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Anti-Inflammatory Effects of Garlic Consumption and Regular Exercise in Sedentary Overweight Individuals

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Abstract

Background: A sedentary lifestyle can result in chronic inflammation, which is a risk factor for Cardiovascular Disease (CVD). Lifestyle modifications, including physical activity and herbal supplements, may have health benefits.

Objectives: The present study aimed to investigate the effect of regular exercise and garlic consumption on some inflammatory biomarkers in sedentary overweight individuals.

Methods: Forty-four sedentary overweight male participants (20 - 30 years) were randomized to the following groups: Exercise + garlic (ES), exercise + placebo (E), garlic (G), and placebo (P). The training protocol included 20 - 45 minutes of walking/running at 60 to 75% of the maximum heart rate, three sessions per week for eight weeks. Participants consumed two capsules containing 500 milligrams of garlic powder or placebo (starch) per day. Before and 48 h after the exercise intervention and supplement administration, blood samples were collected to assess the hs-CRP and TNF-α serum levels. One-way ANOVA and Tukey's post hoc tests were used to analyze the data at a significance level of $P < 0.05$.

Results: A significant difference was observed between the groups regarding the hs-CRP and TNF-α levels after the experimental period ($P < 0.05$). There was a significant difference between EG and placebo groups ($P < 0.05$).

Conclusions: Based on the findings, garlic consumption, along with exercise training could exert anti-inflammatory properties in overweight subjects.

Keywords: Exercise, Inflammation, Garlic, hs-CRP, TNF-α

1. Background

Today, physical inactivity is getting increasingly widespread. In 2010, the World Health Organization (WHO) estimated approximately 3.2 million annual deaths due to a failure to engage in regular physical activity. A sedentary lifestyle is a major contributor to obesity and several diseases and a strong predictor of morbidity and mortality (1). It has been reported that sedentary individuals have elevated levels of inflammatory biomarkers. The C-reactive protein (CRP), for instance, increases due to physical inactivity. An elevation in the circulatory levels of CRP, TNF-α, and IL-6 contributes to cardiovascular disease (CVD), obesity, and insulin resistance. The adipose tissue is the prime origin of IL-6. This biomarker elevates due to fat accumulation and increases the hepatic release of CRP (2). As a marker of systemic inflammation, CRP is a stronger predictor of future cardiovascular events (3). Besides, IL-6 is thought to be a sensitive biomarker for chronic inflammation and a predictor of CVD and non-insulin-dependent diabetes in sedentary populations. A significant elevation in IL-6 and TNF-α is an accurate prognostic predictor of CVD, insulin, and all-cause mortality (4-6).

Lifestyle modification such as physical activity and healthy diet strategies potentially brings about health benefits to sedentary populations. Regular physical activity may favorably modulate inflammatory responses and immune system function as critical processes in the pathogenesis of CVD (7, 8). The effects of exercise training on inflammation and its biomarkers have been investigated in several studies and various results have been reported (9, 10). Several studies have reported an inverse relationship between inflammatory biomarkers, e.g., CRP, and cardiorespiratory fitness in men and women (10). Hewitt et al. (11) indicated that 12 weeks of moderate-intensity aerobic exercise reduced CRP levels in healthy middle-aged individuals. However, a discrepancy also exists in this regard as Zoppini et al. (12), reported that moderate-intensity aer-

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obic exercise for six months did not remarkably affect the CRP levels in the sedentary elderly or diabetic individuals.

Besides, dietary interventions may also alter the generation and release of inflammatory factors. The health benefits of garlic in humans have been claimed for decades. It has the potential to lower blood pressure, LDL cholesterol, triglyceride, and blood glucose (13-15). It may also exert anti-inflammatory properties and reduce pro-inflammatory cytokines such as IL-1B and TNF-α (16, 17). Su et al. (18) showed that 14 days of allicin supplementation reduced IL-6 levels after one session of physical exercise compared to a placebo group. However, Atkin et al. (19) did not support this finding and indicated that the consumption of aged garlic extract over four weeks had no significant effect on vascular inflammation, oxidative stress, and insulin resistance in adults with type 2 diabetes.

