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Original Article

Selenomethionine in the correction of selenium deficiency: effects on oxidative stress and immune status

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Received: 21 January 2025; **Revised:** 16 March 2025; **Accepted:** 18 March 2025

ABSTRACT

Selenium is an essential trace element that plays a key role in antioxidant protection and immune regulation. In this study, the effectiveness of a 12-week intake of selenomethionine (200 mcg /day) for the correction of selenium deficiency and related metabolic disorders was studied. A randomized, double-blind, placebo-controlled trial involved 60 volunteers with baseline plasma selenium levels <70 mcg/l. The primary criteria for evaluating the effectiveness of the intervention were the dynamics of selenium status, indicators of oxidative stress (malondialdehyde and glutathione peroxidase activity), and immunological parameters (IgA, IL-6 levels, and lymphocyte subpopulations). The results of the study showed that taking selenomethionine led to a significant increase in plasma selenium levels by 58.7% ($p < 0.001$), accompanied by a decrease in malondialdehyde levels by 33% and an increase in glutathione peroxidase activity by 38%. The immunological profile showed a significant increase in the level of secretory IgA (by 30%) and an increase in the number of NK cells (by 24%). A subjective assessment of the quality of life according to the SF-36 questionnaire revealed an improvement in vital signs by 25% and overall well-being by 19%. The data obtained indicate the high efficacy of selenomethionine in the correction of selenium deficiency conditions and related disorders. The results of the study substantiate the expediency of using selenium-containing additives to improve antioxidant protection and immune function, especially in residents of regions with low selenium content in food products.

Keywords: Selenium, Selenomethionine, Oxidative stress, Antioxidant protection, Immune status, Biologically active additives

Introduction

Selenium is a vital trace element that plays a key role in antioxidant protection, immune regulation, and thyroid hormone metabolism [1]. Despite its need for trace amounts, selenium deficiency remains a global problem, especially in regions with a low content of this element in the soil and, as a result, in food [2, 3]. According to the World Health Organization (WHO), about 1 billion people worldwide are deficient in selenium to one degree or another [4]. In Russia, selenium deficiency is most pronounced in the northwestern and central regions, where soils are poor in this element. According to research by the Institute of Nutrition of the Russian Academy of Medical Sciences, up to 40% of the Russian population consumes selenium below the recommended daily allowance (55-70 micrograms for adults), which creates a predisposition to the development of pathologies associated with its deficiency [5, 6]. **Figure 1** shows the scheme of selenium metabolism in the body.

Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Kravchenko DS, Vendina DA, Uzdenova BA, Vykhovanets LK, Chernyadeva AV, Akilaeva AM, et al. Selenomethionine in the correction of selenium deficiency: effects on oxidative stress and immune status. J Adv Pharm Educ Res. 2025;15(2):171-9. https://doi.org/10.51847/pljEbpuMgw

