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A Pilot Randomized Controlled Trial on the Effects of Selenium Supplementation Combined with Exercise on Body Composition and Selenium Bioactivity

Ensayo piloto aleatorizado y controlado sobre los efectos de la suplementación con selenio combinada con ejercicio físico en la composición corporal y la bioactividad del selenio

Alongkote Singhato[a,*], Somjet Khongkhon[a,b], Uraiporn Booranasuksakul[a], Narisa Rueangsri[a]

[a] Faculty of Allied Health Sciences, Burapha University, Chonburi, Thailand
[b] Faculty of Thai Traditional and Alternative Medicine, Ubon Ratchathani Rajabhat University, Ubon Ratchathani, Thailand
* alongkote@go.buu.ac.th

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ABSTRACT

Introduction: Selenium (Se) is a crucial trace element that plays an important role in fat metabolism and muscle building. Selenoproteins, such as glutathione peroxidase (GPx) and selenoprotein P (SEPP), are key examples of Se bioactive proteins that contribute to overall physiological processes. In addition, exercise is well known for its beneficial effects on body composition. However, limited data exist regarding the effectiveness of Se supplementation combined with exercise on changes in body composition and Se bioactivity. This pilot randomized controlled trial aimed to determine the effects of Se supplementation combined with exercise on body composition and Se bioactivity, as indicated by GPx and SEPP levels.

Methods: A total of 40 participants were recruited and allocated into two groups: an intervention group (n = 20) that received 200 µg of Se daily combined with regular exercise for 12 weeks, and a control group (n = 20) that performed regular exercise alone without Se supplementation for 12 weeks. Body composition was assessed using gold-standard and bioelectrical impedance methods, including BOD POD and InBody270. GPx and SEPP concentrations were determined using High-Performance Liquid Chromatography–Inductively Coupled Plasma Mass Spectrometry.

Results: The results showed that at the endpoint, participants in the intervention group had a significantly lower percentage of body fat compared with the control group ($p < 0.05$). In addition, fat-free mass, GPx activity, and SEPP concentrations in the intervention group were significantly higher than those in the control group ($p < 0.05$). There were no significant differences in dietary habits between groups, except for Se intake, which was significantly higher in the intervention group at the endpoint ($p < 0.05$).

Conclusions: Se supplementation combined with exercise was effective in improving body composition by reducing body fat percentage, increasing fat-free mass, and enhancing Se bioactivity compared with exercise alone.

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Keywords: bioactivity, body composition, exercise, selenium, selenoproteins

RESUMEN

Introducción: El selenio (Se) es un oligoelemento esencial que desempeña un papel importante en el metabolismo de las grasas y en la formación de masa muscular. Las selenoproteínas, como la glutatión peroxidasa (GPx) y la selenoproteína P (SEPP), son ejemplos clave de proteínas bioactivas dependientes del Se que contribuyen a diversos procesos fisiológicos. Además, es bien conocido que el ejercicio físico tiene efectos beneficiosos sobre la composición corporal. Sin embargo, existen datos limitados sobre la eficacia de la suplementación con Se combinada con ejercicio físico en los cambios de la composición corporal y la bioactividad del Se. Este ensayo piloto aleatorizado y controlado tuvo como objetivo determinar los efectos de la suplementación con Se combinada con ejercicio sobre la composición corporal y la bioactividad del Se, evaluada mediante los niveles de GPx y SEPP.

Métodos: Se reclutó un total de 40 participantes, que fueron asignados a dos grupos: un grupo de intervención (n = 20), que recibió 200 µg de Se al día junto con ejercicio físico regular durante 12 semanas, y un grupo control (n = 20), que realizó únicamente ejercicio físico regular durante 12 semanas sin suplementación con Se. La composición corporal se evaluó mediante métodos de referencia y de bioimpedancia eléctrica, incluyendo BOD POD e InBody270. Las concentraciones de GPx y SEPP se determinaron mediante cromatografía líquida de alta resolución acoplada a espectrometría de masas con plasma acoplado inductivamente (HPLC-ICP-MS).

Resultados: Los resultados mostraron que, al final de la intervención, los participantes del grupo de intervención presentaban un porcentaje de grasa corporal significativamente menor en comparación con el grupo control ($p < 0,05$). Además, la masa libre de grasa, la actividad de GPx y las concentraciones de SEPP fueron significativamente mayores en el grupo de intervención que en el grupo control ($p < 0,05$). No se observaron diferencias significativas en los hábitos dietéticos entre los grupos, excepto en la ingesta de Se, que fue significativamente mayor en el grupo de intervención al final del estudio ($p < 0,05$).