2. Objectives

Overall, reviewing the literature indicates a discrepancy in the effects of exercise and garlic on inflammatory indices. We hypothesized that combining exercise training and garlic supplementation would be more effective than either modification alone. In the present study, we aimed to investigate the effect of aerobic training and garlic supplementation on hs-CRP and TNF-α in sedentary overweight individuals.

3. Methods

3.1. Subjects

In this study, 44 young, healthy, inactive, and overweight volunteers were enrolled (Table 1). First, a complete description of the issue, aims, methods, benefits, and risks of participation was given to the subjects, and they filled out consent forms. The study procedures complied with the codes of the Declaration of Helsinki 1975, as revised in 2000 (available at http://www.wma.net/e/policy/17-c_e.html). The ethical procedure of the study was approved by the Ethics Committee of Tabriz University of Medical Sciences (2595) and the trial was registered with the trial ID UMIN000039566.

The inclusion criteria were a sedentary lifestyle, body mass index (BMI) > 25 kg/m^2, no history of participation in exercise programs, and age range of 20 - 40 years. The exclusion criteria included tobacco use, medical issues such as orthopedic problems, medicine, and supplement intake. All the participants were nonsmokers with no history of heart disease. They were all following a sedentary lifestyle, as confirmed by the Physical Activity questionnaire (PAQ). The subjects were excluded if they exercised more than one time per week for improving their health. The subjects were then simply randomized into the following groups: Exercise + garlic (EG, n = 11), exercise + placebo (EP, n = 11), garlic (G, n = 11), and placebo (P, n = 11). Simple randomization was applied in this study (Figure 1).

3.2. Study Design

The anthropometric parameters (height, weight, and BMI) were performed measured at the beginning and after the experimental period. In these sessions, blood samples were also collected in a fasting state. Subjects in the exercise groups underwent a supervised moderate-intensity aerobic exercise. The exercise program included walking/running on a treadmill at the intensity of 60% - 75% of HR max, 20 - 45 min/session, three sessions per week over eight weeks. The exercise load gradually increased from the beginning to the end. The participants also received supplements (two capsules each containing 500 mg allicin) or placebo (two capsules each containing 500 mg starch) throughout the study. All individuals were asked to follow their usual diets and avoid taking any supplements during the experimental period. Moreover, the participants were given a 24-h diet recall questionnaire to record their diets on the day preceding the first blood sample collection and they were asked to replicate it before the second blood sample collection.

3.3. Measurements

The BMI was calculated using a formula (weight (kg)/height^2 (m)). The skin folds were obtained using a Harpenden skinfold caliper on the right side of the body at the sites, including chest, abdominal area, and thigh. The body fat percentage was estimated by the Jackson Pollock formula. At baseline and 48 h after the experimental period, all subjects were required to attend the lab for blood sample collection after 8 - 10 h of overnight fasting. Blood samples were taken from the antecubital vein and immediately centrifuged at 3500 rpm for 10 min. Serum samples were then used to determine the concentration of hs-CRP (Monobind, USA) with the sensitivity of 0.014 μg/mL and TNF-α (Invitrogen, USA) with the sensitivity of 0.5 pg/mL via the ELISA method.

3.4. Statistical Analysis

The distribution of data was assessed for normality using the Shapiro-Wilk test. To determine the difference between the groups, the posttest data were subtracted from the pretest data (Δ) and then were analyzed using the one-way ANOVA statistical test. Tukey's post hoc test was used to determine the point of differences when ANOVA reached a significance level. Moreover, the paired *t*-test was used

Table 1. Mean ± Standard Deviation of Anthropometric Variables[a]

	Exercise + Garlic	Garlic	Exercise + Placebo	Placebo
Age, y	24.30 ± 1.8	23.9 ± 2.04	25.41 ± 1.53	23.69 ± 1.74
Weight, kg	77.76 ± 6.30	75.25 ± 7.10	73.51 ± 5.30	78.08 ± 7.74
Height, cm	176.49 ± 4.78	177.20 ± 6.17	177.39 ± 6.00	179.22 ± 8.59
BMI, kg/m^2	26.07 ± 2.74	25.70 ± 2.15	25.26 ± 2.51	26.09 ± 1.79

[a]Values are expressed as mean ± SD.