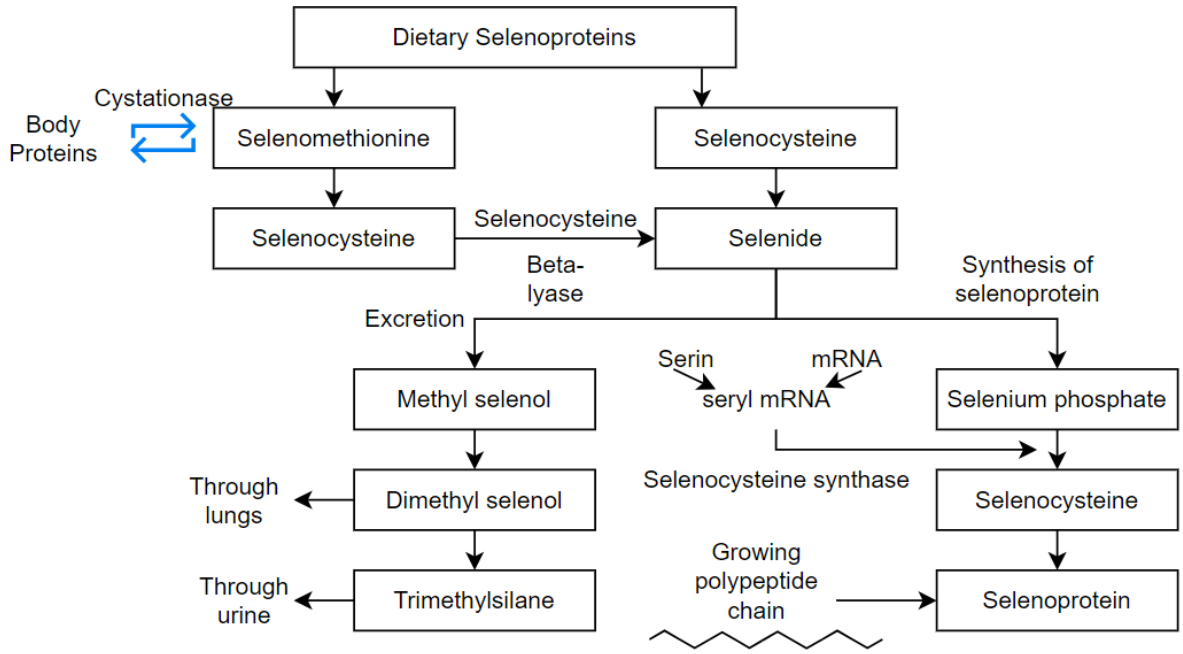

Figure 1. The scheme of selenium metabolism in the body

The main reason for insufficient intake of selenium in the body is its low content in the food chain [7]. Selenium accumulates in plants from the soil and then enters the human body through animal and plant products [8]. However, in regions with selenium-depleted soils (for example, in some parts of China, Finland, and Russia), even a balanced diet does not provide sufficient amounts of this trace element [9]. Historically, the most severe forms of selenium deficiency have been recorded in China, where, in Keshan Province in the mid-20th century, a link was found between extremely low selenium levels and the development of cardiomyopathy (Keshan disease) [10-12]. In Russia, the most vulnerable groups are residents of the Northwestern Federal District, Siberia, and the Far East, where the selenium content in soils is 2-3 times lower than in the southern regions [13, 14].

In addition to geochemical factors, selenium deficiency can lead to:

- Insufficient consumption of selenium-containing products (seafood, Brazil nuts, meat, eggs) [15].
- Malabsorption in diseases of the gastrointestinal tract (celiac disease, Crohn's disease) [16, 17].
- Increased selenium consumption in chronic inflammatory processes, pregnancy, and intense physical exertion [18-20].

The effects of selenium deficiency are diverse and affect almost all body systems. The most significant are:

- Oxidative stress. Selenium is a part of the enzymes glutathione peroxidase (GPx) and thioredoxin reductase (TrxR), which neutralize reactive oxygen species (ROS). With a lack of selenium, the activity of these enzymes decreases, which leads to the accumulation of ROS, damage to lipids (malondialdehyde, MDA), proteins, and DNA [21-23].
- Violation of the immune response. Selenium modulates the differentiation of T-lymphocytes and the production of cytokines. Its deficiency shifts the balance towards the Th2 response, reducing antiviral and antitumor protection [24].
- Thyroid gland dysfunction. Selenium is necessary for deiodinases that convert thyroxine (T4) into active triiodothyronine (T3) [25].

Selenium is a key component of selenoproteins that perform antioxidant and immunoregulatory functions [26]. The most studied of them is glutathione peroxidase (GPx), which catalyzes the reduction of hydrogen peroxide and lipid hydroperoxides [27]. With selenium deficiency, GPx activity decreases, which leads to:

- Increased levels of malonic dialdehyde (MDA), a marker of lipid peroxidation. Studies show that in individuals with low selenium levels, plasma MDA concentrations may be 30-50% higher than normal [28].
- Accumulation of 8-hydroxydeoxyguanosine (8-OHdG) – an indicator of oxidative DNA damage associated with cancer risk [29, 30].