Conclusiones: La suplementación con Se combinada con ejercicio físico fue eficaz para mejorar la composición corporal al reducir el porcentaje de grasa corporal, aumentar la masa

libre de grasa y potenciar la bioactividad del Se en comparación con la práctica de ejercicio físico sin suplementación.

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Palabras clave: bioactividad; composición corporal; ejercicio físico; selenio; selenoproteínas.

HIGHLIGHTS

- Selenium supplementation combined with exercise significantly reduced body fat percentage compared with exercise alone
- Combined intervention significantly increased fat-free mass and improved body composition
- Selenium supplementation markedly enhanced GPx and SEPP concentrations, indicating improved selenium bioactivity
- Changes in selenium metabolism suggest alterations in selenoprotein synthesis and redox regulation

INTRODUCTION

Selenium (Se) is a vital trace element that plays an important role in many human physiological functions [1]. Se deficiency can lead to complications such as immunological impairment, some types of cancer, hypertension, and other disorders [2]. The recommended Se intake for adults is 55 µg/day, whereas individuals with serum Se concentrations below 40–70 µg/L are considered Se deficient, which is possibly caused by inadequate Se intake [3]. The major biological activity of Se is its incorporation into several selenoproteins that are essential for supporting normal physiological functions. Glutathione peroxidase (GPx) and selenoprotein P (SEPP) are examples of the main Se-dependent proteins that play vital roles in immune system enhancement, metabolic support, and reduction of oxidative stress [4]. Although Se deficiency is relatively rare, previous studies have shown that Se supplementation to promote Se bioactivity, particularly GPx and SEPP, is necessary to improve health status among certain populations and to prevent serum selenoprotein levels from falling below optimal ranges [5]. Such suboptimal levels may increase the risk of complications, including autoimmune diseases, cancers, heart failure, endothelial dysfunction, and other non-communicable diseases (NCDs) [6]. In addition, Se supplementation may improve body composition by supporting fat metabolism and stimulating lean body mass synthesis [7], which are key factors in maintaining good health and quality of life throughout the lifespan.

It is well known that regular exercise is strongly recommended for overall health. Efficient circulation, weight control, and enhancement of immune function are examples of the health benefits of exercise [8]. According to current guidelines, 150–300 min of moderate-intensity or 75–150 min of vigorous-intensity physical activity throughout the week, is recommended for generally healthy individuals [9]. In addition to its role in promoting optimal body composition, which is an important factor in maintaining ideal health status , regular exercise has also been reported to enhance immune function by stimulating biomarkers involved in antioxidant defense and Se homeostasis, such as GPx and SEPP [10]. However, there are still limited data on the effectiveness of Se supplementation combined with exercise on changes in body composition and selenium bioactivity, primarily due to the need for advanced mass

spectrometry and analytical techniques to determine selenoproteins concentration in blood. Therefore, this study aimed to determine the effects of Se supplementation combined with exercise on changes in body composition and Se bioactivity, specifically GPx and SEPP, compared with exercise alone.

METHODS

Ethics

The study protocol was approved by the Institutional Review Board of Human Research Ethics, Burapha University (Approval No. IRB1-101/2568). All participants provided written informed consent prior to participation. The trial was registered at the Thai Clinical Trials Registry (TCTR20250818002).

Design

This study was a 12-week pilot randomized controlled trial designed to evaluate the effects of selenium (Se) supplementation combined with exercise on body composition and Se bioactivity compared with exercise alone.

Sampling

A total of 40 participants were recruited using convenience sampling. Sample size was estimated with consideration of dropout rates. Eligible participants were healthy Thai men and women aged 19–50 years. Inclusion criteria: healthy adults aged 19–50 years, no history of food allergies, and willingness to participate. Exclusion criteria: use of medications or dietary supplements, oral or swallowing impairments, and disabilities or underlying diseases.