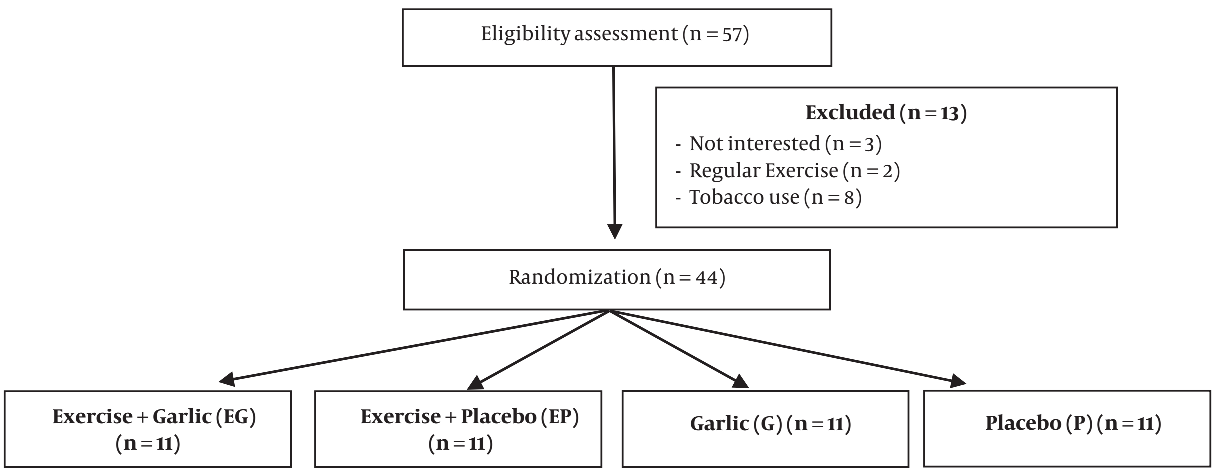

Figure 1. Participants' recruitment flow chart

to determine the changes from pretest to posttest in each group. The statistical significance was set at $P < 0.05$.

4. Results

The baseline characteristics of the subjects are presented in Table 1. The participants were matched and there was no significant difference between the groups at baseline ($P > 0.05$). Table 2 presents the mean ± SD of the variables at baseline (week 0) and after the experimental period (week 8).

The data analysis indicated no differences in the hs-CRP and TNF-α levels between the groups at baseline ($P > 0.05$). The BMI significantly decreased in the EG and EP groups from pretest to posttest with a significant difference between the groups ($F = 10.102$, $P = 0.001$). The post hoc analysis revealed that the EG and EP groups were significantly different from the placebo group ($P = 0.001$ and $P = 0.004$, respectively). We also observed a significant reduction in the hs-CRP levels in the EG and EP groups ($P = 0.013$ and $P = 0.001$), and one-way ANOVA reached the significance level ($F = 3.660$, $P = 0.02$) (Figure 2 and Table 2). Further analysis indicated that the hs-CRP levels were significantly lower in the exercise groups than in the placebo group ($P = 0.03$ and $P = 0.038$, respectively). Moreover, the TNF-α levels significantly decreased in the exercise groups from pretest to posttest ($P = 0.001$ and $P = 0.02$, respectively). One-way ANOVA reached the significance level for the TNF-α levels ($F= 2.976$, $P = 0.043$), and the post hoc analysis revealed a significant difference between the EG and placebo groups ($P = 0.039$) (Figure 3 and Table 2).

5. Discussion

In the present study, we investigated the effect of regular endurance training along with garlic consumption on some biomarkers of inflammation in sedentary overweight individuals. The results showed that exercise training combined with garlic supplementation significantly reduced the serum levels of hs-CRP and TNF-α. Garlic ingestion seems to have an additive effect on the reduction of inflammatory indices caused by exercise training. However, garlic ingestion had no remarkable effect on the hs-CRP and TNF-α levels, per se.

