical causes of death for most women were car accidents and injuries. All of the dead were residents of Obninsk, a small town (about 120,000 inhabitants) in a non-industrial area 105 km southwest of Moscow.

Tissue samples from all victims weighing about 10 g were taken in the right mammary gland in its lower inner quadrant. A scalpel made of high-purity titanium was used for sampling. Available clinical data were reviewed for each subject. None of the subjects had a history of an intersex condition, endocrine disorder, neoplasm, or other chronic disease that would interfere with normal breast development. None of the subjects received drugs that affect the morphology of the mammary gland and the content of ChE in the gland.

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/or national research committee and with the 1964 Helsinki declaration and its later amendments, or with comparable ethical standards.

2.2. Sample preparation

One of the goals of our studies of the content of ChE in the mammary gland in normal and pathological conditions is the search for markers of BC and the development of new diagnostic methods by determining the content of ChE in puncture biopsies of the lesion. When examining a patient with a single puncture biopsy, a material weighing about 10–20 mg can be obtained. Therefore, we initially developed a technique for microwave (MW) acid digestion of breast tissue samples weighing from 10 mg for subsequent determination of the ChE content in them using ICP-AES and ICP-MS analytical methods[58]. To reduce amount of acid used for the sample decomposition an enclose consisting of three mini vessel has been developed. The enclosure is intended for the standard EasyPrep (100 cm^3) autoclave of the MARS-5 MW oven. Analyzed samples of 10 mg and more mass were placed in mini-vessels. In each mini-vessel 1.4 ml of high-purity nitric acid was added. The mini-vessels were closed with a stopper, the stopper was fixed with a lid, and a Teflon condenser tube was inserted into the common hole. Three assemblies of these mini-vessels were enclosed in autoclave. The nitric acid (12.5 mL) of pure for analysis grade was added to the autoclave to provide a vapor pressure equal to the pressure of acids in mini-vessels. The autoclaves with mini-vessels were then placed on the microwave system rotor . One of the autoclaves contained temperature and pressure sensors, as well as a hollow fluoroplast cylinder, the volume of which corresponded to that of the enclosure. The samples were heated to 150 °C for 15 min and hold for 20 min at this temperature. The radiation power in MW was 800 watts at a frequency of 2450 Hz. After cooling the vessels to 300C the contents of the mini-vessels were quantitatively transferred into 10 ml test tubes and the solutions were adjusted to 10 ml with 2% HNO_3 solution. For measurements, the resulting solutions were additionally diluted in two times with a 2% nitric acid solution.

2.3. ICP-AES measurements

Determination of the content of ChE in the studied samples by inductively coupled plasma atomic emission spectrometry (ICP-AES) was carried out using an ICAP-6500 Duo plasma spectrometer (Thermo Scientific). The spectral range (166–847 nm) is recorded by a highly sensitive CID semiconductor detector. The optical unit of the instrument is thermally stabilized and purged with argon. High purity 99.993% argon was used as the plasma gas. The plasma power was 1150 W, the rate of the plasma-forming argon flow was 0.5 L/min, the transport flow was 0.55 L/min, and the cooling flow was 12 L/min. Measurements of ChE in the analyzed solutions were carried out using the iTEVA analytical software.

2.4. Standard solutions and international reference materials

To plot calibration dependences, standard reference solutions by Merck (Merck, KGaA, Darmstadt, Germany) and High-Purity standards (High-Purity Standards, North Charleston, SC, USA) of elements were used. Merck solutions contain the following set of elements: Al, Ba, Ca, Cd Co, Cr, Cu, K, Li, Mg, Mn, Na, Ni, Pb, Sr, Zn (solution IV), Mo, V, Ti (solution XVI), and Zr (solution XVII). For P and S calibration dependences we used single-element reference solutions by High-Purity standards. Working calibration solutions in interval 0.1–10 mg/L were prepared by serial dilutions of initial ones.

