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The Effect of a Combined Training Program with Fenugreek and Green Cumin Supplementation on the Levels of Certain Inflammatory and Anti-Inflammatory Adipokines in Overweight Women

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ABSTRACT

Obesity in older adults can lead to numerous health problems, including cardiovascular diseases, diabetes, hypertension, and a reduced quality of life. These issues are exacerbated by decreased physical activity and metabolic changes associated with aging. Weight management in older adults is of great importance, as it can help prevent these health issues. Additionally, weight control can contribute to maintaining independence and improving the quality of life in older adults. Therefore, this study aimed to investigate the effect of a combined training program with fenugreek and green cumin supplementation on the levels of certain inflammatory and anti-inflammatory adipokines in overweight women. In a quasi-experimental study, 60 overweight older women were randomly assigned to six groups: combined training/placebo (n=16), fenugreek supplement (n=16), green cumin supplement (n=16), combined training/fenugreek supplement (n=16), combined training/green cumin supplement (n=16), and control (n=16). Participants performed the combined training protocol for 8 weeks, with three sessions per week. The fenugreek supplement group consumed two capsules of 335 mg daily, while the green cumin supplement group consumed two capsules of 25 mg daily. The results indicated that in the combined training/placebo ($P<0.001$), green cumin supplement ($P<0.001$), combined training/fenugreek supplement ($P<0.001$), and combined training/green cumin supplement ($P<0.001$) groups, the mean differences in resistin and visfatin levels between pre-test and post-test were significant ($P<0.05$). All four groups resulted in a reduction in inflammatory and anti-inflammatory adipokine levels. In the fenugreek supplement and control groups, no significant differences were found between pre-test and post-test mean values ($P>0.05$). Furthermore, post-hoc test results showed a significant difference in the combined training/green cumin supplement group compared to the other four experimental groups, with a significantly greater reduction observed ($P<0.001$).

Keywords: *Aging, Overweight, Adipokines, Fenugreek, Green Cumin*

1. Introduction

Reports from Iran indicate that nearly 50% of individuals (49% of men and 53% of women) in the 60-70 age group are either obese or overweight, with women having a higher proportion than men. Findings from studies conducted on national data in our country also show a significant increase in the prevalence of obesity among Iranian adults, with women being more affected due to physiological differences and lower physical activity levels than men (1, 2). Obesity is also a precursor to various non-communicable diseases such as type 2 diabetes, cardiovascular diseases, and fatty liver disease, among others. On the other hand, adipose tissue plays a central role in regulating energy homeostasis. This tissue exerts its regulatory effects through the secretion of hormones known as adipokines. Inflammatory hormones produced by adipose tissue are involved in the development of insulin resistance, obesity, and the increased risk of cardiovascular diseases. In contrast, anti-inflammatory adipokines, such as adiponectin and omentin, which promote insulin sensitivity, are reduced in these conditions. Adipose tissue, consisting of fat cells, connective tissue, nerve tissue, a network of blood vessels, and immune cells, not only responds to signals from other hormonal systems and the central nervous system but also influences various physiological functions by secreting a range of protein and non-protein factors (3). Exercise is a powerful non-pharmacological tool for reducing obesity and preventing overweight, and it has been shown to be effective in modulating insulin resistance. Given the relationship between visfatin and insulin resistance, exercise may reduce serum visfatin levels by affecting carbohydrate metabolism (4). Moreover, adiponectin is one of the adipokines secreted by adipose tissue, and its levels decrease with obesity and diabetes. Generally, its levels are lower in obese children and adults compared to other individuals (5). Additionally, adipose tissue, as an active endocrine tissue, plays a role in body weight regulation and, through the secretion of a variety of adipocytokines, contributes to metabolic and inflammatory profiles that explain the relationship between obesity, insulin resistance, and diabetes (6). Recently, a new adipocytokine named adipolin (CTRP12) has been identified. This anti-inflammatory cytokine is synthesized and secreted in adipose tissue and its levels decrease in conditions of obesity and diabetes. Furthermore, adipolin has been shown to improve insulin sensitivity. Adipolin circulates in two forms: intact (fCTRP12) and cleaved (gCTRP12) (7). Studies have shown that only the fCTRP12 isoform of adipolin improves insulin resistance. Therefore, any factor that affects the synthesis or cleavage of adipolin could reduce insulin sensitivity. For instance, insulin itself tends to break down fCTRP12. Thus, lowering insulin levels is an effective approach for improving adipolin function (8). Various therapeutic approaches have been suggested for controlling insulin in diabetes and reducing insulin resistance, with physical activity being one of the most important methods. Therefore, it is possible that exercise can influence the levels of hormones secreted by adipose tissue. Additionally, regular physical activity is an appropriate strategy for treating many metabolic disorders, including type 2 diabetes and obesity. Some of the beneficial effects of exercise are mediated through endocrine glands, including adipose tissue, which plays an important role in energy metabolism, body composition, and insulin resistance (9). Combined exercises (aerobic and resistance) can help reduce body fat and liver fat by increasing energy expenditure, improving fat oxidation, reducing subcutaneous fat, and promoting free fatty acid flow (10). Given that appropriate physical activity can have a significant impact on preventing diseases, their complications, and ultimately the mortality associated with them, a review of scientific literature on the relationship between obesity and physical activity indicates that performing both aerobic and resistance exercises can be effective in reducing the risk of obesity (11).