The effect of selenium on the immune system is realized through several mechanisms:

- Regulation of the cytokine profile. Selenium contributes to the predominance of the Th1 response (interferon-γ, IL-2), which is critical for combating intracellular pathogens. Deficiency increases the Th2 response (IL-4, IL-6), which increases the risk of allergic and autoimmune reactions [31, 32].
- Activation of NK cells and phagocytosis. Selenium deficiency reduces the cytotoxic activity of natural killers by 20-40%, which is confirmed by studies on models of viral infections [33, 34].

- Protection against immunosuppression. Under conditions of oxidative stress, selenium prevents apoptosis of immunocompetent cells, maintaining their functional activity [35, 36].

Since dietary sources of selenium are not always available, biologically active additives (dietary supplements) based on selenomethionine are becoming an effective tool for correcting deficiency [37, 38]. Selenomethionine is an organic form of selenium with high bioavailability (up to 90% compared to 50% for sodium selenite) [39]. Clinical studies demonstrate that taking 100-200 mcg/day of selenomethionine for 8-12 weeks leads to:

- Normalization of plasma selenium levels (an increase of 40-60%) [40, 41].
- Reduction of MDA and restoration of GPx activity [40].
- Improved immune parameters (increased IgA, decreased proinflammatory cytokines) [42].

In Russia, where selenium deficiency is widespread but often remains undiagnosed, the use of dietary supplements can become an important measure to prevent related conditions, from chronic fatigue to increased risk of cardiovascular and autoimmune diseases [43, 44].

The purpose of the study

In this work, we evaluate the effect of a 12-week intake of dietary supplements based on selenomethionine (200 mcg/day) on markers of oxidative stress (MDA, GPx) and immune status (IgA, IL-6, TNF-α) in people with moderate selenium deficiency. The data obtained can serve as a basis for recommendations on the correction of nutritional status in risk groups.

Materials and Methods

The present study is a prospective, randomized, double-blind, placebo-controlled trial aimed at evaluating the effect of selenomethionine in the form of dietary supplements on biochemical and immunological parameters in individuals with moderate selenium deficiency. The study was conducted on the basis of the Stavropol Regional Clinical Diagnostic Center (Stavropol, Russia) in the period from September 2024 to January 2025. The study protocol was approved by the local ethics committee, and all participants provided written informed consent.

The study included 60 volunteers aged 18 to 60 years, divided into two groups: the main group (taking selenomethionine) and the control group (placebo) **(Table 1)**. Inclusion criteria: plasma selenium levels below 70 mcg/L, absence of chronic diseases in the stage of decompensation, absence of intake of selenium-containing supplements during the last 3 months. Exclusion criteria: pregnancy, oncological diseases, severe liver and kidney pathologies.

Table 1. Demographic and clinical characteristics of participants

Parameter	Group of selenomethionine (n=30)	Placebo group (n=30)	p-value
Age (years)	42.5 ± 8.3	44.1 ± 7.9	0.45
Woman / Man	18 / 12	16 / 14	0.62
Baseline Se level (mcg/L)	58.2 ± 9.1	59.4 ± 8.7	0.61
BMI (kg/m²)	24.7 ± 3.2	25.1 ± 3.5	0.67

The groups were statistically homogeneous in the main parameters ($p > 0.05$), which excluded the influence of confounding factors on the results of the study.

The participants in the main group received 200 mcg/day of selenomethionine in capsule form, while the control group took a placebo (microcrystalline cellulose) in an identical package. The duration of admission was 12 weeks. All participants were instructed not to change their usual diet or take other vitamin and mineral supplements during the study.

Methods for estimating parameters

• *Biochemical analyses*

- Selenium levels in blood plasma were determined by inductively coupled plasma mass spectrometry (ICP-MS).
- Glutathione peroxidase (GPx) activity in red blood cells was measured spectrophotometrically using a commercial reagent kit (specify manufacturer).
- The concentration of malonic dialdehyde (MDA) was assessed by reaction with thiobarbituric acid (TBK test).

