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PHARMACOKINETICS OF DIFFERENT SELENIUM SUPPLEMENTS IN HEALTHY INDIVIDUALS AND PATIENTS WITH AUTOIMMUNE THYROIDITIS AFTER ORAL ADMINISTRATION

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Selenium is essential for the function of key selenoproteins such as glutathione peroxidase, thioredoxin reductase, and iodothyronine deiodinase, which have antioxidant properties and support thyroid hormone metabolism. Due to the low selenium content in European soils – particularly in the Southeastern regions, supplementation is often recommended, especially for conditions like Hashimoto's thyroiditis. However, careful consideration of selenium dosage and pharmacokinetics is crucial, as the margin between essential and toxic levels is very narrow. The aim of this study was to investigate the pharmacokinetics of selenium absorption and plasma concentration following oral administration of various selenium doses and chemical forms, both in the short and long term, in healthy individuals and patients with autoimmune thyroiditis. Selenium concentrations in blood plasma were measured using electrothermal atomic absorption spectrometry (ETAAS). The study found that L-selenomethionine is absorbed more efficiently than inorganic sodium selenite, with peak plasma concentrations reached and sustained within 6 – 8 hours. Selenium levels remained elevated 48 hours after ingestion compared to baseline. At a daily dose of 200 μg of selenium as L-selenomethionine, plasma selenium concentrations increased by approximately 30 %, and by about 25 % at 100 μg/day, relative to the initial value. Long-term studies showed that plasma selenium concentrations rose significantly after the first month of supplementation, with a slower increase in subsequent months. After supplementation ended, selenium levels declined rapidly. Interestingly, no significant differences in selenium absorption or excretion were observed between patients with Hashimoto's thyroiditis and healthy controls.

Keywords: selenium; selenomethionine; pharmacokinetics; autoimmune thyroiditis; ETAAS

ФАРМАКОКИНЕТИКА НА РАЗЛИЧНИ СУПЛЕМЕНТИ СО СЕЛЕН КАЈ ЗДРАВИ ЛИЦА И ПАЦИЕНТИ СО АВТОИМУН ТИРЕОИДИТИС ПО ОРАЛНО ВНЕСУВАЊЕ

Селенот е неопходен за функција на клучни селенопротеини како што се глутатион пероксидаза, тиоредоксин редуктаза и јодотиронин дејодиназа, кои поседуваат антиоксидантни својства и имаат особено значење за метаболизмот на тироидните хормони. Поради ниската содржина на селен во почвите низ Европа – особено во југоисточните региони, често се препорачува суплементација, особено кај состојби слични на Хашимотов тиреоидитис. Меѓутоа, потребно е внимателно проучување на дозирањето и фармакокинетиката на суплементите кои содржат селен, имајќи предвид дека границата помеѓу есенцијалната и токсичната доза е многу тесна. Целта на ова истражување беше да се испита фармакокинетиката на апсорпција на селен и неговата концентрација во плазмата по орално внесување на различни дози и хемиски форми на селен, на краток и на долг рок, кај здрави лица и пациенти со автоимун тиреоидитис. Концентрацијата на селен во крвната плазма беше определена со електротермичка атомска апсорпциона спектрометрија (ETAAS). Резултатите од фармакокинетичките испитувања покажаа дека L-селенометионинот се апсорбира поефикасно во споредба со неорганскиот натриум селенит, при што највисоки концентрации во плазма се постигнуваат и одржуваат во рок од 6 до 8 часа. Нивоата на селен остануваат зголемени и 48 часа по внесувањето на суплементот, во споредба со почетната вредност. Во однос на дневната доза, концентрацијата на Se во плазма се зголеми за 30

% при внесување на 200 μg/ден L-селенометионин и приближно за 25 % при доза од 100 μg/ден L-селенометионин, споредено со почетната концентрација. Долгорочните испитувања покажаа значајно зголемување на концентрацијата на селен во плазма по првиот месец од суплементацијата, проследено со побавно зголемување во следните месеци. По прекинот на суплементацијата, нивоата на селен брзо опаѓаат. Интересно е што не се забележани значајни разлики во апсорпцијата или екскрецијата на селен помеѓу пациентите со Хашимото тиреоидитис и здравите испитаници.

Клучни зборови: селен; L-селенометионин; фармакокинетика; автоимун тиреоидитис; ETAAS

1. INTRODUCTION

Selenium is an essential trace element vital for the optimal functioning of the human body. Its importance stems from its incorporation as the 21st proteinogenic amino acid, selenocysteine (SeCys), which is genetically encoded by the UGA codon and integrated into 25 known human selenoproteins.[1] Most of these selenoproteins are enzymes that contain SeCys as their active centre.[2,3]

Selenoenzymes, including members of the thioredoxin reductases (TXNRD) and glutathione peroxidases (GPX) families, play a critical role in mitigating oxidative stress and regulating redox signaling.[4] For example, GPX enzymes inhibit lipid peroxidation, thereby protecting cells and tissues from damage caused by free radicals. These enzymes are also involved in a wide range of biological processes, including signal transduction, cell proliferation, aging, immune function, and the emerging field of ferroptosis.[5,6] TXNRD, in contrast, catalyze the reduction of thioredoxin, various oxidized compounds, and disulfide bonds in proteins, with SeCys serving as the catalysts.[7]