Regarding the effect of exercise on these biomarkers of inflammation, our finding is consistent with those ob-

Table 2. Mean ± Standard Deviation of Variables at Baseline and Posttest[a]

	Exercise + Garlic		Garlic		Exercise + Placebo		Placebo		P
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
Weight, kg	77.76 ± 6.30	75.54 ± 6.04	75.25 ± 7.10	76.10 ± 6.93	73.51 ± 5.30	71.67 ± 8.99	78.08 ± 7.74	77.89 ± 6.60	0.041
BMI, kg/m²	26.27 ± 1.21	25.44 ± 1.15	25.92 ± 1.33	25.89 ± 1.34	26.2116 ± 1.31	25.49 ± 1.35	25.45 ± 1.93	25.51 ± 1.89	0.001
Fat, %	19.94 ± 2.01	19.07 ± 2.18	19.95 ± 1.50	20.06 ± 1.47	18.86 ± 1.46	18.26 ± 1.30	20.28 ± 2.10	20.33 ± 2.18	0.001
hs-CRP, μg/mL	0.92 ± 0.6	0.60 ± 0.4*	0.81 ± 0.4	0.72 ± 0.4	1.05 ± 0.4	0.74 ± 0.4	0.91 ± 0.4	0.95 ± 0.4	0.02
TNF-α, pg/mL	1.81 ± 0.6	1.2 ± 0.6	1.88 ± 0.5	1.78 ± 0.6	1.92 ± 0.4	1.52 ± 0.4	1.9 ± 0.5	‘1.99 ± 0.5	0.0001

Abbreviations: BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein; TNF-α, tumor necrosis factors-alpha.
[a] Values are expressed as mean ± SD.

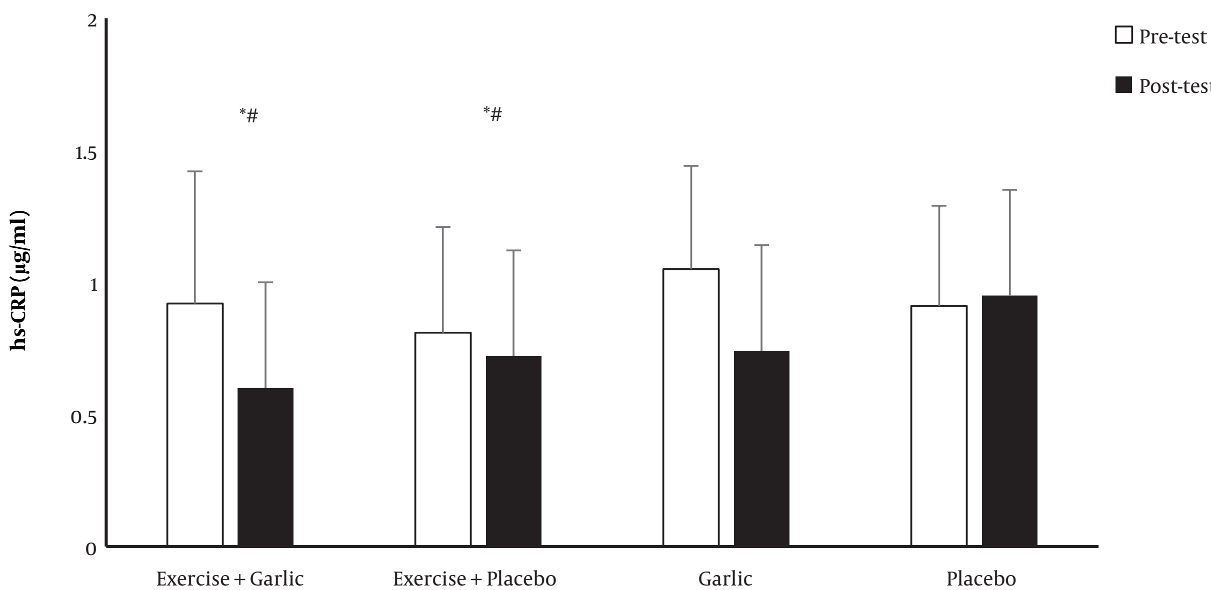

Figure 2. The hs-CRP levels (mean ± SD) from pretest to posttest in groups *, Significantly different from Pretest values ($P < 0.05$).