To check the reliability of the results obtained, the Polish certified reference materials MODAS-5 (Cod Tissue) and MODAS-3 (Herring Tissue), as well as the reference material prepared by the International Atomic Energy Agency IAEA-153 (Powdered milk) were used.

2.5. Statistics

The main statistical parameters, 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 for mass fractions of ChE (mg kg^{-1} of dry mass) were calculated using the Microsoft Office Excel program.

3. Results

Table 1 depicts the mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn obtained by us using the developed ICP-AES method in three different international certified reference materials MODAS-5 (Cod Tissue), MODAS-3 (Herring Tissue) and IAEA-153 (Powdered milk).

Table 1. ICP-AES data (Mean ± SD) of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr, and Zn mass fraction in certified reference material MODAS-5 (Cod Tissue), MODAS-3 (Herring Tissue), and IAEA-153 (Powdered milk) compared to their certified values (mg kg^{-1}, dry mass basis).

Element	MODAS-5		MODAS-3		IAEA-153	
	Certificate	Our result	Certificate	Our result	Certificate	Our result
Al	-	6 ± 1	-	14 ± 1	-	-
Ca	1100	1200 ± 100	36,900	39,800 ± 900	12,870 ± 320	12,900 ± 600
Cu	1.38 ± 0.09	1.5 ± 0.1	3.19 ± 0.22	3.3 ± 0.1	0.57 ± 0.20	0.48 ± 0.03
Fe	13.2 ± 1.1	14.5 ± 2.3	190 ± 13	210 ± 30	2.53 ± 0.91	3.4 ± 1.8
K	19,300 ± 1200	18,100 ± 700	11,800 ± 1300	10,700 ± 500	16,480 ± 1140	16,400 ± 800
Mg	1200 ± 200	1111 ± 43	3000 ± 200	2522 ± 74	1060 ± 75	948 ± 48
Na	3400 ± 200	3100 ± 100	19,400 ± 1700	16,200 ± 700	4180 ± 290	3700 ± 200
P	9600 ± 1200	10,000 ± 400	23,500 ± 3900	26,100 ± 600	10,100 ± 1020	9600 ± 500
S	10,500 ± 1600	12,200 ± 400	9300 ± 1000	10,900 ± 400	-	-
Si	-	-	-	-	17 ± 12	-
Sr	4.07 ± 0.36	3.9 ± 0.3	192 ± 15	177 ± 5	4.09 ± 0.62	4.1 ± 0.2
Zn	20.1 ± 1.1	22 ± 2	111 ± 6	111 ± 3	39.6 ± 1.8	38 ± 2

Mean—arithmetical mean, SD—standard deviation.

Table 2 presents the main statistical parameters (arithmetic mean, standard deviation, standard error of the mean, minimum and maximum values, median, percentiles with levels of 0.025 and 0.975) of mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in normal breast tissue in women aged 16 to 60 years.

Table 2. Basic statistical parameters of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr, and Zn mass fraction in the normal breast tissue of females between ages 16–60 years (mg kg^{-1} on dry tissue).

Element	Mean	SD	SEM	Min	Max	Med.	P0.025	P0.975
Al	3.62	2.44	0.42	1.21	11.1	2.69	1.25	9.60
Ca	77.7	61.8	10.6	11.7	265	60.8	14.4	223
Cu	1.03	1.01	0.18	0.24	5.90	0.75	0.25	3.26
Fe	13.8	12.3	2.1	4.51	66.0	10.1	5.01	43.6
K	194	114	20	53.6	560	173	72.5	475
Mg	18.5	9.0	1.6	7.66	48.0	17.4	8.00	36.4
Na	686	516	91	140	1827	502	145	1745
P	201	74	13	102	371	193	114	352
S	385	224	40	145	940	301	147	902

Table 2. (*Continued*).

