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LITHIUM AND SELENIUM CONCENTRATIONS IN THE DRINKING WATERS OF A MOUNTAINOUS VILLAGE (SĂCALU DE PĂDURE): POTENTIAL RELATIONSHIP TO RESIDUAL THYROID PATHOLOGY (PRELIMINARY RESEARCH)

Mária Melinda VARGA[a*], Attila CSISZÉR[b], Réka BARABÁS[c], Imre Zoltán KUN[d]

ABSTRACT. The lithium excess and selenium deficiency in the body can lead to thyroid disorders (goiter and hypothyroidism). We hypothesize that these elements can contribute to the persistence of thyroid pathology after the universal salt iodination introduced in 2002−2003 in Romania. The concentrations of lithium, selenium, and other micro- and macro-elements, as well as anions, were measured in the well waters used for drinking in the mountain village of Săcalu de Pădure, Upper Mureș Valley. Li concentrations (13 measures), ranging from 9.7 to 69 µg/L, generally exceeded the non-regulatory Health-Based Screening Level (HBSL) of 10 µg/L by 2 to 7 times, sustaining the contribution of Li excess to residual thyroid pathology. Additionally, these waters may be effective in treating mania, suicidal tendencies, Alzheimer's disease, and migraine. The selenium levels, measured in this and 5 surrounding localities (11 assays), were very low, under the detection limit. While the maximum limit for selenium content in drinking water is 20 µg/L (OG 7/2023), no lower limit has been established. Urinary iodine excretion, measured in 22 randomly selected residents, had normal values (100-350 µg/L) in most cases (90.9%), indicating an adequate iodine supply and excluding the iodine role in the residual thyroid pathology.

Keywords: *lithium, selenium, goiter, hypothyroidism, psychiatric use*

[a] *Petru Maior College, Reghin; Faculty of Chemistry and Chemical Engineering, Babeș-Bolyai University, Cluj-Napoca, Romania*
[b] *Regional Center of the National Institute of Public Health, Târgu Mureș, Romania. Email: attila.csiszer@insp.gov.ro*
[c] *Babeș-Bolyai University, Faculty of Chemistry and Chemical Engineering, Department of Chemistry and Chemical Engineering of Hungarian Line of Study, Cluj-Napoca, Romania. Email: reka.barabas@ubbcluj.ro*
[d] *Doctoral School, George Emil Palade University of Medicine, Pharmacy, Science and Technology, Târgu Mureș, Romania. Email: kunimre@gmail.com*
** Corresponding author: vargamariamelinda@yahoo.com*

INTRODUCTION

Data from the 2002−2004 period showed that in Romania, a moderate iodine deficiency exists in 80% of the counties (especially in rural regions), with a prevalence of endemic goiter ranging from 0% to 40% and reduced urinary iodine excretion (UIE) in two-thirds of the studied persons [1]. The introduction of universal and mandatory salt iodination in 2002−2003 eliminated the moderate/mild iodine deficiency that had been typical until then, thus significantly reducing the incidence of goiter and associated thyroid pathology (IDD − Iodine Deficiency Disorders). However, this aim was not achieved in some mountainous areas and among pregnant women. For this program to work effectively and remain sustainable and reliable, it must be followed periodically, especially under the conditions mentioned. Such local controls were carried out by the medical staff of Endocrinology Clinic Târgu Mureș in Mureș Valley (in 1999) and Gurghiu Valley (in 2006 and 2013) [1, 2, 3, 4].

The goals of our research are, on the one hand, to conduct this control, which has not been conducted in the last 11 years, and to identify the factors that maintain residual thyroid pathology in this locality. At the same time, we strive to improve local health parameters by recognizing and treating the existing disorders. Considering that excess lithium (Li) and/or selenium (Se) deficiency in the body can cause thyroid disorders (goiter, hypothyroidism), we hypothesized that these elements may play a significant role in the residual thyroid pathology that persists after the general iodination of table salt from 2002−2003. To investigate this, we measured the presence and concentrations of lithium, selenium, and other micro- and macroelements, as well as some anions (see Table 8), in the drinking water from one of the mountain villages in the Upper Mureș Valley, Săcalu de Pădure.

Regarding the biological properties of lithium, it is worth noting that its exact molecular function is not fully understood. Perhaps because of this uncertainty, the WHO does not currently consider it an essential nutrient [5]. However, several studies found a correlation between higher levels of lithium in the diet and lower risks of dementia, Alzheimer's disease, and suicide. Recently, the adults' daily requirement of Li was estimated at 1 mg, amounts we naturally consume without dietary supplements. The primary dietary sources of Li are cereals, potatoes, tomatoes, cabbage, and mineral waters from specific locations [6, 7]. According to estimates, cereal grains and vegetables can provide between 66 and 90% of the daily Li consumed [8]. Animal-derived foods, drinking water, and beverages supply the remainder.