tained by Devries et al. (20), Jankord et al. (21), and Hewitt et al. (11). Devries et al. (20), reported that the serum levels of hs-CRP and the markers of oxidative stress reduced following 12 weeks of endurance training in both lean and obese women. Hewitt et al. (11), also observed that 12 weeks of moderate-intensity exercise (65% of the maximal oxygen uptake) reduced the concentration of hs-CRP in healthy middle-aged individuals with normal weight (21). Our findings in line with these reports support the hypothesis that exercise training can exert an anti-inflammatory effect (22). There could be several mechanisms whereby exercise training decreases the levels of inflammatory factors. Some researchers have attributed the decrease in the hs-CRP levels to the changes in body composition, decreased body fat, and weight loss following regular exercise (23). Hammett et al. (24), suggested that the association between greater physical fitness and lower serum CRP levels is explained, at least in part, by lowered body fat following long-term regular exercise. Jae et al. (23), also reported that lifestyle changes, including regular exercise training decreased hs-CRP in overweight adults, and this was associated with weight loss.

Following the exercise intervention, a significant reduction was observed in the BMI and fat parentage in the present study which, at least in part, might explain the changes in inflammatory biomarkers, including TNF-α and hs-CRP levels in sedentary overweight individuals. In contrast, some researchers suggest that despite a significant weight loss, hs-CRP levels may not change and this reduction may be independent of body fat and weight changes (22). Okita et al. (25), for instance, reported that regular exercise reduced the hs-CRP levels, but the changes were independent of weight changes. Thus, this theory proposes that hs-CRP changes are independent of the changes in body fat content and its levels only decrease through an increase in physical fitness. Thus, the train-

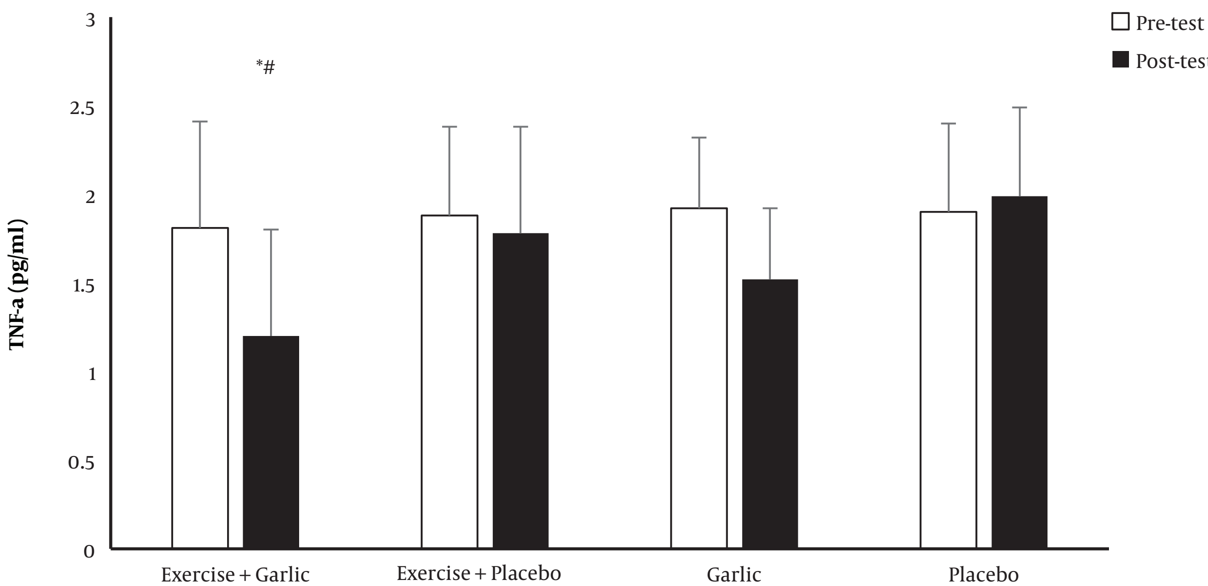

Figure 3. The TNF-α levels (mean $\pm$ SD) from pretest to posttest in groups *, Significantly different from Pretest values ($P < 0.05$).