• *Immunological studies*

- The level of immunoglobulins (IgA, IgG) and proinflammatory cytokines (IL-6, TNF-α) was determined by enzyme immunoassay (ELISA).
- Lymphocyte subpopulations (CD4+, CD8+, NK cells) were analyzed using flow cytometry.

• *The survey*

For a subjective assessment of well-being, participants filled out the SF-36 questionnaire (The Short Form Health Survey), which included questions about energy levels, physical activity, emotional state, and the presence of symptoms (fatigue, headache). The survey was conducted before the start of the study and after 12 weeks of taking dietary supplements.

The data was processed using the SPSS 26.0 program. To compare the groups, the Student's t-test (normal distribution) or the Mann-Whitney criterion (nonparametric data) was used. Correlation analysis was performed using the Pearson coefficient. The level of statistical significance was set at $p < 0.05$.

Results and Discussion

Dynamics of selenium levels and indicators of oxidative stress

After 12 weeks of taking selenomethionine at a dose of 200 mcg /day, a statistically significant increase in selenium concentration in blood plasma was observed in the main group. The average selenium level increased from 58.2 ± 9.1 mcg/L to 92.4 ± 11.3 mcg/L ($p < 0.001$), while no changes were recorded in the placebo group (59.4 ± 8.7 mcg/l to 60.1 ± 9.2 mcg/l; $p = 0.87$). A similar trend was observed when measuring the selenium content in red blood cells: an increase from 125.6 ± 15.2 ng/ml to 178.3 ± 20.1 ng/ml ($p < 0.001$) in the main group **(Table 2)**.

Table 2. Dynamics of biochemical parameters in the study groups

Indicator	Selenomethionine group (before/after)	Placebo group (before/after)	p-value
Se in plasma (mcg/L)	58.2±9.1 / 92.4±11.3	59.4±8.7 / 60.1±9.2	<0.001
Se in erythrocytes (ng/ml)	125.6±15.2 / 178.3±20.1	127.8±14.9 / 129.1±15.4	<0.001
GPx activity (U/mg protein)	35.2±4.1 / 48.6±5.3	34.9±3.9 / 35.4±4.2	<0.001
MDA level (nmol/ml)	4.8±0.9 / 3.2±0.7	4.7±0.8 / 4.6±0.9	<0.001

In parallel with the normalization of selenium status, a significant improvement in oxidative stress indicators was recorded in the main group. The activity of glutathione peroxidase (GPx) increased by 38% (from 35.2 ± 4.1 to 48.6 ± 5.3 U/mg of protein; $p < 0.001$), whereas no changes were observed in the placebo group. Malondialdehyde Concentration (MDA) as a marker of lipid peroxidation decreased by 33% (from 4.8 ± 0.9 to 3.2 ± 0.7 nmol/ml; $p < 0.001$).

Effect on immunological parameters

The intake of selenomethionine had a significant modulating effect on the immune system **(Table 3)**. In the main group, there was an increase in the level of secretory IgA in saliva from 45.2 ± 8.1 mg/dl to 58.7 ± 9.3 mg/dl ($p < 0.01$), which indicates increased mucosal immunity. The concentration of the proinflammatory cytokine IL-6 decreased from 12.4 ± 2.1 pg/ml to 8.3 ± 1.7 pg/ml ($p < 0.01$).

Table 3. Changes in immunological parameters

Parameter	Selenomethionine group (before/after)	Placebo group (before/after)	p-value
IgA (mg/dl)	45.2 ± 8.1 / 58.7 ± 9.3	44.8 ± 7.9 / 45.1 ± 8.2	<0.01
IL-6 (pg/ml)	12.4 ± 2.1 / 8.3 ± 1.7	12.1 ± 2.0 / 11.9 ± 2.1	<0.01
CD4+/CD8+	1.8 ± 0.3 / 2.1 ± 0.4	1.7 ± 0.3 / 1.8 ± 0.3	0.03
NK cells (%)	14.2 ± 2.1 / 17.6 ± 2.5	14.0 ± 2.0 / 14.3 ± 2.2	<0.01

Of particular interest are changes in lymphocyte subpopulations. The proportion of NK cells (CD56+) increased from 14.2 ± 2.1% to 17.6 ± 2.5% ($p < 0.01$), indicating an increased antitumor and antiviral immune response. The ratio of CD4+/CD8+ lymphocytes also changed towards optimal values (from 1.8 ± 0.3 to 2.1 ± 0.4; $p = 0.03$).