Element	Mean	SD	SEM	Min	Max	Med.	P0.025	P0.975
Si	8.75	6.22	1.08	2.00	32.1	7.33	2.40	21.7
Sr	0.50	0.24	0.04	0.19	1.06	0.46	0.20	0.98
Zn	3.29	1.65	0.30	1.30	9.60	2.95	1.52	7.28

M—arithmetic mean, SD—standard deviation, SEM—standard error of mean, Min—minimum value, Max—maximum value, Med.—median, P0.025—percentile with 0.025 level, P0.975—percentile with 0.975 level.

Comparison of our results with literature data for the mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr, and Zn in normal breast tissue of adult women is shown in **Table 3**.

Differences between the mean values of mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in normal breast tissue of adult women (results of this work) and the reference values of these ChE content in blood serum, adipose tissue, as well as in the prostate and thyroid parenchyma are presented in **Table 4**.

Age-related changes in the elemental composition of the mammary gland are reflected in **Table 5**. The parametric Student's t-test and nonparametric Wilcoxon-Mann-Whitney U-test were used to estimate differences between the mean values of mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in normal breast tissue of healthy women aged 16–40 and 41–60 years.

4. Discussion

The developed ICP-AES method makes it possible to determine the content of twelve ChE in breast tissues: Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr, and Zn. Acceptable agreement between the values of the content of these ChE obtained by us in the international certified reference materials MODAS-5 (Cod Tissue), MODAS-3 (Herring Tissue) and IAEA-153 (Powdered milk) with the data of the corresponding certificates (**Table 1**) testified to the sufficient accuracy of the results of measuring the mass fractions of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in breast tissue samples using the developed ICP-AES technique (**Tables 2–4**).

Table 3. Median, minimum and maximum value of means of chemical element mass fractions (mg kg^{-1}, dry mass basis) in normal breast tissue of healthy females according to data from the literature in comparison with this work results (Females aged 16–60 years).

Element	This work	Published data [Reference]		
	M ± SD	Median of means (*n*)*	Minimum of means M or M ± SD, (*n*)**	Maximum of means M or M ± SD, (*n*)**
Al	3.62 ± 2.44	6.7 (4)	0.103 (52)[40]	38.4 (20)[41]
Ca	77.7 ± 61.8	262 (7)	52.6 ± 10.6 (-)[42]	680 (2)[43]
Cu	1.03 ± 1.01	2.56 (18)	0.48 ± 0.30 (20)[44]	2280 ± 140 (-)[45]
Fe	13.8 ± 12.3	21.8 (14)	5.1 (46)[46]	75.6 (20)[47]
K	194 ± 114	676 (7)	272 (20)[41]	4600 (-)[48]
Mg	18.5 ± 9.0	85.5 (4)	9.9 ± 1.8 (-)[42]	680 (4)[43]
Na	686 ± 516	2000 (7)	392 ± 56 (-)[42]	5380 (3)[43]
P	201 ± 74	2000 (8)	280 (-)[49]	56,000 ± 5460 (-)[45]
S	385 ± 224	4000 (6)	2000 (-)[50]	7600 (-)[48]
Si	8.75 ± 6.22	0.235 (5)	0.00024 ± 0.00003 (-)[51]	0.24 ± 0.39 (16)[52]
Sr	0.50 ± 0.24	0.45 (3)	0.12 (-)[49]	1.4 ± 0.4 (-)[42]
Zn	3.29 ± 1.65	8.3 (17)	2.88 (46)[46]	27.8 ± 5.0 (20)[53]

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

The contents of ChE mentioned above were determined in all or in most of the samples, therefore, for these ChE, the mean value of the mass fraction (M), standard deviation (SD), standard error of the mean (SEM), minimum, maximum, median, and percentiles with levels of 0.025 and 0.0975 was calculated (**Table 2**). The obtained 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 the median, range (minimum-maximum) and percentiles with the level of 0.025 and 0.0975 were calculated, which are valid for any law of distribution of the results of ChE content in breast tissue.