On the other hand, fenugreek has been used for many years as a substitute remedy for various pains and diseases (12). Today, it is more commonly used as a dietary supplement. The remarkable effects of fenugreek in the treatment of diabetes, blood sugar control, increasing milk production in breastfeeding mothers, and many other diseases cannot be overlooked. Fenugreek contains copper, antioxidants, choline, trigonelline, yamogenin, sarsasapogenin, and diosgenin, and these chemical components contribute to its medicinal properties (13). Studies have shown that fenugreek contains saponins, ginseng, and fiber, which can be effective in treating many diseases. Today, alongside physical activity, fenugreek supplements help lower blood cholesterol levels, particularly low-density lipoprotein (LDL) cholesterol, thereby reducing

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the risk of atherosclerosis, heart attacks, and strokes. Fenugreek is rich in fiber, which helps cleanse cholesterol from blood cells and arteries. By reducing cholesterol accumulation in blood vessels, the risk of blood clotting is also significantly reduced (14). Moreover, cumin (Cuminum cyminum) has been used as an anti-obesity, anti-convulsant, anti-epileptic, diuretic, and stomach tonic medicine. Its primary active component, cuminaldehyde, inhibits two enzymes, alpha-reductase and aldose reductase, involved in carbohydrate metabolism, which is thought to contribute to its anti-diabetic properties (15). Jafari and colleagues (2016) demonstrated in a study that cumin has a positive and significant effect on fasting glucose level (16)s, while in the study by Taghizadeh and colleagues (2014), no significant effect of cumin on fasting glucose was observed in overweight individuals (14). In the study by Morovati and colleagues (2017), the use of cumin did not have a statistically significant effect on blood glucose, anthropometric indices, or lipid profile (17). Given the beneficial effects of both fenugreek and cumin and the positive outcomes of physical exercise on obese and elderly individuals, the present study aims to investigate the effects of 8 weeks of supplementation with fenugreek and cumin, with and without combined exercises, on the levels of certain adipokines in elderly overweight women.