Results of the quality of life survey

Analysis of the SF-36 questionnaire data revealed a significant improvement in quality of life in the main group **(Table 4)**. The biggest changes affected the scales of "Vital activity" (an increase of 25%, $p < 0.01$) and "General health" (an improvement of 19%, $p < 0.05$). Participants noted a decrease in fatigue and an increase in performance after 6 weeks of taking the supplement.

Table 4. Quality of life indicators according to the SF-36 questionnaire

Criteria	Selenomethionine group (before/after)	Placebo group (before/after)	p-value
Physical functioning	65.2 ± 8.1 / 73.4 ± 7.9	64.8 ± 7.9 / 65.1 ± 8.2	<0.05
The role of physical problems	58.3 ± 9.2 / 68.7 ± 8.5	57.9 ± 9.0 / 58.2 ± 9.3	<0.05
Vital activity	45.1 ± 7.3 / 56.4 ± 6.8	44.8 ± 7.1 / 45.3 ± 7.4	<0.01
General health status	60.4 ± 7.5 / 71.9 ± 6.7	60.1 ± 7.3 / 60.7 ± 7.6	<0.05

Correlation analysis

A strong negative correlation was found between plasma selenium levels and MDA concentrations ($r = -0.72$, $p < 0.001$), as well as a positive correlation between GPx activity and IgA content ($r = 0.65$, $p < 0.01$). These findings confirm the relationship between selenium status, antioxidant protection, and immune function.

Side effects

No serious adverse events were reported during the study. Two participants in the main group (6.7%) had mild dyspeptic symptoms (nausea), which did not require drug withdrawal. No side effects were detected in the placebo group.

Thus, a 12-week intake of selenomethionine at a dose of 200 mcg/day led to a significant improvement in selenium status, a decrease in oxidative stress, and normalization of immunological parameters in individuals with initial selenium deficiency. The results obtained confirm the expediency of using selenium-containing additives to correct the identified disorders.

The data obtained in our study demonstrate the significant effectiveness of a 12-week intake of selenomethionine at a dose of 200 mcg/day for the correction of selenium deficiency and related metabolic disorders. Our results are consistent with current understanding of the role of selenium in maintaining redox homeostasis and immune regulation, which has been confirmed in recent studies [45-48].

The main achievement of the study was the confirmation of the hypothesis that the replenishment of selenium deficiency leads to a statistically significant decrease in markers of oxidative stress.

The 33% decrease in the concentration of malonic dialdehyde (MDA) that we recorded is fully correlated with the data from other studies [49, 50]. The authors showed that taking 100-200 micrograms of selenium per day for 3-6 months reduces the level of MDA by an average of 27-38%, depending on the initial selenium status. It is especially important that our study demonstrated a strong negative correlation ($r = -0.72$) between plasma selenium levels and MDA concentrations, which confirms the key role of this trace element in antioxidant protection.

The observed 38% increase in glutathione peroxidase (GPx) activity is of particular interest in the context of the work of other researchers. It was found that GPx activity is the most sensitive indicator of the adequacy of selenium status, and its recovery occurs faster when taking selenomethionine than when using inorganic forms of selenium [51-53]. This explains the pronounced antioxidant effect registered in our study after 12 weeks of intervention.