Beyond its antioxidant functions, selenium is essential for regulating the basal metabolic rate in various tissues and plays a significant role in thyroid hormone synthesis.[8] Selenoenzymes, particularly iodothyronine deiodinases (DIO), are responsible for converting inactive thyroxine (T4) into its active form, triiodothyronine (T3), thereby modulating thyroid activity.[9]

Selenoprotein P (SELENOP) plays a central role in the storage and transport of selenium in peripheral tissues, further underscoring the systemic importance of this trace element.[10-12] Dietary selenium is primarily obtained from plant or animal sources.[13] However, soils in Macedonia and the Balkan Peninsula are notably low in selenium, resulting in plants that contain only trace amounts. Consequently, selenium intake among children and adults in these regions falls below recommended levels.[14]

Optimal selenium intake is crucial for preventing both deficiency or toxicity-related disorders, making it a pressing public health concern.[15] In selenium deficiency, cells prioritize the synthesis of essential selenoproteins, establishing a cellular hierarchy. Conversely, acute selenium toxicity from high-dose exposure can lead to rapid and potentially fatal outcomes. Chronic selenosis, caused by prolonged moderate overexposure, manifests in symptoms such as hair loss, dermatitis, and gastrointestinal complaints.[16]

The role of selenium in thyroid health has attracted significant attention, particularly in autoimmune thyroiditis, such as Hashimoto's thyroiditis. Several clinical trials have explored the potential of selenium supplementation to improve thyroid function and reduce autoimmune responses.[17] For example, studies by Gartner et al. and Duntas et al. demonstrated a significant reduction in anti-thyroperoxidase antibodies (TPOAb) following selenium supplementation, accompanied by improvements in thyroid echogenicity and overall well-being.[18,19]

In a study by Tian et al., 40 patients with euthyroid autoimmune thyroiditis (AIT) received 200 μg/day of selenium for 3 months, while a control group received a placebo. The selenium group showed a significant reduction in TPOAb titers and oxidative stress markers, suggesting that selenium's antioxidant properties may mediate its beneficial effects.[20] However, studies by Nacamulli et al.[21] and Deng et al.[22] reported mixed results regarding selenium's impact on thyroid echogenicity and antibody levels, highlighting the need for further comprehensive assessments.

However, these studies had several limitations, including the lack of monitoring of selenium concentrations and a primary focus on thyroid antibody levels as the main outcome measure.[23] Consequently, despite the observed benefits, there are currently no definitive recommendations for routine selenium supplementation in patients with autoimmune thyroiditis.

In conclusion, while selenium supplementation shows promise in improving thyroid antibody levels and certain aspects of thyroid health, further research is necessary to establish clear clinical guidelines. These guidelines should consider not only selenium status but also comprehensive thyroid function parameters.

Determining selenium bioavailability is essential for developing effective supplementation strategies to support optimal health. Pharmacokinetic analyses – designed to assess the rate and extent of selenium absorption and its availability at the site of action – are fundamental to this effort.[24] Several methods contribute to our understanding of selenium pharmacokinetics and bioavailability in humans, including monitoring plasma selenium concentrations, measuring glutathione peroxidase activity, and using stable selenium isotopes to trace endogenous selenium forms in food.[25,26]

In more recent clinical studies, sodium selenite and L-selenomethionine have been the most commonly used forms of selenium supplements.[27] However, comparative research has revealed significant differences in their pharmacokinetic and therapeutic profiles, with selenomethionine generally preferred over sodium selenite.[28]

Se-methylselenocysteine is another selenium compound used in supplementation, notable for its ability to form methylselenol – a metabolite believed to play a role in cancer therapy.[29] Despite the cytotoxic potential of sodium selenite in selectively targeting malignant cells, organic selenium compounds such as selenomethionine are gaining increasing favor, particularly in the treatment of thyroid disorders.[30]

Different selenium compounds exhibit distinct pharmacokinetic profiles, with organic forms generally demonstrating greater efficacy than inorganic compounds.[31,32] Moreover, the therapeutic potential of selenium extends beyond thyroid disorders, showing promise in areas such as cancer therapy and intensive care settings.[33,34] While some studies report favorable outcomes, inconsistencies in pharmacokinetics and clinical responses emphasize the need for tailored approaches and more rigorous investigation.[35]

The aim of this study was to evaluate and compare the pharmacokinetics of selenium in healthy individuals and patients with autoimmune thyroiditis following oral administration of various doses and chemical forms. Both short- and long-term daily intake was assessed to identify and recommend the optimal dose and chemical form of selenium for effective supplementation.

2. MATERIALS AND METHODS

2.1. *Study design*

2.1.1. *Short-term pharmacokinetic testing of selenium*

Pharmacokinetic testing was conducted on three groups of healthy volunteers over a 48-hour period. The first group consisted of 5 volunteers (3 men and 2 women) with an average age of 47 years. This group received a single oral dose of 100 μg of selenium in the form of L-selenomethionine. The tablet contained 100 μg of elemental selenium along with the following inactive ingredients: microcrystalline cellulose, maltodextrin, croscaramellose sodium, calcium hydrogen phosphate, silicon dioxide, and magnesium stearate. The second group consisted of 4 participants (2 men and 2 women) with an average age of 44 years. This group received a single oral dose of 100 μg of selenium in the form of inorganic selenium (sodium selenite). Each tablet contained 100 μg of elemental selenium and included the following bulking agent: powdered cellulose and hydroxypropyl methyl cellulose (capsule shell). The third group consisted of 4 participants (2 men and 2 women) with an average age of 41 years. They were administered a single oral dose of 200 μg of selenium in the form of L-selenomethionine. Pharmacokinetics testing was also performed on a group of six women diagnosed with Hashimoto's thyroiditis, with an average age of 59 years. This group received a single oral dose of 100 μg of selenium in the form of L-selenomethionine. The characteristics of the study population are presented in Table 1. In all groups, selenium kinetics were monitored by measuring plasma selenium concentrations prior to administration and at 2, 4, 6, 8, 12, 24, and 48 hours post-dose.