Li concentrations measured in *drinking waters* in *various countries* varied by three orders of magnitude, and the published mean concentrations ranged from 0.48 to 56 µg/L [12]. Several other studies [9, 10] examined the Li content of groundwater (bank-filtrated and karst waters) and surface

waters (rivers, lakes, open reservoirs) used to supply drinking water in the *United States*. Li concentrations in groundwater ranged between *1 and 396 µg/L (median 8.1 µg/L) for public supply wells and 1–1700 µg/L (median 6 µg/L) for domestic supply wells nationwide.* Sharma et al. [10] investigated the presence of Li in water sources (ground and surface water) across the United States in 21 drinking water facilities. In groundwater, Li concentrations ranged from 0.9 to 161 µg/L (median 13.9 µg/L), and in surface water, they ranged from 0.5 to 130 µg/L (median 3.9 µg/L). Li in drinking water is not regulated in the United States. Still, the United States Geological Survey (USGS), in collaboration with the U.S. Environmental Protection Agency (US-EPA), provides a non-regulatory Health-Based Screening Level (HBSL) of 10 µg/L, which provides a human health context for Li in drinking water sources. Li levels were higher than the HBSL of 10 µg/L in 56% of the groundwater and 13% of the surface water [10]. The authors also discovered a strong correlation between Li and Na concentrations. Additionally, the Li concentration in source water and treated drinking water was remarkably similar. A 2023 review article presents a meta-analysis of 76 papers on Li concentrations, stratified by water resource type and country subgroups, using a random effects model (REM) [11]. The overall pooled concentration of Li was 5.374 µg/L (95 % CI: 5.261–5.487 µg/L). The pooled concentration of Li in groundwater (40.407 µg/L) was 14.53 times that of surface water (2.785 µg/L). The highest water Li content was attributed to Mexico (2,209.05 µg/L), Bolivia (1,444.05 µg/L), Iraq (1,350 µg/L), and Argentina (516.39 µg/L). At the same time, the lowest water Li content was associated with Morocco (1.20 µg/L), Spain (0.46 µg/L), and India (0.13 µg/L). Dobosy et al. (2023) [12] found in Hungary that Li concentrations in bank-filtrated river water, surface water from open reservoirs, and groundwater varied between 0.90–4.23, 2.12–11.7, and 1.11–31.4 µg/L, respectively, while the median values were 3.52, 5.02, and 8.55 µg/L, respectively. In bottled Hungarian mineral waters, concentrations ranged from 4.2 to 209 µg/L, with a median of 17.8 µg/L. Additionally, only a correlation between Li and K concentrations was found. At ten sampling locations in the Hungarian segment of the Danube River, the mean and median lithium concentrations were 2.78 and 2.64 µg/L, respectively. In Romania, in the Dobrogea region, half of the studied waters had Li concentration ranging 3.00−12.2 µg/L, while in the Banat region, between 1.40-1.46 µg/L. Despite the high Li content in soil, Li was mainly unavailable for plant uptake and bioaccumulation [13]. Iordache et al. (2024) [14] found Li concentrations in bottled and spring water between 0.06–1.557 and 0.09–984 µg/L, respectively, and a strong positive correlation among Li, Na, and Mg. Li exceeded the Health-Based Screening Level (HBSL) in 41.37% and 19% of bottled and spring water samples, respectively. Their results showed that the Li values in drinking waters were extremely high in Covasna County,

and high in Harghita and Mureș Counties. Romania does not have a maximum allowed concentration of lithium in drinking water [15], as do the European Union and the WHO. Due to the high-water consumption of the hydrothermal recycling process for spent Li batteries, Li concentrations are expected to rise, particularly in rivers where treated industrial wastewater is discharged.

Regarding the *biological effects* of lithium, its neuroprotective and regenerative properties can be stressed [16]. Due to its normothymic effects, Li has been commonly used in psychiatry since 1949, mainly for bipolar disorders, treating acute mania and manic episodes [17, 18]. The typical therapeutic oral dosages of lithium carbonate per day vary from 600 to 1200 mg [19]. Using highly bioavailable orotate chelate, a low-dose Li therapy was also developed [20]. Several studies have investigated the relationship between Li concentration in drinking water and the risk of suicide, homicide, and arrest rate for drug use [21−24]. Most of these studies indicate a link between higher Li concentrations in drinking water and a lower risk of suicide [12]. It has been observed that the suicide rate is significantly reduced when drinking water with a high lithium content [12]. It can also have anti-osteoporosis effects. Recently, lithium in drinking water was linked to generally reduced cancer risk [25]. Long-term lithium exposure via drinking water was reported to potentially disrupt thyroid function in a study conducted in the Puna region in Argentina, where local lithium in drinking water ranged from 8 to 1.005 µg/L [12, 26, 46]. In the thyroid gland, lithium (e g, in the form of carbonate) inhibits iodine uptake, the coupling of iodotyrosines, proteolysis, and thus hormone secretion. In the periphery, it blocks the formation of active T3 from T4 by inhibiting the 5'-deiodinase enzyme that activates it. Its spectrum of action is narrow; therefore, it is used successfully only for short-term thyroid inhibition, under lithium control (0.8-1.0 mmol/L content in the blood), mainly in iodine-induced severe hyperthyroidism [27, 28]. Because it inhibits ADH action in the kidney, it can be used to treat water intoxication ('water poisoning,' Schwartz-Bartter syndrome) when used to induce diabetes insipidus. Its effect on the bone marrow can be beneficial in some circumstances, stimulating leukopoiesis. It must be stressed that it is contraindicated in pregnant women because it can cause fetal developmental abnormalities (Ebstein anomaly). Of the lithium salts, lithium carbonate (Li_2CO_3) and lithium citrate ($Li_3C_6H_5O_7$) are most used. The active moiety of these salts is the lithium ion: Li^+.