2. Methods and Materials

2.1. Population and Sample

This applied semi-experimental study was conducted involving elderly women from the retirement and senior citizen centers in Sanandaj, with an age range of 60 to 67 years and a body mass index (BMI) greater than 25 kg/m². Inclusion criteria for the study included being over 60 years old, non-smoker, no history of regular physical activity (30 minutes, 3 days a week) in the last 6 months, no use of medications that affect muscle amino acid metabolism (such as beta-blockers, beta-agonists, calcium channel blockers, and corticosteroids), no osteoporosis or related bone and joint problems, no severe mobility disorders, and no cardiovascular or respiratory conditions, or chronic diseases such as diabetes. Exclusion criteria included muscle injuries, inability to perform exercises, missing more than three training sessions, and withdrawal from the study due to personal reasons. Out of the initial 84 applicants, 17 were excluded for not meeting the inclusion criteria and 7 withdrew from the study. A total of 60 participants were randomly assigned to six groups: combined exercise/placebo (10 participants), fenugreek supplement (10 participants), green cumin supplement (10 participants), combined exercise/fenugreek (10 participants), combined exercise/green cumin (10 participants), and control (10 participants). During the course of the study, 1 participant from the exercise/placebo group, 2 participants from the exercise/fenugreek group, and 1 participant from the green cumin supplement group withdrew due to personal issues, leaving 56 participants to complete the study.

2.2. Exercise Protocol

The participants performed a 10-minute warm-up at the beginning of each session, including walking on a treadmill and stretching exercises, followed by a 5-minute cool-down with walking and stretching. To determine the intensity of aerobic exercise, each participant's target heart rate was calculated using the Karvonen method as follows: Resting Heart Rate + (Exercise Intensity Percentage × (Maximum Heart Rate - Resting Heart Rate)) = Target Heart Rate. Exercise intensity was controlled by heart rate. Additionally, the maximum leg press and chest press strength of the participants were assessed before and after the 8-week intervention using the standard 1RM test. The combined exercise protocol (aerobic/resistance) lasted for 8 weeks, with 3 sessions per week (exercise/placebo, exercise/fenugreek, and exercise/green cumin groups) at 16:30 on alternate days. The combined exercise groups performed both aerobic and resistance training simultaneously. Aerobic training consisted of 20 minutes of treadmill running at 55-65% of maximum heart rate, while resistance training included 5 stations at 55-65% of 1RM with 10-12 repetitions per set for 3 sets, with 60-second rest intervals between each set. After completing 3 sets, participants had 120 seconds of active rest before proceeding to the next station. The exercise stations included: chest press, leg press, front leg stretch, back leg press, and shoulder press.

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2.3. Measurements

To determine the sample size, G*Power software was used based on previous studies with a significance level of 0.05 and a statistical power of 0.80. Weight was measured without shoes and minimal clothing using a digital scale (made in China) with a precision of 100 grams. Height was measured using a non-elastic tape measure while participants stood against a wall. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m).

2.4. Blood Sampling

To measure blood indices, 5 milliliters of venous blood were drawn from participants after a 12-hour fasting period, 48 hours before the first session and 48 hours after the last session in the morning. The blood samples were centrifuged at 3500 rpm for 5 minutes, and the serum was separated and stored in microtubes at -70°C. Serum adiponectin levels were measured using a Biomedical Group Australia kit with a sensitivity of 0.14 picomoles per liter. Resistin and visfatin levels were measured using a Cusabio kit (China) with sensitivities of 0.80 ng/mL and 1.0 ng/mL, respectively. Serum Asprosine levels were measured using the ELISA method with a catalog kit (LS-F55600) from the United States. Lipocalin-2 levels were measured by the ELISA method and a Liosion reader (USA) using a ZLBio research kit (Germany). Serum adipolin levels were measured using a CUSABIO Human Orexin A ELISA kit (E08859h) from Japan.

2.5. Supplement Preparation and Consumption

Participants in the fenugreek supplement group consumed two 335 mg capsules (Glucorex B) containing dry fenugreek seed extract daily, one in the morning and one at noon. Participants in the green cumin supplement group consumed two 25 mg capsules daily, one in the morning and one at noon.