T a b l e 1

Characteristics of the study population in which selenium pharmacokinetics were evaluated over a 48-hour period

	I group	**II group**	**III group**	**IV group**
Type of individuals	healthy	healthy	healthy	with Hashimoto's thyroiditis
Chemical form of selenium	selenomethionine	sodium selenite	selenomethionine	selenomethionine
Dose of Se	100 μg	100 μg	200 μg	100 μg
Number of participients	5	4	4	6
Average age (years)	47	44	41	59

2.1.2. *Long-term pharmacokinetic testing of selenium*

Long-term pharmacokinetic testing was conducted over a period of 5 months on two groups of healthy volunteers and one group of patients with Hashimoto's thyroiditis. The first group, consisting of 5 volunteers (2 men and 3 women) with an average age of 43 years, received a daily oral dose of 100 μg of selenium in the form of L-selenomethionine. The second group, which included 3 participants (1 male and 2 females) with an average age of 37 years, received a daily oral dose of 200 μg of selenium, also in the form of L-selenomethionine. The third group consisted of 6 patients diagnosed with Hashimoto's thyroiditis (2 men and 4 women) with an average age of 50 years. This group received a daily oral dose of 100 μg of L-selenomethionine. The characteristics of the study population are presented in Table 2.

Selenium pharmacokinetics of these three groups were monitored by measuring plasma selenium concentrations before supplementation, after 1, 2, and 3 months of continuous L-selenomethionine intake, and again at 1 and 2 months following cessation of supplementation. To avoid artificially elevated readings, selenium concentrations were measured 48 hours after the last oral dose in all cases.

All participants provided informed consent to have their blood selenium levels tested.

T a b l e 2

Characteristics of the study population in which long-term selenium pharmacokinetics were evaluated

	I group	**II group**	**III group**
Type of individuals	healthy	healthy	with Hashimoto's thyroiditis
Chemical form of selenium	selenomethionine	selenomethionine	selenomethionine
Dose of Se	100 μg/day	200 μg/day	100 μg/day
Number of participients	5	3	6
Average age (years)	43	37	50

2.2. *Sampling procedure and Se analysis by ETAAS*

The procedure was based on the method previously developed by Sherovski et al.[36] for the determination of selenium in plasma and blood samples. Blood samples were collected using a plastic intravenous cannula with an injection valve, and sodium citrate was used as an anticoagulant. Plasma was prepared by centrifuging the blood for at least 15 minutes at 2500 rpm. After centrifugation, 500 μl of the clear supernatant plasma was diluted 1:2 with a sample diluent (0.2 % Triton X-100 in 0.1 % HNO_3), and 10 μl of this mixture was added to the graphite furnace along with 5 μl of a palladium modifier.

The method was validated using the standard additions technique, yielding satisfactory results with recoveries ranging from 98.25 to 102.65 %. The precision of the method ranged from 1.55 % to 2.63 %.

Selenium content was determined by injecting each sample three times into the graphite furnace, which was operated under the conditions specified in Table 3. A Varian SpectrAA 640Z Zeeman electrothermal atomic absorption spectrometer (ETAAS), equipped with a GTA-100 graphite furnace and a PSD-100 autosampler (Varian, USA), was used.

Pyrolytically coated graphite tubes served as atomizers. A Varian selenium hollow cathode lamp was employed, and measurements were performed at a wavelength of 196.0 nm. Argon was used as a protective gas, and 10 μl of each sample was injected into the graphite furnace. The instrumental parameters utilized for selenium quantification via Zeeman ETAAS are listed in Table 3. Peak height was used for quantification.

T a b l e 3

Optimal analytical parameters for selenium determination using Zeeman ETAAS

Parameter	Se
Wavelength	196.0 nm
Lamp current	10.0 mA
Calibration mode	Absorbance, peak height
Background correction	Zeeman
Drying	
Temperature	85; 95; 120ºC
Time	5; 40; 10 s
Pyrolysis	
Temperature	1100 °C
Ramp time	5 s
Hold time	30 s
Atomization	
Temperature	2500 °C
Ramp time	0 s
Hold time	3 s
Cleaning	
Temperature	2500 °C
Time	2 s
Gas	Argon

2.3. *Reagents*

All reagents and standards were of analytical grade. The stock standard solution for selenium (1000 µg/ml) was obtained from Solution Plus Inc. (USA). Working standard solutions that were prepared weekly by appropriate dilution were stored at 4 °C. The palladium matrix modifier solution (500 ppm) was prepared by diluting a palladium nitrate [$Pd(NO_3)_2$] solution containing 10 g/l of Pd (Merck, Darmstadt, Germany) in 20 % HCl (v/v) (Merck, Darmstadt, Germany). The sample diluent – nitric acid at a concentration of 0.2% (v/v), and the corresponding detergent solution, also at 0.2% (v/v), were prepared by diluting trace-pure concentrated nitric acid (65%, w/w) (Merck, Darmstadt, Germany) and Triton X-100 (Merck, Darmstadt, Germany), respectively. Double-distilled water with a conductivity of 0.3 µS/cm was used for all procedures. All disposable devices were rigorously cleaned before use by briefly immersing them in hot concentrated nitric acid, washing with tap water and detergent, and rinsing twice with double-distilled water.