Selenium is an essential mineral that is naturally present in many foods and added to others; it is also available as a dietary supplement. Selenium is a constituent of 25 selenoproteins, including thioredoxin reductases, glutathione peroxidases, and selenoprotein P [29]. Selenoproteins play critical roles in thyroid hormone metabolism, DNA synthesis, reproduction, and protection from oxidative damage and infection [30, 31]. It exerts a general antioxidant effect. Selenium concentration is higher in the thyroid gland than in

any other organ and plays essential roles in thyroid hormone synthesis and metabolism [32]. Selenoproteins play critical roles in the conversion of T4 to the active T3 (acting in the opposite direction to that of Li), via 5'-deiodinase, which is rich in selenoproteins. In the structure of the iodothyronine deiodinases, Se is incorporated as selenocystein [33]. In addition, the selenoproteins glutathione peroxidase and thioredoxin reductase help protect the thyroid gland from the hydrogen peroxide produced during thyroid hormone synthesis [32, 34]. Selenium is frequently used in autoimmune thyroiditis (Hashimoto), reduces TPOAb levels, and is effective in mild forms of hypothyroidism [33, 35−37]. Selenium may reduce the risk of cardiovascular mortality associated with selenium deficiency. Both its low and high serum levels were associated with depression [38]. In Romania, the maximum allowed concentration for selenium in drinking waters is 20 µg/L [15].

RESULTS AND DISCUSSION

Săcalu de Pădure is a village of 301 people [39] in the Upper Mureș Valley, and it is administratively part of Brâncovenești. This village is not supplied with tap water, so the residents obtain water for their needs from their own wells or other local sources, e g, the two wells in the center. In the villages Brâncovenești and Lueriu, the residents use tap water.

Clinical examinations. Twenty-three subjects, randomly selected and of different ages, were clinically examined: 14 women and nine men. We found thyroid pathology in 11 cases, which means 47.82% suffering from some form of thyroid disease: most of them (9 persons) have various degrees of goiter, some (5) hypothyroidism, one chronic autoimmune thyroiditis, and one papillary thyroid cancer (the latter was operated on and irradiated). Some patients are suffering from combined disorders. At the same time, we found psychological symptoms in 8 persons (34.78%): severe depression, bipolar disorders with repeated, persistent periods of depression, and generalized anxiety disorders with panic attacks.

Determination of urinary iodine excretion (UIE) was conducted on 22 residents in August 2024 in Săcalu de Pădure. The participants were randomly allocated. The average UIE value was 208.09 ± 67.38 µg/L, the median 190 µg/L.

Table 1. The indicators of iodine status (August 2024)

Iodine status indicators (µg/L)	Săcalu de Pădure
Average UIE	208.09
Average ± SD	208.09 ± 67.38
Median value of UIE	190

Table 2. Percentage distribution of UIE

UIE values (µg/L)	>350	100−350	<100	<50
Percentage distribution (in parentheses, the number of subjects)	9.09% (2/22)	90.90% (20/22)	0% (0/22)	0% (0/22)

As Table 2 shows, most cases (90.9%) have normal (100-350 µg/L) [5] values. None of the values were below 100 µg/L, indicating iodine deficiency, and only two exceeded 350 µg/L, pleading for excessive iodine intake. These results suggest *an adequate iodine supply*; there were no cases of UIE below 100 µg/L. The two high values (>350 µg/L, i e 9.09%) suggest even *excessive iodine intake.* This can be attributed to significant environmental exposure to iodine, primarily through alimentation. Thus, monitoring iodine supplementation is essential not only to detect iodine deficiency but also to avoid excessive iodine intake, which can promote the development of certain diseases, including hypothyroidism, hyperthyroidism, autoimmune thyroiditis, and perhaps thyroid cancer [5].

Table 3. Distribution of subjects by age

Age distribution	<20	20-30	30-40	40-50	50-60	60-70	70-80	80-90
Nr. of subjects	3	2	2	4	5	2	2	2