2.6. Data Analysis

Descriptive statistics, including frequency distribution, mean, and percentage, were used to describe the variables. To compare the differences in pre-test and post-test scores between groups, analysis of covariance (ANCOVA) was performed, followed by post-hoc LSD tests. A significance level of $p < 0.05$ was considered statistically significant.

3. Findings and Results

The variables of age, weight, height, body mass index (BMI), and other study variables were described based on central tendency and dispersion indices in Table 1.

Table 1

Mean and Standard Deviation of Age, Height, Weight, and BMI of Participants in the Six Groups

Variable	Exercise/Placebo	Fenugreek	Green Cumin	Exercise/Fenugreek	Exercise/Green Cumin	Control
Age (years)	63.01 ± 1.36	62.37 ± 1.38	62.72 ± 1.12	63.18 ± 1.28	63.46 ± 1.11	62.78 ± 1.58
Weight (kg)	Pre-test	72.47 ± 1.58	74.35 ± 2.24	73.29 ± 1.89	72.77 ± 2.78	73.59 ± 2.84
	Post-test	70.93 ± 1.16	74.28 ± 1.55	72.16 ± 2.15	70.52 ± 1.78	73.77 ± 2.77
	p = 0.04	p = 0.92	p = 0.04	p = 0.03	p = 0.002	p = 0.88
Height (cm)	162.60 ± 1.39	163.17 ± 1.82	164.68 ± 2.79	162.68 ± 1.84	163.29 ± 2.31	163.23 ± 1.79
BMI (kg/m²)	Pre-test	26.88 ± 0.76	26.42 ± 1.1	26.42 ± 1.1	27.08 ± 0.86	26.34 ± 0.76
	Post-test	25.75 ± 1.04	26.92 ± 0.79	25.92 ± 0.79	26.68 ± 0.76	25.35 ± 0.76
	p = 0.03	p = 0.72	p = 0.03	p = 0.03	p = 0.003	p = 0.93

Based on the results of within-group comparison tests, the mean levels of asprosine in the combined exercise/placebo, combined exercise/fenugreek supplement, and combined exercise/green cumin supplement groups significantly decreased ($p < 0.05$). The observed p-values in the exercise/placebo group ($p < 0.001$), exercise/fenugreek ($p < 0.0001$), and exercise/green cumin ($p < 0.001$) indicated significant differences in the mean asprosine levels between pre-test and post-test for all three groups; this means all three protocols led to a decrease in asprosine levels. No significant difference was found between pre-test and post-test mean values in the fenugreek supplement ($p = 0.65$), green cumin supplement ($p = 0.40$), and control ($p = 0.89$) groups (Figure 1).

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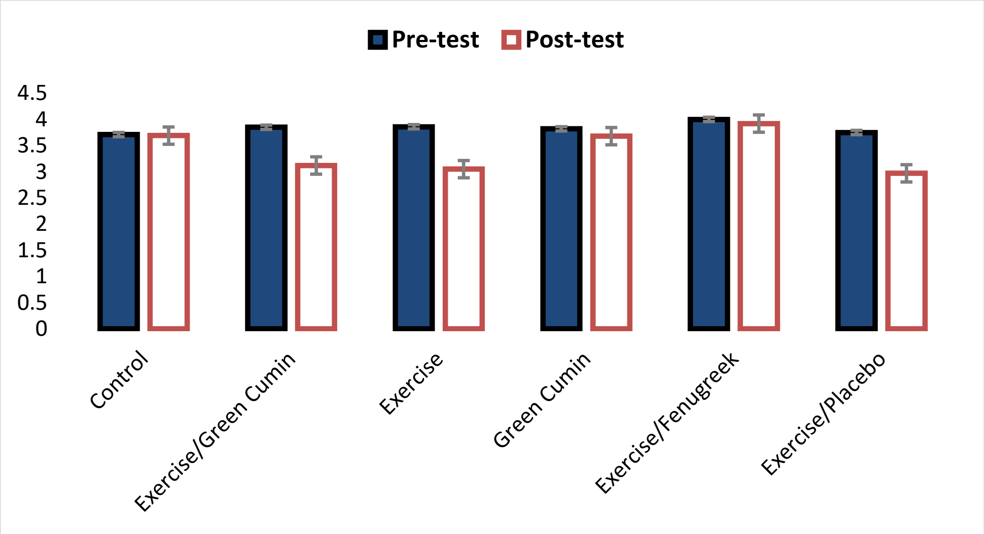
Figure 1