Interventions

The participants in the intervention group were asked to follow the protocol: Se supplementation (200 µg/day as selenomethionine; Swanson®, North Dakota, USA). Participants were instructed to take the supplement once daily after a main meal, independent of the timing of exercise sessions, to ensure consistency and minimize gastrointestinal discomfort. Exercise program was assigned. Briefly, participants performed aerobic exercise 3–5 sessions per week (frequency), with each session lasting 30–60 minutes (time), including activities such as brisk walking, jogging, or cycling (type). Exercise intensity

was prescribed at 50–85% of maximal heart rate (HRmax) and was continuously monitored using a wearable smartwatch (Xiaomi Mi Band 6). Heart rate data were used to ensure participants remained within the target zone, and intensity was adjusted individually as needed throughout the intervention period. Progression was implemented by gradually increasing exercise duration and/or intensity based on participant tolerance and performance. Participants were initially instructed and periodically supervised by the research team, with ongoing self-monitoring during the 12-week intervention. For control group, they were asked to follow protocol: Exercise only (same protocol) Exercise included aerobic activities (walking, jogging, cycling) at 50–85% HRmax for 12 weeks. Compliance monitored via LINE application and activity logs. The adherence rates of exercsie (both 2 groups) and supplement intake (only intervention group) were 70 and 75%, respectively.

Measurements

Body composition were determined using BOD POD (COSMED Inc., Rome, Italy) and InBody270 (InBody Co., Seoul, South Korea). For the BOD POD assessment, participants wore light, tight-fitting clothing and a swim cap, and the device was calibrated before each session according to the manufacturer's instructions. Participants then underwent the measurement in a seated position inside the chamber, and body fat percentage was obtained from the device output. For the InBody270 assessment, participants stood barefoot on the analyzer and held the hand electrodes according to the standard operating procedure after device calibration. Skeletal fat-free mass and related body composition variables were obtained directly from the device output. These procedures have now been described more clearly in the Methods section to improve transparency and reproducibility. In this study, the BOD POD was used as the primary reference method for body composition assessment. The device provided measurements including percentage of body fat, thoracic gas volume, and additional derived parameters such as total body fluid, fat-free mass, basal metabolic rate, and total energy requirement. Among these, body fat percentage was considered the principal outcome derived from the BOD POD. The InBody270 was used to obtain mineral-related body composition data, specifically body weight by mineral content.

Biochemical analyses in blood samples were analyzed using HPLC-ICP-MS (Thailand National Institute of Metrology). The following biomarkers were quantified GPx (U/g) and SEPP (mg/L). All measurement were performed at baseline (week 0) and endpoint (week 12).

Participants were instructed to fast overnight for at least 8 hours prior to all measurements. All assessments were conducted in the morning to minimize diurnal variation. Dietary intake was assessed using a 3-day food record at final week. Nutrient intake was calculated using nutrient analysis software, INMUCAL for Nutrients version 4.0, developed by the Institute of Nutrition, Mahidol University, Thailand.

Randomization

In this study, participants were assigned to either the intervention or control group using a simple random allocation procedure. Specifically, participants were asked to draw a concealed allocation label (intervention or control) from a container, ensuring that assignment was random at the individual level. To maintain equal group sizes (n = 20 per group), a restricted allocation approach was applied such that once one group reached its target sample size, the remaining participants were assigned to the other group. Allocation concealment was maintained by using identical, non-transparent labels placed in a closed container, preventing participants and researchers from predicting group assignment prior to selection.

Standardization

For standardization on dietary habits, participants were instructed to maintain habitual diet throughout study, record 3-day dietary intake during week 11, avoid additional supplements, and fasting blood samples were collected at baseline and week 12.

Order Effects

All measurements were conducted in the same order at baseline and endpoint to minimize procedural variability.

Statistical analyses

Data on sex and education level were presented as percentages. Continuous variables, including body mass index (BMI), body composition parameters, and GPx and SEPP concentrations, were expressed as mean ± standard deviation (SD). Independent t-tests were used to compare mean differences between the intervention and control groups, while paired t-tests were performed to evaluate within-group changes from baseline to the endpoint. Effect sizes were calculated using Cohen's d. Additionally, estimation statistics were performed using Gardner–Altman plots to visualize mean differences and 95% confidence intervals. All statistical analyses were conducted using Predictive Analytics Software Statistics (SPSS Inc., Chicago, IL, USA), version 25.0. A two-tailed *p*-value < 0.05 was considered statistically significant.

RESULTS

Regarding the background characteristics of the participants, both groups consisted of females, with no significant difference in mean age. In addition, participants had a normal BMI, and most held a bachelor's degree as their highest level of education. No significant differences in participant characteristics were found between the groups (Table 1).