Table 4. Distribution by gender

Woman (number/percentage)	14	63.63%
Man (number/percentage)	8	36.36%

In 1999, the staff of the Endocrinology Clinic from Târgu Mureș (Balázs et al.) showed a moderate iodine deficiency in a group of 508 schoolchildren in the Upper Mureș Valley (around the town of Deda): average UIE was 59.95 ± 30.22 mg/L, while the estimated mean value of UIE was 52.29 µg/L [3]. After that, in 2006 and then in 2013, Kun et al. carried out similar tests in Gurghiu Valley, finding a gradual improvement in the iodine deficiency. In 2006, the UIE was 85.37±60.05 µg/L, with a mean of 74.88 µg/L, confirming a slight iodine deficiency; 30.8% of the children had a normal value. In 68.1% of children, urinary iodine levels did not reach the usual lower limit (100 µg/L), while in 30.3%, they did not even reach 50 µg/L. With

slight differences among the three investigated locations (Caşva, Glăjărie, Largă), hypothyroidism due to iodine deficiency was present in 15% of the examined schoolchildren (11 clinical forms and nine subclinical forms) [1]. In 2013, the average UIE for 120 children from the Gurghiu Valley was 345.15±201.40 µg/L. The mean UIE was 297.5 µg/L, with individual urinary iodine levels differing significantly (SD ± 197.13 µg/L*)*. Urinary iodine levels exceeded the normal range (> 350 µg/L) in 35.83% of children. These high values indicate excessive iodine intake [5].

Table 5. Comparison of iodine status (reflected by UIE) and thyroid pathology in the Upper Mureș and Gurghiu Valley between the years 1999 -2024

Year	Geographical zone, authors	UIE Mean ±SD(µg/L)	Median (µg/L)	Iodine status	Thyroid changes
1999	Mureș Valley (Balázs et al.) [3]	59.95 ± 30.22	52.29	moderate iodine deficiency	33.7% goiter
2006	Gurghiu Valley (Kun et al.) [1].	85.37 ± 60.05	74.88	slight iodine deficiency, 68% reduced iodine intake	15% hypothyroidism (11 overt, 9 subclinical form), 20% goiter
2013	Gurghiu Valley (Kun et al.) [5].	345.15 ± 201.40	297.5	excessive iodine intake in 36% of children	7% subclinical hypothyroidism 6% goiter, autoimmunity increases
2024	Săcalu de Pădure (Varga, Kun et al.)	208 ± 67	190	adequate iodine intake	goiter (total: 9), 56%; (>Gr.1/a: 5), 31%; hypothyroidism (2), 12.5%; cancer (1), 6.25%, from 16 subjects

Nearly 11 years have passed since the last study, underscoring the need for a new understanding of thyroid pathology that remains relevant today, even if it has decreased in both number and significance. Despite the use of iodized salt, thyroid pathology can still be found in the Upper Mureș Valley, though to a much lesser extent. Our survey shows that iodine coverage improved significantly after the introduction of universal use of iodized table salt in 2002-2003, compared with earlier results. Mountain settlements known to be mildly/moderately deficient in iodine have now become iodine sufficient. Looking to the future, we must emphasize the importance of

constant and accurate monitoring. Given that iodine deficiency has practically disappeared, other factors may explain the persistence of thyroid pathology, such as excessive lithium exposure and/or selenium deficiency.

The lithium concentrations in drinking water. Measured in Săcalu de Pădure wells, the Li-concentrations showed relatively high values compared to other settlements of Upper Mureș Valley, such as Lueriu and Brâncovenești (Table 6). Similarly, when we compare these values with the Li-concentrations measured in different areas of Romania [13, 14], in Hungary [12], and in other parts of the world [10, 11, 26], they can be classified as relatively high. It can be assumed that the geological conditions (clay soil) in Săcalu de Pădure are such that the wells may even have a composition close to mineral water, with a relatively elevated lithium content.

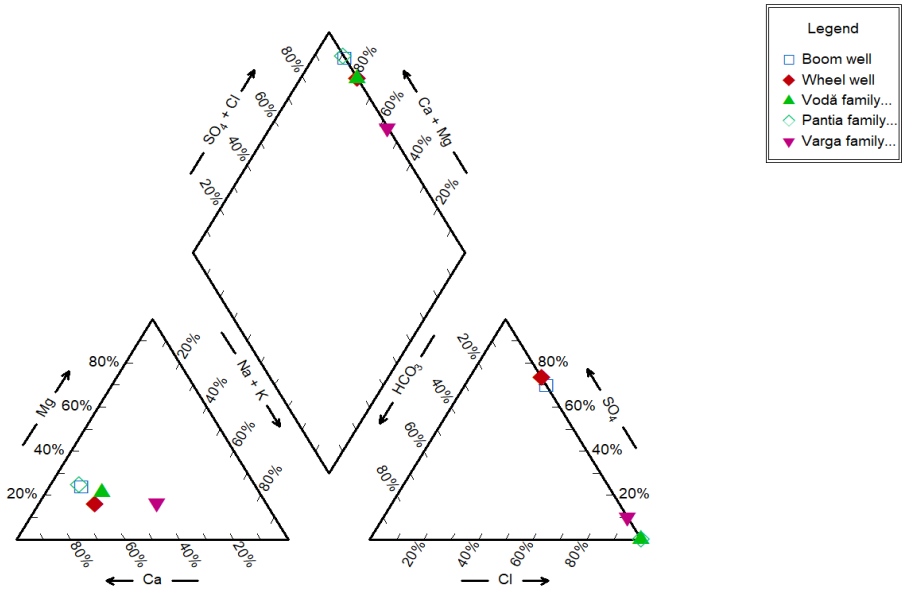

Figure 1. Piper diagram

To determine the water typology, the Piper diagram and the Gibbs plot are employed in several studies to analyze the hydrochemical facies and the correlation among groundwater chemistry and geomorphological processes [40, 41]. The Piper diagram shows that in the cation triangle, all points cluster toward the calcium corner, with only small contributions from magnesium and very low sodium–potassium levels, indicating a clear Ca-dominant character.