Table 4. The comparison of the means of some chemical element mass fraction (mg kg^{-1}, wet mass basis) in normal breast tissue of adult females (this work results) with those in blood serum, adipose, prostate, and thyroid tissue [Reference data].

El	Our result*	Reference data				Ratios			
	Breast tissue	Blood serum [5,54]	Adipose [2,55]	Prostate [56]	Thyroid [34,57–60]				
	I	II	III	IV	V**	I/II	I/III	1/IV	I/V
Al	1.81	0.23	0.79	7.0	2.6	7.87	2.29	0.26	0.70
Ca	38.9	97	35.6	500	420	0.40	1.00	0.08	0.09
Cu	0.52	1.19	0.28	1.9	1.02	0.44	1.86	0.27	0.51
Fe	6.9	1.09	18.5	24	55.6	6.33	0.37	0.29	0.12
K	97	191	117	2355	1605	0.51	0.83	0.04	0.06
Mg	9.3	21.7	6.5	210	74	0.43	1.43	0.04	0.13
Na	343	3251	337	2200	1732	0.11	1.02	0.16	0.20
P	101	142	-	1530	1073	0.71	-	0.07	0.09
S	193	1200	-	2180	2065	0.16	-	0.09	0.09
Si	4.4	6.9	-	25	12.7	0.64	-	0.18	0.35
Sr	0.25	0.03	0.044	0.51	0.95	8.33	5.68	0.49	0.26
Zn	1.65	1.15	1.68	210	23.7	1.43	0.98	0.01	0.07

El—element;
* We calculated these values using mean for water-50%[61];
** We calculated these values using mean for water-75%[62].

Most often, in studies of ChE in the mammary gland, samples of visually intact tissue adjacent to the tumor are used. However, we have previously shown that the intact tissue adjacent to the thyroid tumors in terms of the level of ChE content is not identical to the normal thyroid gland tissue of apparently healthy individuals[59,60]. Therefore, in our review of reported data, only results obtained from the study of normal mammary glands of apparently healthy women were used. The results obtained for most of the investigated ChE are in good agreement with the medians of the previously published mean values of the content of ChE in healthy breast tissue (**Table 3**). The only exceptions are P and S, the content of which is approximately one mathematical order lower than the median of the published data, as well as Si, the average content of which is more than 36 times higher than the median of the previous reports. At the same time, our mean values of the content of P, S, and Si do not even fit into the range of data available in the literature. However, it should be noted that the variations of published mean values for some of the studied ChE are very large and amounts to several mathematical orders.

Table 5. Differences between means (M ± SEM) of determined elements mass fraction (mg kg^{-1}, dry tissue) in normal female breast tissue of two age groups (AG).

Element	Female breast tissue				Ratio
	AG1	AG2	*t*-test	*U*-test	AG2 to AG1
	16–40 years	41–60 years	*p*<	*p*	
	n = 22	n = 16			
Al	4.13 ± 0.66	2.94 ± 0.40	0.133	> 0.05	0.71
Ca	85.2 ± 13.1	67.0 ± 17.8	0.418	> 0.05	0.79
Cu	1.05 ± 0.14	0.99 ± 0.36	0.888	> 0.05	0.94
Fe	16.2 ± 3.4	10.3 ± 1.2	0.117	> 0.05	0.64
K	226 ± 29	153 ± 23	0.059	< 0.05*	0.68
Mg	22.1 ± 2.3	13.9 ± 1.4	0.005*	< 0.01*	0.63
Na	882 ± 129	434 ± 92	0.009*	< 0.01*	0.49
P	219 ± 18	178 ± 17	0.114	> 0.05	0.81
S	475 ± 58	270 ± 33	0.005*	< 0.01*	0.57
Si	9.36 ± 1.71	7.91 ± 1.09	0.481	> 0.05	0.85
Sr	0.51 ± 0.07	0.48 ± 0.05	0.745	> 0.05	0.94
Zn	3.65 ± 0.48	2.82 ± 0.25	0.140	> 0.05	0.77