Table 1. Background characteristics of the participants

Characteristics	Control group (n=20)	Intervention group (n=20)	p value
Sex			
Male, n (%)	7 (35)	5 (25)	0.73[a]
Female, n (%)	13 (65)	15 (75)	
Age (year), mean (SD)	24.45 (3.33)	24.70 (3.40)	0.24[b]
BMI, mean (SD)	22.16 (2.97)	21.27 (2.29)	0.29[b]
Educational level			
Bachelor's degree, n (%)	16 (80)	12 (60)	0.30[a]
Graduate's degree, n (%)	4 (20)	8 (40)	

[a]Fisher's exact test, [b]Independent t-test

The effects of Se supplementation combined with exercise, compared with exercise alone, are presented in Table 2. The results revealed that at the endpoint (week 12), participants in the intervention group had a body fat percentage of 20.25%, which was significantly lower than that of the control group (22.15%) ($p < 0.05$). In addition, fat-free mass in the intervention group (22.18 kg) was significantly higher than in the control group (20.44 kg) at the endpoint ($p < 0.05$). Furthermore, GPx and SEPP concentrations in the intervention group at the endpoint were 58.62 U/g and 5.88 mg/L, respectively, which were significantly higher than those in the control group (42.84 U/g and 2.89 mg/L, respectively) ($p < 0.05$). In addition, estimation plots (Figure 1A–D) demonstrated consistent between-group differences at endpoint. The intervention group showed lower body fat percentage and higher fat-free mass, GPx, and SEPP compared with the control group, with confidence intervals not crossing zero, indicating robust effects.

Table 2. Body compositions and Se bioactivity of the participants

Body composition and Se bioactivity	Baseline		Endpoint		Cohen's d for control	Cohen's d for intervention
	Control	Intervention	Control	Intervention		
Percentage of body fat, mean (SD)	22.98 (2.70)	22.30 (3.29)	22.15 (2.87)	20.25 (2.46)*.^	0.29	0.70
Total body fluid (L), mean (SD)	32.93 (3.52)	33.85 (3.33)	32.11 (4.25)	33.42 (2.72)	0.21	0.14
fat-free mass (kg), mean (SD)	19.72 (3.57)	20.19 (2.96)	20.44 (2.82)^	22.18 (2.55)*.^	-0.22	-0.72
Mineral weight (kg), mean (SD)	2.59 (0.29)	2.67 (0.36)	2.64 (0.41)	2.84 (0.27)	-0.14	-0.53
Basal metabolic rate (kcal), mean (SD)	1,826.50 (211.50)	1,830.00 (224.79)	1,858.20 (202.42)	1,849.60 (188.03)	-0.15	-0.09
Total energy requirement (kcal), mean (SD)	2,186.90 (358.13)	2,100.80 (268.47)	2,426.60 (285.86)^	2,491.80 (131.01)^	-0.73	-1.85
Thoracic gas volume (L), mean (SD)	3.10 (0.23)	3.18 (0.25)	3.16 (0.25)	3.25 (0.17)	-0.24	-0.32
GPx as Se (U/g), mean (SD)	43.63 (3.38)	42.48 (4.14)	42.84 (2.45)	58.62^ (4.45)	-3.75	-1.87
SEPP as Se (mg/L), mean (SD)	2.96 (0.57)	2.74 (0.41)	2.89 (0.50)	5.88^ (0.98)	-4.18	-2.09

* Significant differences between groups at endpoint were determined using an independent t-test at $p < 0.05$

^Significant differences within groups compared with baseline were determined using a paired-sample t-test at $p < 0.05$

Percentage of body fat was estimated via BOD POD, while fat-free mass was estimated via BIA.