Figure 2. Map of the settlements: Săcalu de Pădure, Lueriu, Brâncovenești

Table 6. Lithium concentrations in drinking water. Comparison of the values in Săcalu de Pădure with the data of surrounding settlements (Lueriu, Brâncovenești)

Maximum value of lithium (µg/L) allowed in drinking water [10, 12, 42]:10 µg/L					
No.	Settlement	Origin of sampling	2024 Nov.	2025 April	2025 May
1	Săcalu de Pădure	Central boom well	24.74	22	25.9
2		Central wheel well	38.44	-	-
3		V. family well	25.56	24.5	-
4		P. family well	31.92	-	-
5		B. V. family well	-	40.3	-
6		B. V. family well, Glodeșel 1	-	10	-
7		Glodeșel 2 (Fountain Valley)	-	9.7	-
8		S. C. family well, 96 m deep drilled fountain	-	69	-
Other settlements					
9	Lueriu	tap water (mains)	1.66	-	-
10	Brâncovenești	well water (M. V. well)	1.04	-	-

‘’**–** “: not measured.

Table 6 shows that the Li values found in Săcalu de Pădure wells are higher than those in the surrounding localities of Lueriu and Brâncovenești. Lithium concentrations measured in the wells of Săcalu de Pădure ranged between 9.7 and 69 µg/L (the latter, highest value, was found in the water of a drilled well); three Li values measured at several-month intervals in the water of the central boom wells provided concordant results. Similar concordance can be seen in the case of V. family’s well.

Table 7. Li concentration indicators

Indicators (µg/L)	Săcalu de Pădure	Other settlements
Average	29.09	1.35
Average ±SD	29.09 ± 11.5	1.35 ± 0.35
Median value	25.56	1.35

Although there is no legal limit for lithium [12, 42], the water cannot be considered usual [43, 44], as it generally exceeds the 10 µg/L limit by 2−7 times. Related to this limit, we already mentioned in the introduction that, in Romania, as in the whole of Europe, Li in drinking water is not regulated. The situation is similar in the United States, where a *non-regulatory Health-Based Screening Level* (HBSL) *of 10 µg/L* for Li in drinking water sources has been accepted [10]. This value was later generally accepted as the maximum limit in drinking water. Considering the daily water consumption of 2 liters (as indicated in literature), this means a lithium intake of approximately 20-140 µg/day [42]. Of course, food sources also contribute significantly to its total daily intake.

Until now, the inhibitory effect of Li on *thyroid function* was known only at high therapeutic doses (0.6-1.2 g/day). It can be assumed that long-term intake, even at low doses, may elicit a similar effect, as has already been demonstrated in psychiatry. The literature is scarce regarding the possible role of Li-excess in the persistence of postiodination residual goiters and the associated pathological changes. In this sens two important sources should be mentioned: Stewart A.G. and Pharoah P.O.D. [45], called to attention to this possibility (1996), and the study of Broberg K. et al. (2011), and Concha G. et al. (2010), conducted in Puna region in Argentina − where local lithium in drinking water ranged from 8 to 1.005 µg/L −, concluding: exposure to lithium via drinking water and other environmental sources may affect thyroid function, consistent with known side effects of medical treatment with lithium. This emphasizes *the need to screen for lithium in all drinking water sources* [26, 46]. In high daily doses (e. g., Li carbonate 0.6-1.2 g), used in bipolar disorders, lithium can inhibit all steps of thyroid hormone biosynthesis, as well as their secretion in the bloodstream. Similarly, lithium inhibits 5'-deiodinase, blocking the conversion of T4 to active T3. Its clinical application for the treatment of hyperthyroidism is limited by the side effects observed at these doses; it is used mainly in special circumstances for thyrotoxic states. For the subtle mechanism of lithium's thyroid effects, it is assumed that in the formation of the goiter, in addition to hypothyroidism, which leads to the hyperstimulation of TSH secretion, lithium affects the

insulin-like growth factor, tyrosine kinase, and Wnt, exerting its effect on beta-catenin pathways, too [44, 47, 48]. It is not yet known whether lithium can induce autoimmune thyroiditis [48], but there is much data in this respect.