3. RESULTS AND DISCUSSION

In order to investigate the pharmacokinetics of selenium, a series of tests were conducted to determine its absorption and excretion times, as well as the plasma concentrations achieved at different doses. Selenium pharmacokinetics – specifically its absorption and plasma concentration, were examined over both a short-term period of 48 hours and a long-term period of three months, followed by a two-month washout phase. The studies were carried out using two daily doses: 100 µg and 200 µg, administered in the form of either organic selenium (L-selenomethionine) and inorganic selenium (sodium selenite).

3.1. *Pharmacokinetics of selenium over 48 hours*

Based on the obtained results, the average baseline plasma selenium concentration in individuals from the first group was 39.95 ± 2.23 µg/l. Two hours after ingestion of 100 µg of selenium as L-selenomethionine, the plasma selenium concentration began to rise, reaching 48.08 ± 3.13 µg/l. The maximum concentration was observed 6 hours post-ingestion, at 62.55 ± 2.43 µg/l. These findings indicate that elevated plasma selenium concentrations are achieved and maintained between 6 and 8 hours after intake.

Selenium excretion was observed beginning 8 hours after ingestion. After 48 hours, the plasma selenium concentration remained 13.4 % above the baseline value. The results are illustrated in Figure 1.

In the second group of individuals, who were orally administered a single dose of 100 µg of selenium as sodium selenite (Na_2SeO_3), the plasma selenium concentration followed a trend similar to that observed in the first group, although absorption was approximately 10 % lower. The average plasma selenium concentration in this group was 40.48 ± 2.59 µg/l. Maximum absorption of 57.58 ± 3.67 µg/l was reached 6 hours after ingestion, and after 48 hours, the selenium level was only 4% higher than the baseline concentration. A detailed graphical representation is shown in Figure 2.

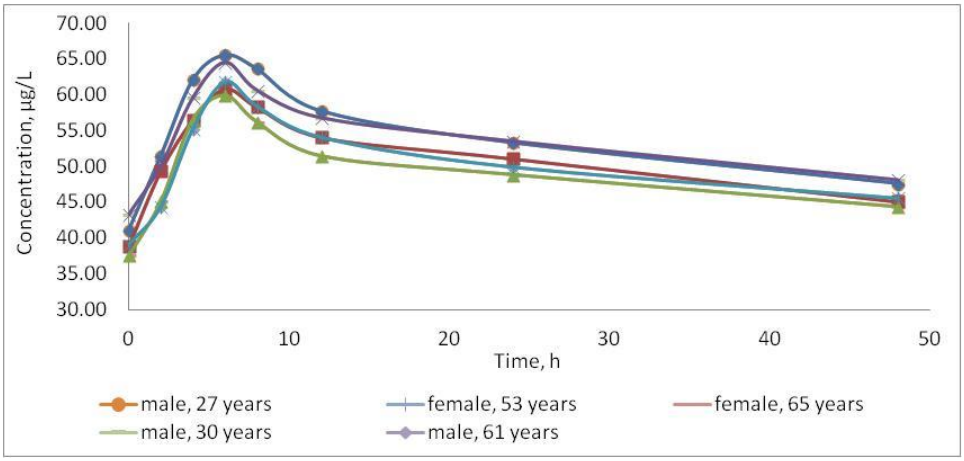

Fig. 1. Graphical representation of selenium pharmacokinetics over 48 hours following a single dose of 100 µg of selenium as L-selenomethionine

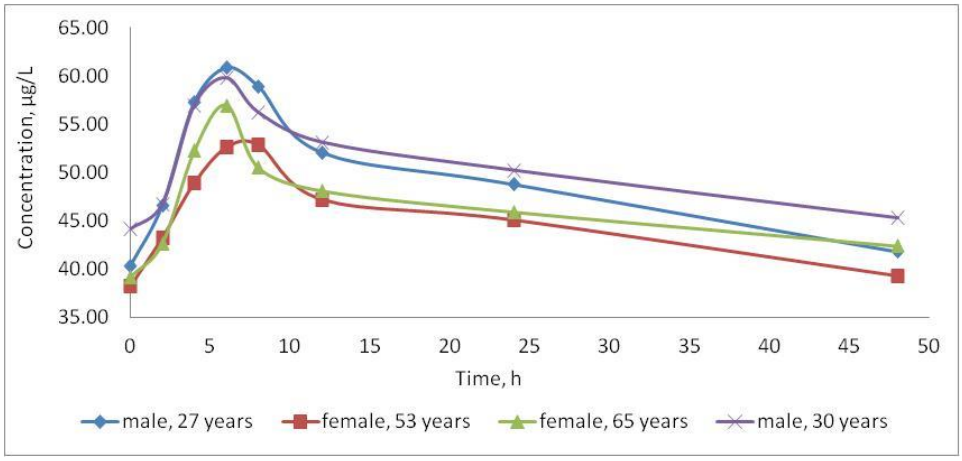

Fig. 2. Graphical representation of selenium pharmacokinetics over 48 hours following a single dose of 100 µg of selenium as sodium selenite

The results obtained from the third group of individuals, who were supplemented with 200 µg of selenium as L-selenomethionine, showed the same increasing and decreasing trends as observed in the two previous groups. As expected, the selenium concentration in this group was higher than in the other groups due to the higher dose of selenium. The average baseline concentration (pre-supplementation) was 41.20 ± 3.56 µg/l. Plasma selenium levels began to rise 2 hours after ingestion, with the maximum concentration of 80.83 ± 3.51 µg/l reached at 6 hours (Fig. 3). Similar to the first group, the highest concentrations were observed between 4 and 8 hours, after which the levels began to decline. After 48 hours, the selenium concentration remained 21 % above the baseline, reaching 52.98 ± 4.68 µg/l.