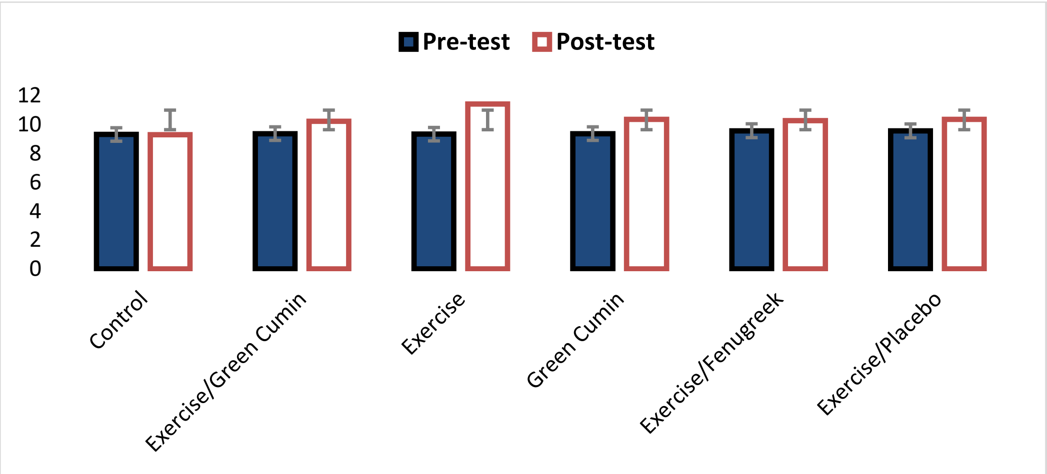
Changes in Pre-test and Post-test Asprosine Levels in Six Experimental Groups



Based on the results of within-group comparison tests, the mean levels of adiponectin in all five groups (combined exercise/placebo, fenugreek supplement, green cumin supplement, combined exercise/fenugreek supplement, and combined exercise/green cumin supplement) significantly increased ($p < 0.05$). The observed p-values in the exercise/placebo group ($p < 0.02$), fenugreek supplement ($p < 0.048$), green cumin supplement ($p < 0.04$), exercise/fenugreek supplement ($p < 0.0001$), and exercise/green cumin supplement ($p < 0.02$) showed significant differences in the mean adiponectin levels between pre-test and post-test for all five groups; indicating that all protocols led to an increase in adiponectin levels. No significant difference was found in the control group ($p = 0.96$) (Figure 2).

Figure 2

Changes in Pre-test and Post-test Adiponectin Levels in Six Experimental Groups



Based on the results of within-group comparison tests, the mean levels of adipolin in the combined exercise/placebo, combined exercise/fenugreek supplement, and combined exercise/green cumin supplement groups significantly increased ($p < 0.05$). The observed p-values in the exercise/placebo group ($p < 0.0001$), exercise/fenugreek (p