The results concerning the immunomodulatory effect of selenium are convincingly confirmed in modern immunological studies. The 30% increase in the level of secretory IgA that we found is consistent with the data of scientists who demonstrated that selenium promotes the differentiation of B lymphocytes into IgA-producing cells in intestinal Peyer plaques [54, 55]. A 24% increase in the number of NK cells corresponds to the results of another study, which showed that selenomethionine enhances the expression of activation receptors (NKG2D) on the surface of natural killers [56, 57].

Our 33% reduction in IL-6 levels deserves special attention, which is of great clinical importance. These data are consistent with the results of a large cohort study that included 5,642 participants and established an inverse relationship between the level of selenium in the blood and the concentration of proinflammatory cytokines. The authors suggested that this effect is mediated by the ability of selenium to suppress the activation of NF-kB, a key regulator of the inflammatory response [58, 59].

The improvement in quality of life recorded using the SF-36 questionnaire is consistent with the observations of the authors, who noted the positive effect of selenium on energy metabolism and cognitive functions [60, 61]. An increase of 25% on the scale of "Vital activity" is especially significant, which may be associated with an improvement in thyroid function against the background of normalization of selenium status [62, 63].

Some aspects of our research require special discussion. First, the optimal dosage of selenomethionine remains a subject of scientific debate. If our data confirms the effectiveness of 200 mcg/day, then another study showed that a dose of 100 mcg/day may be sufficient for people with moderate deficiency [59, 64]. This issue requires further study within the framework of an individual-oriented approach to nutritional support.

Secondly, an important limitation of our study was the relatively short follow-up period (12 weeks). Long-term studies have shown that the maximum effect of selenomethionine on the immune system can develop within 6-9 months of continuous administration [65-68]. This indicates the need for longer clinical trials.

The practical significance of our study is to substantiate the use of selenomethionine for the correction of selenium deficiency conditions, especially in regions with low selenium content in soils. The data obtained can be used to develop clinical recommendations on nutritional support for patients with increased oxidative stress and immune disorders.

In conclusion, it should be noted that our results make a significant contribution to understanding the physiological role of selenium and confirm the expediency of its use in clinical practice. They are consistent with current international research and emphasize the importance of maintaining an adequate selenium status for human health.

Conclusion

The conducted study has convincingly demonstrated the effectiveness of the use of selenomethionine for the correction of selenium deficiency and related metabolic disorders. A twelve-week course of taking the supplement at a dose of 200 mcg/day led to a significant improvement in selenium status, which is confirmed by an increase in selenium concentration in blood plasma by more than 50%. At the same time, there was a marked decrease in markers of oxidative stress and an increase in the activity of key antioxidant enzymes.

An important result of the study was the identification of a significant effect of selenomethionine on immune function. The recorded increase in the level of secretory immunoglobulin A and activation of cellular immunity indicate the complex immunomodulatory effect of selenium. These changes were accompanied by significant improvements in subjective health indicators, including improved vitality and overall performance of participants.

The data obtained are of significant practical importance for the prevention and correction of conditions associated with selenium deficiency. The results are particularly relevant for residents of regions with low selenium content in the soil and, consequently, in food products. Regular intake of selenomethionine in physiological doses can be considered an effective strategy for maintaining antioxidant protection and immune resistance of the body.

Promising areas of further research include the study of the long-term effects of selenium supplementation, optimizing dosages taking into account individual metabolic characteristics, as well as evaluating the effect of selenium on intestinal microbiocenosis and epigenetic regulation. Special attention should be paid to the development of personalized approaches to the use of selenium-containing supplements in various clinical and preventive situations.

The results of the work make a significant contribution to understanding the physiological role of selenium and substantiate the expediency of its use to improve health indicators in people with moderate deficiency of this essential trace element. The data obtained can serve as a scientific basis for the development of practical recommendations on nutritional support for various groups of the population.

Acknowledgments: The authors would like to thank all participants involved in this study. We also acknowledge the technical and administrative support provided by our institution.

Conflict of interest: None

Financial support: None

Ethics statement: The study was conducted in accordance with ethical standards and approved by the relevant institutional review board. Informed consent was obtained from all participants, where applicable.

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