In addition to the observed thyroid changes, Li may also induce many *neuropsychological* and psychiatric effects. The daily intake of 20-140 µg in Săcalu de Pădure corresponds to low and slightly higher doses exerting different psychological actions [42]. In tiny doses, Li can be used for suicide prevention and dementia prevention (threshold for anti-aggressive/anti-impulsive effects may occur at 0.0008 mEq/L in the blood). Recently, it was supposed that the reduction of testosterone secretion in men also contributes to the acute anti-aggressive effects [49]. It was demonstrated that as the dose increases, not only does the strength of the effect increase, but its *quality* also changes. This can be imagined as follows: increasing the dose will cause lithium to act on more attack points [50]. The effect does not always increase linearly with dose; the relationship can be exponential or sigmoidal. Many factors influence the strength of the effect, but the importance of elimination must be emphasized. Given that there is a long-term and permanent intake, lithium – even in small daily amounts – can accumulate in the body and cause long-lasting effects. At the same time, natural lithium in drinking water *can increase lifespan.*

Regarding the *neuropsychiatric* effects of Li, it was mentioned that its principal therapeutic utilization is for bipolar disorders (usually in daily doses between 0.6-1.2 g), acutely in the manic phase, and chronically for preventing recurrences of these disorders. In chronic, permanent use, it can cause depression, too. This latter effect can be attributed to the induced hypothyroidism and neurobiological alterations resulting from chronic exposure. Low levels of lithium cause mood swings, but very high levels can cause severe poisoning [51].

The subtle *mechanisms of action of lithium in the CNS have* not been elucidated. It is now likely that, first, it affects the secondary messenger processes of neurotransmitters, the current fashionable hypothesis being that it acts through *phosphoinositide,* that can affect myoinositide depletion, thereby enhancing synaptogenesis [43, 52]. Similarly, Li reduces phosphoinositide levels in cell membranes and, consequently, the formation of second messengers, inositol triphosphate and diacylglycerol, thereby reducing the sensitivity of different brain structures to neurotransmitters and hormones in acute manic states. Lithium can affect a wide range of levels, from macroscopic brain structures to intracellular organelles. Modulation of neurotransmission is essential to its mechanism of action; thus, it inhibits dopaminergic and NMDA (glutamate)-ergic transmission and stimulates *GABA*-ergic transmission. It exerts a neuroprotective effect by influencing brain-derived neurotrophic factor (BDNF) and B-cellCLL/lymphoma (Bcl-2), with antiapoptotic actions. At

trace doses (i e, nanolithium), it may act mainly by inhibiting glycogen synthase kinase-3 beta (GSK-3β) [49]. Li acts as a neuroprotective agent against neurodegeneration by preventing inflammation, oxidative stress, apoptosis, and mitochondrial dysfunction using PI3/Akt/GSK3β and PI3/Akt/CREB/BDNF signaling pathways [16]. Regarding the molecular mechanism of Li action, it may exert its effects by directly altering the fate of sodium ions. Even if not perfectly, it can replace sodium ions and influence their movement back and forth during cell firing. This is directly related to the assumption that the main characteristic of lithium is a membrane-stabilizing effect.

From a biological point of view, lithium can be considered a double-edged sword: it is required in small quantities for the normal course of certain biochemical processes, but in large quantities, it has harmful effects: depression, ataxia, tremor, thyroid failure, diabetes insipidus, kidney lesions up to kidney failure, cardiovascular disorders (e.g. cardiac arrhythmias), and metabolic disorders, liver damage, etc. [4, 53, 54]. The inhibitory effect of lithium excess on the thyroid can probably be prevented – at least partially – by selenium supplementation, since both act, inter alia, at the level of the *5'-deiodinase* enzyme, Li inhibiting, and Se stimulating it. The competition between the two elements has already been proven in some aspects in animal experiments [55]. Similarly, some authors have found that Li can interact with Mg ions. Experimental studies showed an activation of thyroid gland synthetic activity by ingestion of magnesium chloride [56]. Mg can indirectly influence deiodination, which catalyzes the conversion of T4 to the more active T3 form [57]. Recently, Ahmed et al. (2025) [58] observed that neonatal hypothyroidism induced by lithium exposure via breast milk could be minimized with iodine supplements, as iodine successfully competed with Li. This may be another way to prevent the adverse thyroid effects of Li excess, in states without pregnancy, too.

Selenium concentration in drinking water. The selenium concentration in drinking water (mains, spring, and stream water) in Săcalu de Pădure, Brâncovenești, and in four localities situated in Gurghiu Valley (Gurghiu, Caşva, Largă, and Glăjărie), a total of 11 measures, was below the limit of quantification (LOQ=2.32 µg/L). However, this result is not consistent with a Se deficiency in the human body, because the intake of Se is attributed mainly to the alimentary route: consumption of selenium-containing foods, food supplements, dairy products, drinking water, multivitamins, and other selenium-containing medicines. So, our current studies are not suitable for answering this problem. Nevertheless, as a first step in the research, we measured its concentrations in drinking water, noting that this question can be answered only by measuring Se serum levels in the future. The maximum limit for selenium in drinking water was 10 µg/L until 2022; it has now been raised to 20 µg/L [15]. There is no established lower limit for its normal concentration because the amount of

selenium in water depends on soil composition. Since elemental selenium is not or only slightly soluble in water, how much is dissolved from rocks under given soil conditions depends on the oxidation state. The selenium concentration in drinking water is low − usually between 0.006 and 10 µg/L − and, on average, does not exceed 3 µg/L. Thus, the relative contribution of drinking water to daily selenium intake is considered not significant compared to that from food, even in regions with high selenium content (e g China, approx. 50 µg/L). Selenites and selenates are generally the more mobile selenium compounds that are soluble in water. The release of these compounds into water is also significantly influenced by soil pH. Magnesium deficiency impacts the bioavailability and tissue distribution of selenium, resulting in reduced levels [59].