Based on the 48-hour pharmacokinetic results, it can be concluded that L-selenomethionine is better absorbed than sodium selenite. To ensure meaningful comparison between different forms of selenium, tablets containing the same amount of elemental selenium – regardless of the chemical form, were used. Specifically, tablets containing 100 µg of elemental selenium in the form of sodium selenite correspond to 230 µg of sodium selenite, while tablets with 100 µg elemental selenium in the form of L-selenomethionine contain 250 µg of L-selenomethionine.

L-selenomethionine is a naturally occurring form of selenium that is incorporated into proteins during translation. For this reason, most commercially available dietary supplements provide selenium in the form of selenomethionine (SeMet). SeMet is directly utilized in the SeMet cycle for protein synthesis. Selenium from SeMet also serves as a precursor for the synthesis of selenocysteine (SeCys), which is essential for the formation of selenoproteins.

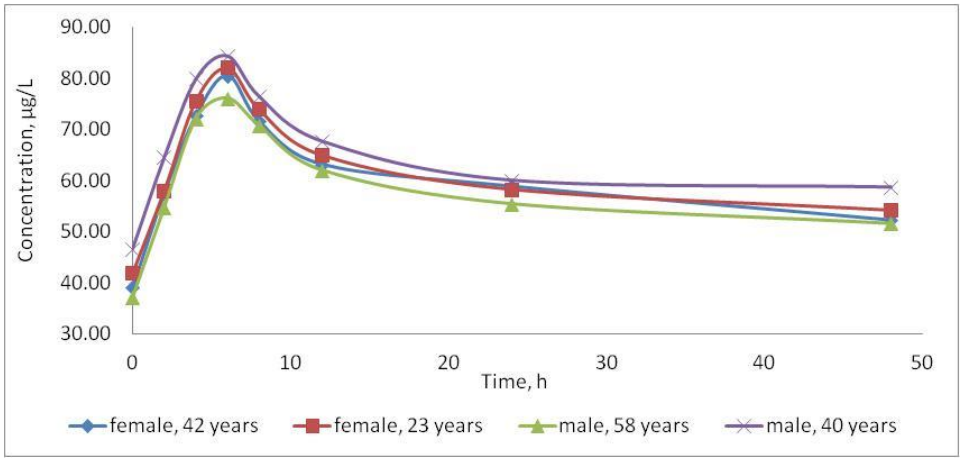

Fig. 3. Graphical representation of selenium pharmacokinetics over 48 hours following a single dose of 200 µg of selenium as L-selenomethionine

Other selenium compounds – including inorganic forms such as selenite and selenate, as well as organic forms like glutathione selenide, selenodiglutathione, and selenized triglycerides, are metabolized to hydrogen selenide (H_2Se). H_2Se is a key intermediate in the biosynthesis of SeCys-tRNA(Ser)SeCys and selenoproteins.[3] The structure of various selenium compounds and their metabolic precursors are illustrated in Figure 4.

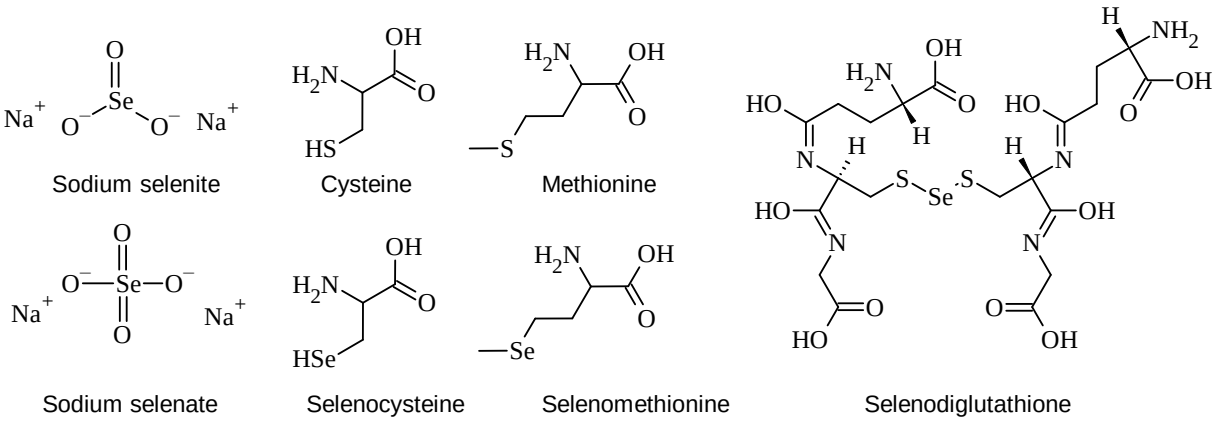

Fig. 4. Structural representations of various selenium compounds and their biochemical precursors

In addition to the chemical form in which selenium is consumed as a dietary supplement, previous studies have shown that several individual factors – such as baseline selenium levels, age, alcohol consumption, smoking, and hormone therapy, significantly influence selenium absorption and pharmacokinetics.[37,38]