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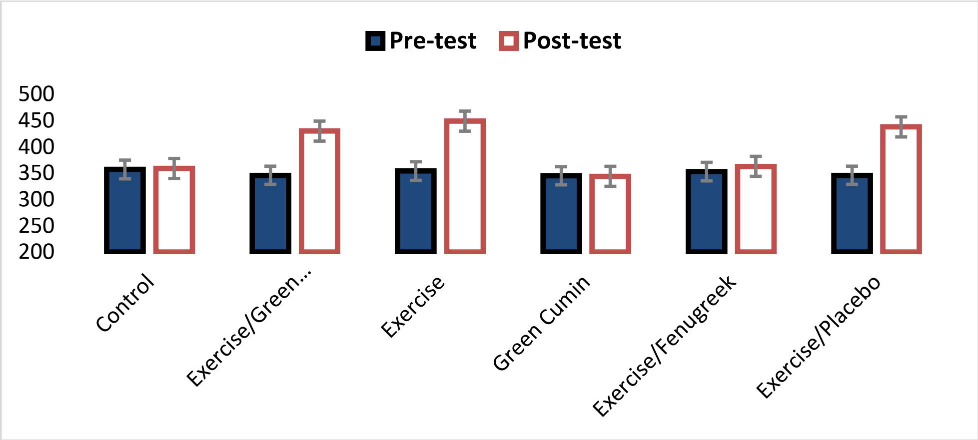
< 0.0001), and exercise/green cumin (p < 0.0001) indicated significant differences in the mean adipolin levels between pre-test and post-test for the three groups; this means that the protocols in these three groups, along with exercise, led to an increase in adipolin levels. No significant difference was found between pre-test and post-test mean values in the fenugreek supplement (p = 0.24), green cumin supplement (p = 0.94), and control (p = 0.71) groups (Figure 3).

Figure 3

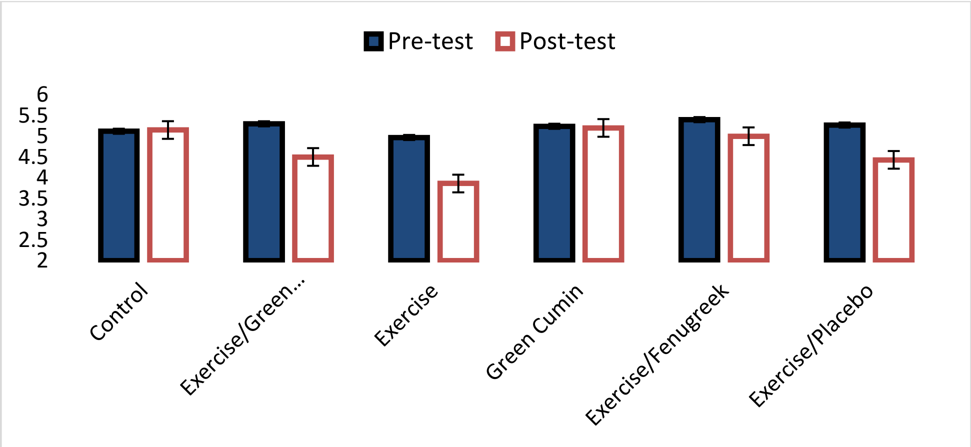
Changes in Pre-test and Post-test Adipolin Levels in Six Experimental Groups



Based on the results of within-group comparison tests, the mean levels of lipocalin in the combined exercise/placebo, combined exercise/fenugreek supplement, and combined exercise/green cumin supplement groups significantly decreased (p < 0.05). The observed p-values in the exercise/placebo group (p < 0.001), exercise/fenugreek (p < 0.0001), and exercise/green cumin (p < 0.001) showed significant differences in the mean lipocalin levels between pre-test and post-test for the three groups; meaning that all three protocols caused a reduction in lipocalin levels. No significant difference was found in the fenugreek supplement (p = 0.16), green cumin supplement (p = 0.83), and control (p = 0.89) groups (Figure 4).