Other micro- and macroelements, and anions in drinking waters:

Table 8. Concentrations of macro-, microelements, and anions in the tested waters

µg/l mg/L [15, 60, 61]	Maximum value allowed in drinking water	Săcalu de Pădure				Brânco-venești	LOD, LOQ mg/L µg/L
		Boom well	Wheel well	V. family well	P. family well	V. family well	
K	− mg/L	29.60	53.80	33.70	11.90	4.87	LOD=0.038
Na	200 mg/L	15.1	16.60	21.74	21.8	115	LOD=0.032
Ca	− mg/L	150	125	99.50	148	94.70	LOD=0.039
Mg	− mg/L	18.3	11.1	10.05	20.08	13.7	LOD=0.023
Al	200 µg/L	<LOQ	<LOQ	<LOQ	<LOQ	−	LOQ=5.3
Cr	0.05 mg/L	<LOD	<LOD	<LOD	<LOD	<LOD	LOD=0.048
Mn	0.05 mg/L	<LOD	<LOD	<LOD	<LOD	<LOD	LOD=0.015
Fe	0.2 mg/L	<LOD	0.09	<LOD	<LOD	<LOD	LOD=0.066
Ni	20 µg/L	6.72	5.72	5.63	7.02	−	LOQ=1.41
Cu	2 mg/L	<LOD	<LOD	0.08	<LOD	<LOD	LOD=0.038
Zn	5 mg/L	<LOD	<LOD	0.058	0.011	<LOD	LOD=0.004
Cd	5 µg/L	<LOQ	<LOQ	<LOQ	<LOQ	−	LOQ=0.84
Pb	5 µg/L	<LOQ	<LOQ	<LOQ	<LOQ	−	LOQ=1.53
F^-	1.5 mg/L	0.10	0.09	0.26	0.11	0.09	LOQ=0.05
Cl^-	250 mg/L	41.9	26.2	27	45.7	390	LOQ=0.05
NO_2^-	0.5 mg/L	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	LOQ=0.05
NO_3^-	50 mg/L	51.9	15.9	11	15.2	16.6	LOQ=0.05
PO_4^{3-}	0.5 mg/L	<LOQ	2.03	0.079	<LOQ	<LOQ	LOQ=0.05
SO_4^{2-}	250 mg/L	130	96.5	77.4	150	56.4	LOQ=0.05

LOD − Limit of detection; LOQ − Limit of quantification; "− ": Not measured.

For the elements and anions K, Na, Ca, Mg, Al, Cr, Mn, Fe, Ni, Cu, Cd, Pb, F-, Cl-, NO_2^-, NO_3^-, and SO_4^{2-}, the maximum values allowed in drinking water were taken from OG 7/2023. For the elements K, Ca, and Mg, there are no legally established maximum concentration limits. These ions are considered essential minerals and part of natural water hardness. The maximum concentrations of Zn and PO_4^{3-} in drinking water are not specified in the legal regulations [15]. Their mentioned upper normal concentrations are cited from other sources [60, 61].

The measured *Ca- and Mg*-concentrations (ranging between 99.5−150, and 10.05−20.08 mg/L, respectively) are comparable with those of some known bottled mineral waters (e g, Biborțeni – from Bățanii, source F1, Sâncrai, Borsec, Stânceni, Poiana Negrii, Aqua Carpatica, etc.) [62]. The Ca and Mg have a natural sedative effect helpful in the prevention and treatment of depression and stress reactions [63, 64]. Both elements play a fundamental role in the intrinsic functions of living cells, particularly in their excitability and motility. Both are necessary for bone health. Hypocalcemia induces neuromuscular hyperexcitation, which can progress to tetanic convulsions. Similarly, hypomagnesemia increases neuromuscular excitability, causes insulin resistance, and perhaps depression. Mg is needed for the activation of over 600 enzymes in the body [65, 66]. *Chloride* ions are present in higher concentrations in the water of the V.M. family well in Brâncovenești, which the proximity of the salt lake can probably explain. In this sense, Na has a relatively high concentration compared to other water sources.

The increased *phosphate* content detected in the wheel well can promote algae growth in the water. The pollution of the Săcalu de Pădure waters is primarily reflected in the increased *nitrate* content of the boom well. This excess is especially dangerous for infants, who may suffer from methemoglobinemia, as nitrates are converted into nitrites in the digestive system, which, when bound to hemoglobin, disrupt oxygen binding. This can lead to a hypoxic state in infants, which manifests itself in a blue discoloration. In adults, it causes stomach irritation. It should be noted that the two wells in the center of Săcalu de Pădure are currently under warning due to contamination: *Not suitable for human consumption!* But this is not indicated in the other wells in the settlement!