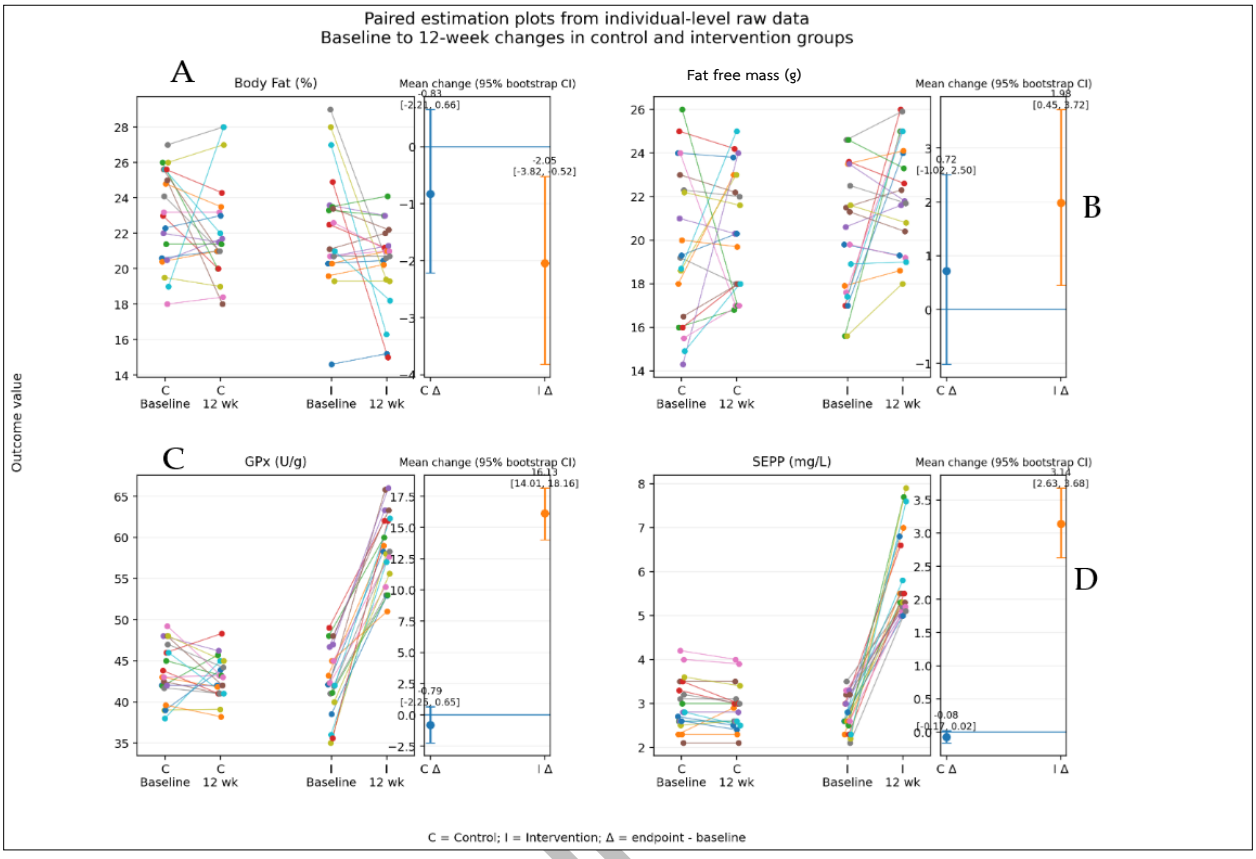

Figure 1. Gardner–Altman estimation plots showing mean differences between intervention and control groups at endpoint. (A) Body fat percentage, (B) fat-free mass, (C) GPx, and (D) SEPP. Points represent mean differences (intervention minus control), and error bars indicate 95% confidence intervals. The horizontal line at zero represents no difference between groups.

For dietary habits of participants, the results indicated that there were no significant differences between the groups, except for daily Se intake. Participants in the intervention group who received Se supplementation had a significantly higher Se intake than those in the control group ($p < 0.05$) (table 3).

Table 3. Dietary habits of participants.

Nutrients consumed	Control group (n=20)	Intervention group (n=20)	p value
%kcal distributed from carbohydrate, mean (SD)	58.70 (4.30)	56.85 (5.29)	0.27
%kcal distributed from protein, mean (SD)	13.65 (2.43)	14.00 (2.38)	0.59
%kcal distributed from fat, mean (SD)	27.65 (4.80)	29.15 (5.89)	0.42
Amount of estimated daily Se intake, mean (SD)	80.85 (16.65)	281.50 (16.32)	<0.05*

*Significant differences between groups were determined using an independent t-test at $p < 0.05$

DISCUSSION

Regular exercise is well acknowledged for supporting various health outcomes. Previous studies have focused on the benefits of exercise in promoting optimal body composition through enhanced body fat metabolism and stimulation of muscle building[11,12]. In the present study, although participants in the control group who performed exercise alone did not show a reduction in percentage body fat and had lower fat-free mass compared with the intervention group at the endpoint, their fat-free mass was significantly improved compared with baseline. These results support previous findings that exercise can promote lean body mass development in humans[13,14]. Previous studies have demonstrated that Se plays a crucial role in the human immune system primarily through its incorporation into selenoproteins, such as GPx, thioredoxin reductases (TrxR), and SEPP. These selenoproteins regulate cellular redox balance, thereby protecting immune cells from oxidative damage during activation and proliferation[15]. Adequate Se status modulates redox-sensitive signaling pathways, including nuclear factor-κB (NF-κB), leading to controlled inflammatory responses and reduced cytokine overproduction. In addition, Se supports both T- and B-cell function, enhances

antibody production, and contributes to effective antiviral defense, collectively promoting optimal immune competence[16].