One study on the bioavailability of L-selenomethionine found that a single tablet increased plasma selenium levels by approximately 10 % after 3 hours and 7 % after 12 hours. Doubling the dose initially slowed absorption but resulted in a peak concentration at 6 hours that was 16 % above baseline and remained elevated for 24 hours. Prolonged administration of the doubled dose led to a significant 32% increase from baseline, indicating a sustained elevation in blood selenium levels. Pharmacokinetic modeling revealed a half-life of approximately 19 hours and demonstrated a linear relationship between dose and bioavailability. These conclusions were based on plasma selenium concentrations measured using hydride generation atomic fluorescence spectroscopy.[31]

In present study, high absorption and slow excretion of selenium in the form of L-selenomethionine were observed, consistent with findings reported in the literature.[31,32] One likely reason for individual differences in selenium absorption is the timing of selenium intake relative to meals. Research has shown that, aside from its chemical form, one of the most important factors influencing selenium absorption is its concentration in plasma. Studies indicate that the body's selenium content plays a crucial role in regulating the homeostatic metabolism of ingested selenium,[39] likely due to the body's adaptation to varying intake levels.[40]

The results indicate that excretion begins after the eighth hour and that selenium concentrations in plasma remains elevated even 48 hours after supplementation. This sustained elevation is likely due to selenium binding to proteins or being stored in the liver and muscles. These conclusions are supported by a selenium kinetics study by Bügel et al.,[41] in which participants ingested a high single dose of 327 mg of the stable selenium isotope ^{77}Se. The study found that selenium levels in the body remained elevated even 14 days after supplementation, suggesting the possibility of enterohepatic recirculation. It was found that a significant portion selenium passing through the liver (46 %) returns to the intestine.[42]

Although selenium concentrations in urine and feces were not monitored in this study, other research has shown that selenium is primarily excreted through these routes.[40] Additionally, Bügel and coworkers[41] found that higher excretion occurred within the first 24 hours after ingestion of ^{77}Se, followed by a decline to low levels. A similar trend was observed for fecal excretion, with high levels in the first 24 hours and relatively elevated levels continuing between 48 and 72 hours post-ingestion.

A kinetic model for selenomethionine in the body was also proposed by Patterson et al.,[43,44] who suggested that selenomethionine undergoes recirculation, passing through the liver, pancreas, and peripheral tissues multiple times before being

excreted. Further supporting this model is the detection of labelled ^{77}Se in feces up to two weeks after ingestion.

3.2. *Pharmacokinetics of selenium after a 3-month intake*

As short-term pharmacokinetic studies have shown that selenomethionine is better absorbed than sodium selenite, long-term pharmacokinetic studies were conducted exclusively using varying does of selenomethionine. The results, shown in Figure 5, indicate that the average plasma selenium concentration in individuals from the first group – who received 100 µg/day of selenium as selenomethionine – was 39.60 ± 2.24 µg/l prior to supplementation. After one month of supplementation, the concentration increased to 48.96 ± 3.19 µg/l. Following two and three months of continuous supplementation, the concentrations were 50.71 ± 3.47 µg/l and 52.55 ± 3.45 µg/l, respectively.

These findings suggest that plasma selenium concentration increases significantly after the first month of supplementation, while the rate of increase becomes less pronounced during the second and third months.

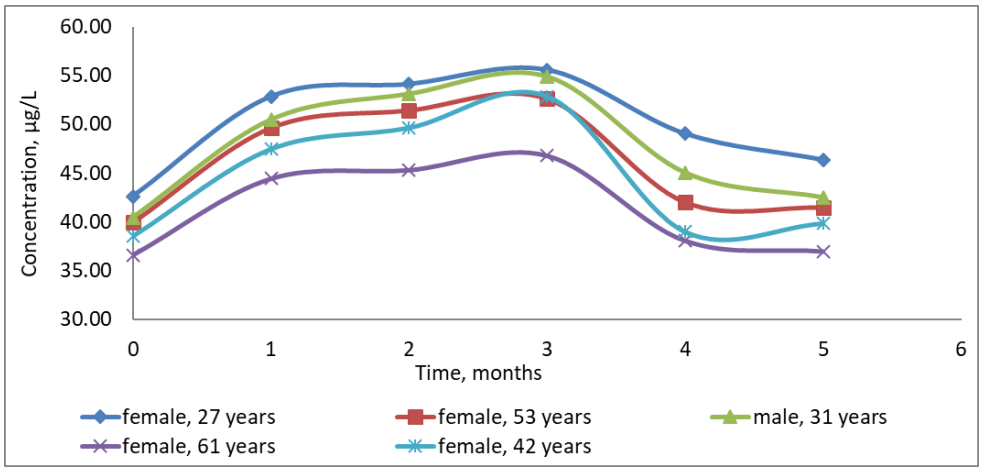

Fig. 5. Graphical representation of selenium pharmacokinetics during a 3-month supplementation period with 100 µg/day of selenium as selenomethionine, followed by a 2-month post-supplementation phase.

On the other hand, plasma selenium concentration significantly decreased one month after supplementation was discontinued. Specifically, one month after stopping supplementation, the selenium concentration dropped to 42.62 ± 4.51 µg/l, only 7 % above the initial concentration of 39.60 ± 2.24 µg/l. Two months after discontinuation of the 100 µg/day selenomethionine supplementation, the plasma selenium concentration had nearly returned to baseline, measuring just 4 % above the initial value.