ing variables including volume and intensity, duration, and frequency, seem to be sufficient to affect the body fat content and the markers of inflammation. Esposito et al. (26) reported that fitness resulted from regular exercise was the main factor in reducing the hs-CRP levels because the losses in weight and body fat mass were insignificant in response to six months of training while hs-CRP levels dropped significantly. Some previous studies suggest that exercise training reduces the expression and blood levels of leukocyte adhesion molecules, inhibits interactions between monocytes and endothelial cells, decreases the production of pro-inflammatory cytokines, and increases the production of anti-inflammatory cytokines by mononuclear cells (27). It has been suggested that CRP production is stimulated by IL-6 and, to a lesser extent, by IL-1 and TNF-α. Physical activity could decrease resting levels of IL-6 and TNF-α and, ultimately, CRP production (28).

On the other hand, several studies have investigated the effects of garlic consumption on the levels of inflammatory and anti-inflammatory markers. Then, an emphasis was put on the potential anti-inflammatory effects of garlic because of the observations of studies that garlic decreased cytokine production, suggesting distinct anti-inflammatory properties (29). For instance, Hodge et al. (30), demonstrated that garlic extract reduced the levels of leukocytes, IL-6, IL-1α, IL-8, and TNF-α cytokines and increased the levels of IL-10 in patients with abdominal inflammation. Su et al. (18), also investigated the effects of 14 days of allicin supplementation on exercise-induced muscle damage, IL-6 levels, and antioxidative capacity in well-trained athletes. The results showed that 14 days of allicin supplementation reduced the IL-6 levels. They also reported that allicin supplementation induced a higher value of total antioxidant capacity at rest, and this higher value was maintained 48 h after exercise. They concluded that allicin might be a potential agent to reduce exercise-induced muscle damage (18).

The mechanism of the anti-inflammatory property of garlic was investigated in several studies. Ban et al. (31) found that thiacremonone, a novel sulfur compound found in garlic, exerted its anti-inflammatory properties through the inhibition of NF-κB activation via an interaction with the sulfhydryl group of NF-κB molecules. Furthermore, Wilson et al. (17), suggested that garlic exerts its effects on human health via multiple different functions, including antioxidant, anti-inflammatory, and antibacterial properties. Organosulfur compounds in garlic can scavenge oxidizing agents and inhibit the oxidation of fatty acids, thereby preventing the formation of pro-inflammatory messengers; they also inhibit bacterial growth via interactions with sulfur-containing enzymes (17). Our data showed that garlic supplementation alone had no significant effect on hs-CRP and TNF-α levels. However, the data indicated that garlic, in combination with exercise training, may have additive effects on inflammatory markers, which is more pronounced for TNF-α levels. We assume that a longer supplementation period or higher doses of supplementation may be required to observe a remarkable alteration in these variables by garlic ingestion alone.

5.1. Conclusions

In the present study, we investigated the effect of endurance training on the hs-CRP and TNF-α levels in sedentary overweight individuals. As observed, BMI, TNF-α, and hs-CRP significantly decreased in the exercise + garlic group, indicating that garlic may have slight additive effects on the anti-inflammatory potential of exercise. However, garlic was not effective per se in this period of supplementation. We assume that the changes in the biomarkers of inflammation would be accompanied by changes in body composition.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

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Footnotes

Authors' Contribution: The study was designed by Farhad Gholami and Jabar Bashiri. The data were collected by Naser Amanollahi and Farhad Gholami. The data were interpreted by Farhad Gholami and Jabar Bashiri. The manuscript was prepared by Farhad Gholami. The final version of the manuscript was approved by all authors.

Clinical Trial Registration Code: The clinical trial registration code was UMIN000039566.

Conflict of Interests: The authors declare no conflict of interest.

Ethical Approval: The study protocol complied with the ethical guidelines of the 1975 Declaration of Helsinki. The ethical procedure of the study was approved by the Ethics Committee of Tabriz University of Medical Sciences (code: 2595).

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Informed Consent: All the participants were informed of the study procedure, and written consent was obtained from each participant.

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