Furthermore, Se contributes to body fat metabolism and fat-free mass maintenance mainly through its effects on redox regulation, mitochondrial function, and endocrine signaling[17]. As a component of selenoproteins such as GPx, SEPP, and TrxR, Se reduces oxidative stress, improves insulin sensitivity, and enhances lipid metabolism, thereby supporting reduced fat accumulation[18]. Se is also involved in thyroid hormone metabolism via iodothyronine deiodinases (DIO), which regulate energy expenditure and basal metabolic rate, influencing both fat oxidation and muscle protein turnover[19]. In skeletal muscle, adequate Se status protects myocytes from exercise-induced oxidative damage, supports mitochondrial efficiency, and facilitates muscle recovery and hypertrophy, ultimately contributing to increased fat-free mass and improved body composition[20,21]. These pathways, when combined with exercise, may explain the findings of this study, in which Se supplementation enhanced the effects of exercise on reducing percentage body fat and supporting fat-free mass in participants. In addition, the results are consistent with previous studies showing that GPx and SEPP levels at baseline were comparable to those reported in earlier investigations of these selenoproteins[22,23]. Furthermore, supplementation has been shown to increase selenoprotein concentrations, such as GPx and SEPP, thereby enhancing the biological activity of Se in the body[24-26]. These results can be explained by changes in selenocysteine concentrations may indicate alterations in Se utilization for selenoprotein synthesis, which plays a central role in antioxidant defense and redox homeostasis. Moreover, the observed variation in other selenometabolites may reflect adaptive changes in Se metabolic pathways, including Se storage, recycling, and detoxification processes, which together regulate Se availability and biological activity within the cell[27]. However, this study was used HPLC-ICP-MS to quantify GPx and SEPP as selenium-containing biomarkers, selenium speciation (e.g., selenocysteine and selenomethionine) was not directly measured in this study. Therefore, interpretations regarding changes in selenium metabolism should be made with caution.

Dietary habits, particularly energy distribution from macronutrients, did not differ between groups. However, participants in the intervention group who received Se supplementation had a significantly higher Se intake. Therefore, these results minimized potential confounding effects from differences in other nutrient intakes and allowed the effects of varying Se intake levels on study outcomes to be more clearly evaluated. Interestingly, although participants in the control group did not receive Se supplementation, their Se intake met the recommended intake of 55 µg/day[28]. This finding suggests that participants in this study were not at risk of Se deficiency, likely due to residing in coastal areas with abundant access to marine foods, which are rich sources of Se[29-31]. The limitations of this study include selenium speciation (including selenocysteine, selenomethionine, and other selenometabolites) was not quantified in the present analysis and should be investigated in future studies. In addition, the lack of assessment of additional selenoproteins, such as TrxR and DIO, which play important roles in regulating thyroid hormone activation and inactivation and, consequently, energy metabolism, body fat regulation, and muscle protein turnover[32]. Therefore, future studies are recommended to determine these selenoproteins to further elucidate the effects of Se supplementation combined with exercise. Moreover, studies with larger sample sizes and longer intervention periods are warranted to confirm these findings.

CONCLUSIONS

In conclusion, Se supplementation combined with exercise was effective in improving body composition by reducing body fat and increasing fat-free mass, as well as enhancing GPx and SEPP concentrations, thereby supporting Se bioactivity more effectively than exercise alone.

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AUTHORS' CONTRIBUTIONS

AS designed the study. AS, SK, UB and NR collected the data. AS sought funding. Data analysis and interpretation was performed by SK. AS, UB, and NR reviewed the results. Writing of the original draft was performed by AS and revisions of the manuscript by UB and NR. All authors approved the final version of the manuscript.

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CONFLICTS OF INTEREST

The authors state that there are no conflicts of interest when writing the manuscript.

DATA AVAILABILITY

Provision of data on request to the corresponding author.

PROTOCOL REGISTRATION NUMBER: TCTR20250818002

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