In the second group, which received 200 µg/day of selenium as selenomethionine, the trends in plasma selenium concentration – both the increases during supplementation and decreases afterward, were similar to those observed in the first group. The average plasma selenium concentration in the individuals in this group was 42.03 ± 3.45 µg/l prior to supplementation. After one month of supplementation, the concentration increased to 55.56 ± 4.61 µg/l. Following two and three months of continuous supplementation, the concentrations were 58.34 ± 5.11 µg/l and 60.23 ± 4.51 µg/l, respectively. Selenium concentration rose significantly after the first month, with smaller increases in the subsequent months. After 1 month, the concentration increased by 24 % and after 2 and 3 months, it rose by 27 % and 30 %, respectively, compared to the initial level (Fig. 6). As expected, plasma selenium concentrations in this group were higher due to the increased dose of selenomethionine, although the average baseline concentration before supplementation did not differ significantly from that of the first group.

In the second group of participants, plasma selenium concentration also significantly decreased one month after supplementation ended. At that point, the concentration remained approximately 18 % above the initial level, while two months after discontinuation, it was only 11 % above baseline. These results suggest that supplementation with 200 µg/day of selenium in the form of selenomethionine significantly increases plasma selenium levels, and that the elevated concentrations persist longer after supplementation ends.

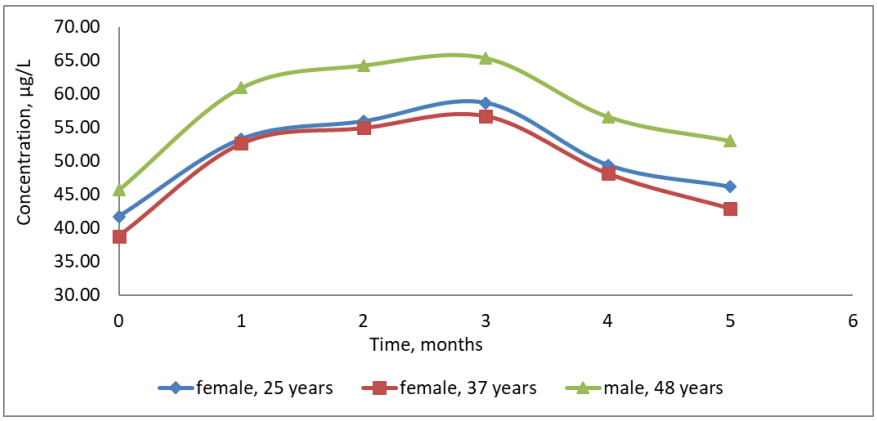

Fig. 6. Graphical representation of selenium pharmacokinetics during a 3-month supplementation period with 200 µg/day of selenium as selenomethionine, followed by a 2-month post-supplementation phase

These findings are consistent with existing literature on long-term selenium kinetics. According to Clark et al.,[45] plasma selenium concentration increases significantly during the initial months of long-term selenomethionine supplementation and reaches a plateau after 8 – 9 months. They also observed that this plateau is maintained even after 9 years of continuous supplementation.

It is important to note that, at the studied doses of selenomethionine, plasma selenium concentrations did not approach toxic levels (400 µg/l) during the observation period. However, caution is warranted, as prolonged intake of high selenium doses may lead to adverse effects.

Based on these results, definitive conclusions about selenium bioavailability cannot be drawn, as bioavailability largely depends on the conversion of absorbed selenium into its biologically active form and its retention in tissues. Nevertheless, it can be assumed that elevated plasma selenium concentrations may facilitate a more rapid transformation into the active form.

3.3. *Pharmacokinetics of selenium in patients with autoimmune thyroiditis*

Based on the results from healthy individuals, it can be concluded that selenomethionine is better absorbed than sodium selenite, and that plasma selenium levels increase significantly with an oral intake of 200 µg/day of selenomethionine compared to 100 µg/day.

Although the increase plasma selenium concentration in more pronounced with 200 µg/day than with 100 µg/day, we recommend 100 µg/day of selenomethionine as the optimal supplementation dose. This recommendation is based on several considerations. First, supplementation with 200 µg/day results in a 30 % increase in plasma selenium concentration, while 100 µg/day yields an increase of approximately 25 %. This suggests that a substantial improvement can be achieved with the lower dose, minimizing exposure to unnecessarily high selenium levels.

Additionally, most commercially available selenium supplements are formulated as 100 µg tablets, making them more convenient to use. This also avoids the psychological burden of taking multiple tablets at once or spreading them throughout the day. Finally, using the lower dose reduces the risk of side effects associated with high selenium intake, such as nausea, vomiting, and hair loss.

To investigate the pharmacokinetics of 100 µg selenium in the form of selenomethionine over a 48-hour period in patients diagnosed with Hashimoto's thyroiditis, six women with an average age of 59 years were included in the study. The results are presented in Figure 7.

Based on the obtained results, it can be concluded that there is no significant difference in the absorption and excretion of selenium between patients diagnosed with Hashimoto's thyroiditis and healthy individuals. In this group, serum selenium levels increased rapidly following oral administration of selenomethionine, indicating good absorption of the supplement. The rise in concentration began 2 hours after ingestion, with peal levels of 59.86 ± 3.73 µg/l reached at 6 hours. Selenium concentrations remained elevated compared to baseline even 48 hours after intake. These findings suggest that Hashimoto's thyroiditis does not impair selenium absorption.