LIMITATIONS OF THE STUDY

Although the study was conducted using a rigorous methodology, certain limitations should be acknowledged. The applied random method for subject selection, the partially identical subjects across the different

groups, the relatively small sample size, and the various times of determination could influence the results. Similarly, we do not know the conditions before the introduction of iodination in different settlements, only the global situation of the Upper Mureș Valley. Nevertheless, it can be assumed that iodine deficiency was more severe in the mountainous region (Săcalu de Pădure) than in the flat areas (Brâncovenești, Lueriu). Due to time and resource constraints, the study focused only on the most relevant variables. Yet, the results provide valuable insights into the investigated phenomenon and serve as a basis for further research.

CONCLUSIONS

The relatively high lithium content (between 9.7 − 69 µg/L) of the drinking water in Săcalu de Pădure, Romania, exceeding generally 2−7 times the non-regulatory Health-Based Screening Level of 10 µg/L − considered its maximum standard limit − may contribute to the residual thyroid pathology, given that the iodine supply was found to be normal. It is true that until now, thyroid disorders (hypothyroidism and goiter) have only been detected after larger, therapeutic doses of lithium (typically Li carbonate 600-1200 mg/day, used primarily in bipolar disorders, and rarely in thyrotoxic states), but it can be assumed that the constant intake of small amounts of lithium (20−140 µg/day) can induce similar changes, too. This has already been demonstrated in connection with the psychological effects of lithium used in very low doses. This study cannot address the possible role of selenium deficiency in this process, as selenium is mainly obtained from food rather than drinking water. Residual goiter and related disorders should be treated according to well-established therapeutic guidelines.

EXPERIMENTAL SECTION

The clinical examinations, consisting of a brief familial and personal history, general clinical and endocrine examinations (mainly thyroid), were performed on 23 randomly allocated persons. This exam was conducted by a member of the authors (KIZ), who has practiced endocrinology for more than 4 decades.

Urinary iodine excretion (UIE). The standard Sandell-Kolthoff method was used to determine urinary iodine excretion in 22 residents randomly allocated at the Regional Center of the National Institute of Public Health, Târgu Mureș.

Sample collection and storage. The locations of county seats, the water wells, are illustrated in image 1. Water samples were collected from Săcalu de Pădure and the surrounding localities (Lueriu and Brâncovenești) at multiple time points − November 2024, and April and May 2025 − for comparative analysis. The samples were collected unfiltered in clean plastic bottles that had been rinsed three times with the local sampling water before collection, without any preservation steps. The water samples were stored at refrigeration temperatures (1–2 months) until laboratory processing. The samples were transported in a cooler bag to maintain the appropriate temperature throughout transit.

Reagents and solution. A multielement standard solution IV (1000 mg L^{-1}, Merck, Darmstadt, Germany) was used to prepare the calibration solutions by dilution with 2% (v/v) HNO_3. Nitric acid 63% (m/m) for analysis (Merck, Darmstadt, Germany) was used to prepare the 2% (v/v) HNO_3 blank solution by dilution with double-distilled water produced using a Cyclon bidistiller (Fistreem International, Cambridge, UK).

Sample preparation. Samples were filtered through 4 µm ashless filter paper (Macherey-Nagel, Düren, Germany). Aliquots of 125 mL were evaporated to dryness on a sand bath (ST 82, Gestigkeit Harry GmbH, Düsseldorf, Germany), then taken up with 5 mL of 65% (m/m) HNO_3 and diluted to volume in 25 mL volumetric flasks, resulting in a five-fold preconcentration of the sample.

Instrumentation. Lithium concentrations in the water samples were determined using high-resolution continuum source flame atomic absorption spectrometry on a ContraAA 300 spectrometer (Analytik Jena, Jena, Germany) equipped with a Xe short-arc lamp and an air-acetylene flame. The working conditions employed were those recommended by the manufacturer: 670.784 nm analytical line, air-acetylene flow rate of 70 L/h, and a burner height of 6 mm. Calibration curves were constructed in the range of 0–1 mg L^{-1} Li (n = 6) using peak height measurements, with signals obtained by 5-pixel integration of the analytical line, yielding an R^2 of 0.9999. The limit of detection (LOD) of the method was 0.074 µg/L, calculated using the 3σ criterion based on the standard deviation of 11 blank sample measurements and the calibration curve slope, considering the 5-fold preconcentration of the samples. Measures were first taken in November 2024, and subsequently in April and May 2025; in April 2025, the determinations were extended to the other wells in the village.

The technique used to analyze the anions was ion chromatography. These measurements were performed on an IC 761 Compact type, manufactured by Methrom A. G. (Switzerland). The eluent used was 0.0027 mol-1 sodium carbonate and 0.001 mol-1 sodium bicarbonate. The mobile phase speed

was 0.7 ml/min. The calibration curve was prepared using a 1000 mg/L multicomponent standard solution (NO_3^-, SO_4^{2-}, Cl^-, F^-, PO_4^{3-}). A separate standard stock solution was prepared for the determination of nitrite. All reagents were Sigma-Aldrich brand.

Selenium concentration in drinking water was determined with an inductively coupled plasma mass spectrometer (UltraMass 700, Varian, Australia) at the Regional Center of the National Institute of Public Health in Târgu Mureș. An internal standard of 89Y at 100 ppb was used. Limit of quantification (LOQ): 2,32 µg/L.

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