Figure 4

Changes in Pre-test and Post-test Lipocalin Levels in Six Experimental Groups



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4. Discussion and Conclusion

A substantial body of scientific evidence indicates that certain hormones secreted by adipose tissue play a role in adipogenesis, energy metabolism, and inflammation. Previous research has focused on the impact of exercise on adipokines such as resistin, visfatin, and others (18, 19). The main findings of the present study showed that after completing the exercise regimen and green cumin supplementation, the levels of both adipokines investigated significantly decreased. Aging and obesity are involved in many mechanisms related to pathophysiological conditions; however, their synergistic effects may increase the likelihood of diseases such as type 2 diabetes and cardiovascular diseases, leading to higher mortality rates in older individuals (20). It has been reported that insulin contributes to the increase of inflammation and oxidative stress. In this context, previous research has demonstrated that obesity leads to insulin resistance and an increase in oxidative stress due to the infiltration and hypertrophy of intermuscular and intracellular adipocytes. This can, through fat toxicity, disrupt mitochondrial function and cause skeletal muscle degradation (21). Numerous studies have highlighted the increase in adiponectin following physical activity. In line with the present study's findings, Rostamzadeh et al. (2019) investigated the effects of 8 weeks of resistance training on adiponectin levels, insulin resistance, insulin sensitivity, and glycosylated hemoglobin in overweight men. The results showed that resistance training led to increased adiponectin levels and improved insulin sensitivity (21). In another study, Torabi et al. (2018) examined the effect of high-intensity interval training on adiponectin levels and insulin resistance in adolescents with attention-deficit/hyperactivity disorder. Their findings showed that 6 weeks of high-intensity interval training led to a significant increase in serum adiponectin levels in the experimental groups, while insulin resistance significantly decreased (22). Adiponectin plays a role in glucose and lipid homeostasis, thus contributing to the pathogenesis of insulin resistance. Moreover, adiponectin is recognized as an insulin-sensitizing hormone that works by reducing triglyceride content in the liver and muscle through increased AMPK activity and the expression of energy-consuming molecules. Therefore, this hormone has properties similar to exercise as it enhances glucose uptake in muscles and suppresses glucose production in the liver (23). Studies show that recombinant adiponectin administration in rodents results in increased glucose uptake, decreased plasma free fatty acids, increased fatty acid oxidation in muscles, and a reduction in hepatic glucose production. Additionally, it improves insulin sensitivity throughout the body. Mice with adiponectin deficiency show insulin resistance and glucose intolerance. Beyond its effects related to insulin sensitivity, this hormone may also alter insulin secretion in the pancreas within the body (24). On the other hand, in addition to being stimulated by these environmental actions, adiponectin has been shown to modulate food intake and energy expenditure during fasting (increased food consumption from glucose metabolism and decreased energy consumption) and refeeding (opposing effects) through its impact on the central nervous system (24). Changes in serum adiponectin levels have been shown to play a major role in the onset of obesity-related complications such as atherosclerosis and type 2 diabetes. However, multiple studies have demonstrated that circulating adiponectin levels are significantly reduced in the presence of obesity and in patients with cardiovascular diseases, with an inverse relationship between adiponectin levels and body mass index (BMI) (25).

Authors' Contributions

H. L. contributed to the conceptualization and design of the study, participant recruitment, and data collection. J. B. B. was responsible for developing the training protocol, supervising the intervention process, and interpreting the results. S. K. performed the statistical analysis, contributed to data interpretation, and manuscript drafting. E. E. assisted in supplement formulation, literature review, and ensured adherence to ethical guidelines. All authors contributed to the manuscript's revision, approved the final version, and take responsibility for its content and integrity.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

Data are available for research purposes upon reasonable request to the corresponding author.

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Declaration of Interest

The authors report no conflict of interest.

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Ethics Considerations

The study placed a high emphasis on ethical considerations. Informed consent obtained from all participants, ensuring they are fully aware of the nature of the study and their role in it. Confidentiality strictly maintained, with data anonymized to protect individual privacy. The study adhered to the ethical guidelines for research with human subjects as outlined in the Declaration of Helsinki. Ethical considerations included obtaining informed consent, ensuring confidentiality and anonymity, and avoiding any harm to participants (Ethical approval: IR.IAU.NAJAFABAD.REC.1401.184)).

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