Notably, the initial serum selenium concentration in this group was 35.35 ± 7.13 µg/l, which is lower than that observed in healthy individuals. The reduced baseline may be linked to inflammatory responses and increased activity of selenoproteins,

which help counteract free radical production resulting from autoimmune attacks on the thyroid gland.[46]

There is limited data in the literature on selenium pharmacokinetics in patients with autoimmune thyroiditis. For example, a study by Duntas et al. reported that serum selenium levels increased rapidly after oral administration of selenomethionine in such patients, further supporting the conclusion of effective absorption.[19]

Long-term studies show that selenium concentrations increase significantly after the first month of supplementation, with smaller increases in subsequent months. Additionally, selenium levels decline markedly one month after supplementation ends and return to near-baseline levels after two months (Fig. 8).

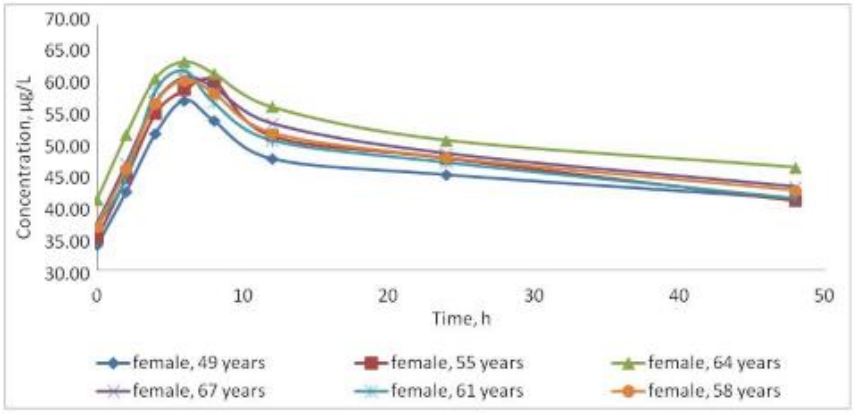

Fig. 7. Graphical representation of selenium pharmacokinetics over 48 hours following a single dose of 100 µg of selenium as selenomethionine in patients with autoimmune thyroiditis

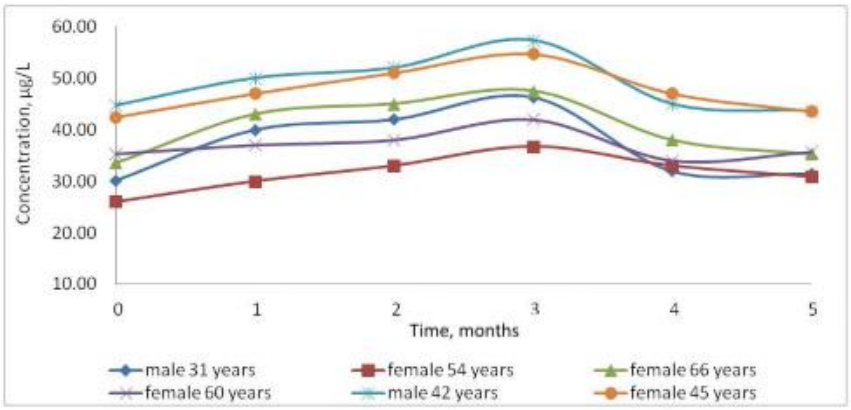

Fig. 8. Graphical representation of selenium pharmacokinetics during a 3-month supplementation period with 100 µg/day of selenium as selenomethionine, followed by a 2-month post-supplementation phase in patients with autoimmune thyroiditis

4. CONCLUSION

Selenium, an essential trace element, holds significant pharmacological importance due to its wide range of biological effects. Addressing selenium deficiency or excess has become a global health priority. This study highlights the value of selenium supplementation, particularly for individuals living in regions with selenium-deficient soils and food sources.

Understanding selenium metabolism is crucial, as it varies depending on the chemical form of selenium ingested and an individual's baseline selenium status. Pharmacokinetic analyses provide valuable insight into selenium's bioavailability and the potential risk of adverse events following supplementation.

The results demonstrate a rapid increase in plasma selenium levels after oral intake of selenomethionine, indicating efficient absorption of this organic form. Short-term studies show a 30 % increase in plasma selenium levels with 200 µg/day supplementation and a 25 % increase with 100 µg/day, both of which remain elevated for up to 48 hours post-ingestion.

Long-term supplementation leads to a significant rise in plasma selenium levels during the first

month, followed by a more gradual increase in subsequent months. However, after supplementation is discontinued, selenium levels decline rapidly, underscoring the complexity of selenium bioavailability.

Optimal supplementation appears to be achievable with 100 μg/day of selenium in the form of selenomethionine. This dosage results in a meaningful increase in plasma selenium levels while minimizing the risk of adverse effects. Moreover, this dose aligns with most commercially available supplements, simplifying adherence and reducing the likelihood of side effects.

Importantly, no significant differences in selenium absorption and excretion were observed between patients with Hashimoto's thyroiditis and healthy individuals. Although patients with Hashimoto's had lower baseline serum selenium levels, their absorption remained unaffected, suggesting that the disease does not impair selenium uptake.

While definitive conclusions about selenium bioavailability cannot yet be drawn – since it depends on the conversion of adsorbed selenium into biologically active forms and its retention in tissues, the data suggest that selenomethionine is rapidly converted into active forms following supplementation.

Overall, these findings underscore the importance of adequate selenium intake for maintaining health, particularly in selenium-deficient regions, while also emphasizing the need for careful dosing to avoid potential adverse effects.

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