M—arithmetic mean, SEM—standard error of mean, AG1—age groups 1, AG2—age groups 2, *t*-test—Student's t-test, *U*-test—Wilcoxon-Mann-Whitney U-test, Al—aluminum, Ca—calcium, Cu—copper, Fe—iron, K—potassium, Mg—magnesium, Mn—manganese, Na—sodium, P—phosphorus, S—sulfur, Si—silicon, Sr—strontium, Zn—zinc, * Significant values.

The obtained data of the studied ChE content in healthy breast tissue were compared with the reference values of the content of these ChE in blood serum[5,54], adipose tissue[2,55], prostate[56] and thyroid[34,57-60] human gland (**Table 4**). Wherein, published data on the water content in breast tissue[61] and the results of report No. 23 of the International Commission on Radiation Protection[62] were used to recalculate the results for wet mass. The comparison (**Table 4**) showed that in terms of the content of Ca, Cu, K, Mg, P, Si and Zn, breast tissue almost does not differ from blood serum, while the content of Al. Fe, and Sr are significantly higher, and, vice versa, the contents of Na and S are noticeably lower. Thus, the ability of breast tissue to absorb trace elements such as Al, Fe, and Sr from the interstitial fluid seems to be quite real. Almost a mathematical order of magnitude lower levels of Na compared to serum is due to the fact, that this electrolyte is mainly contained in the extracellular space.

As noted above, breast tissue consists of a glandular component, adipose tissue, and stroma. On average the ratio by mass of the glandular component and adipose tissue together with the stroma is approximately 1:1[63]. From a comparison of the data obtained for the mammary gland with adipose tissue, it follows that ChE such as Al, Cu and Sr accumulate mainly in the glandular tissue of the mammary gland (**Table 4**).

Comparison of the content of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in the mammary gland with the content of these ChE in the prostate and thyroid gland showed that the mass fractions of all studied ChE in the mammary gland are significantly lower than in other glands (**Table 4**). This is due to the fact that approximately half of the breast tissue consists of adipose tissue, in which the ChE content is significantly lower than in glandular tissues (**Table 4**).

Using the parametric Student's t-test and the non-parametric Wilcoxon-Mann-Whitney U-test to compare two age groups it was found that the content of K, Mg, Na, and S in normal breast tissue decrease with age. The results obtained may be useful for a more complete understanding of age-related changes in the physiology and biochemistry of the mammary gland. and probably also for the diagnosis of pathological conditions of this organ.

5. Conclusion

The developed ICP-AES method allows obtaining reliable data on the content of Al, Ca, Cu, Fe, K, Mg, Na, P, S, Si, Sr and Zn in breast tissue samples. An important advantage of the developed technique is the possibility of determining the content of ChE in samples weighing only a few milligrams, which makes it possible to use materials from puncture tissue biopsies for analysis.

The ability of mammary gland tissue to absorb Al, Fe, and Sr from the interstitial fluid was found. This phenomenon should be taken into account in further studies on the role of ChE in the etiology of breast pathologies, as well as in the development of methods for the differential diagnosis of diseases of this organ, for example, benign and malignant tumors of the gland, based on the study of the elemental composition of the breast lesion.

The phenomenon of the age-related decrease of K, Mg, Na, and S contents in the normal mammary gland, discovered for the first time, requires further detailed study.

Author contributions

Conceptualization, VZ and VK; methodology, DD, IG and VK; software, DD, IG and VK; validation, VZ, VK and DD; formal analysis, VZ, investigation, VZ; resources, VK; data curation, VZ; writing—original draft preparation, VZ and VK; writing—review and editing, VZ and VK; visualization, VZ and VK; supervision, VZ; project administration, VK. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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