Jorjani Biomedicine Journal

Online ISSN: 2645-3509

Protective Effect of Aerobic Training with Blue-Algae Spirulina Supplementation on Endothelial Dysfunction and Insulin Resistance in Overweight Adults Men

Ammar Raoufi Sangachin[1], Ahmad Abdi[1*], Alireza Barari[1]

1. Department of Physical Education and Sport Science, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran

Article Type:

Original Article

Article History:

Received: 1 Dec 2021
Revised: 10 Jan 2021
Accepted: 25 Jan 2022

****Correspondence:***

Ahmad Abdi,

Department of Physical Education and Sport Science, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran.

a.abdi@iauamol.ac.ir

DOI: 10.29252/jorjanibiomedj.10.1.26

Abstract

Background and Objective: Aging is the major risk factor for the development of cardiovascular diseases as aging increases plasma levels of pro-inflammatory mediators and endothelial dysfunction. Physical exercise and spirulina improve the endothelial dysfunction and chronic inflammation that accompanies aging. This study aimed to evaluate the effects of Aerobic Exercise (AT), with blue-algae Spirulina Supplementation (SP) on the indicators of endothelial dysfunction and insulin resistance in overweight adult men.

Material and Methods: In this clinical trial study, 40 overweight adult men (age 57.50±4.84 years, Body mass index: BMI 26.90±2.85 kg/m2) were selected from Bandar-e-Anzali and randomly allocated into five groups; including Control-Normal (CN), Overweight (OW), Overweight-Aerobic Training (OWAT), Overweight-Spirulina (OWSP) and Overweight-Aerobic Training -Spirulina (OWATSP). Training groups participated in an aerobic exercise program for eight weeks, five sessions per week (with an intensity of 65 to 85% of peak heart rate, 40 minutes). The OWSP and OWATSP groups were provided with two 500 mg SP tablets daily in the morning and evening. Data were analyzed using an independent t-test and ANCOVA at a significance level of $P<0.05$.

Results: The levels of endothelin-1(ET-1), Intercellular Adhesion Molecule 1 (ICAM-1), Selectin-E, and HOMA-IR index in the OW group were higher than CN ($P\leq0.05$). AT and SP significantly reduced ET-1, ICAM-1, Selectin-E, and HOMA-IR ($P\leq0.05$). In the OWATSP group, the levels of ET-1, ICAM-1, Selectin-E, and HOMA-IR were significantly lower than OW and OWSP ($P\leq0.05$). NO levels significantly decreased in OWATSP and OWAT ($P\leq0.05$).

Conclusion: Aerobic training and spirulina supplementation could improve the endothelial function in overweight adult men, by altering the levels of ET-1, ICAM-1, Selectin-E, and NO. However, the simultaneous effect of AT with SP on these indices was better. Improved endothelial function was associated with an improvement in insulin resistance index.

Keywords: Exercise [MeSH]; Spirulina [MeSH]; Insulin Resistance [MeSH]; Obesity [MeSH] ; Vascular System Injuries [MeSH]

Highlights

- Aerobic exercise and royal jelly reduce endothelial dysfunction in the adult by altering ET-1, ICAM-1, Selectin-E, and NO.
- Royal jelly has a synergistic effect on aerobic exercise results.

Introduction

Obesity and atherosclerosis are associated with Endothelial Dysfunction (ED) (1). ED is caused by an imbalance between endothelial-derived vasodilators and vasoconstrictors. Endothelin-1 (ET-1) is the strongest vasoconstrictor (2). Vascular dilators include vascular prostaglandins, Nitric Oxide (NO), and endothelium-dependent hyperpolarization factors (3). Activation of endothelial cells occurs by endothelial expression of cell surface adhesion molecules, especially Intercellular Adhesion Molecule 1 (ICAM-1), soluble Vascular Cell Adhesion Molecule 1 (sVCAM-1). The endothelial leukocyte adhesion molecule (known as selectin-E) facilitates the uptake and attachment of circulating leukocytes to the vessel wall (4). Apart from the effects of ET-1 vasoconstriction, its overexpression in endothelial cells causes the expression of adhesion molecules and vascular inflammation. The ET-1 signal has been shown to induce lipogenesis and reduce insulin sensitivity in adipocytes, while inhibition of ET-1 signaling improves insulin function in adipocytes (5). In addition, circulating ET-1 concentrations increase as a result of obesity and are associated with impaired glucose tolerance in humans (6). Therefore, obesity is thought to be up-regulation of ET-1, which in turn increases inflammation, and by activating adherent cells, it affects vascular function and also leads to dysregulation of blood sugar. However, the correlation between adhesive molecules and ET-1 is also affected by sex. A study showed that despite the correlation between ET-1 and ICAM-1 in women with metabolic syndrome, this correlation was not observed in men with metabolic syndrome (7). Aging also appears to be associated with evident changes in the cardiovascular system that reflect alterations of biochemical adaptive mechanisms (8) as aging is associated with endothelial dysfunction and low systemic inflammation (9). Several authors suggested that cardiovascular diseases and diabetes mellitus are linked to endothelial dysfunction (10, 11), and all of them are strictly related to aging. In general, the vasoconstriction induced by vascular modulators is increased in the elderly, while agonist-mediated endothelial vasodilation is attenuated. Furthermore, a reduced chronic adaptive capacity of older hearts and vessels has been reported in animal models and humans (12). Aerobic exercise improves arterial health in many populations (13) and is involved in reducing the risk of heart disease. Regular exercise along with diet control is considered an important factor in preventing obesity. Previous studies have shown that vascular endothelial function in obese adolescents can be improved by aerobic exercise and resistance training (14), as well as a combination of exercise and diet (15). In addition to exercise training, some plants have been shown to play a role in controlling obesity and its complications. Spirulina is an alga belonging to the family Oscillatoraceae. This plant grows in marine and freshwater environments and is referred to as a superfood that has several biological activities such as antioxidant, anti-diabetic, cholesterol control, and insulin resistance (16). Spirulina-derived protein has also been reported to inhibit the production of NO and angiotensin-2-induced reactive oxygen species in human endothelial cells and reduce the expression of Nitric Oxide Synthase (iNOS) and ET-1 (17). In another study, spirulina was shown to reduce endothelial damage and oxidative stress indices in patients with systemic arterial hypertension (18).

Aerobic exercise as a non-pharmacological treatment as well as spirulina as a safe food has several important biological effects that can affect obesity and its complications. However, the effect of spirulina, as well as the simultaneous effect of aerobic exercise and spirulina on contractile and non-contractile factors (vasodilators) derived from the endothelium, has not been well studied. This study aimed to evaluate the protective effect of aerobic training with blue-algae spirulina supplementation on endothelial dysfunction indices (ET-1, NO, ICAM-1, and selectin-E) and insulin resistance in overweight adult men.

Materials and Methods

In this double-blind clinical trial study, 136 overweight adult men in Bandar-e-Anzali (Gilan, Iran) in the age range of 55-65 years were purposefully selected by a physician after reviewing their files. For this purpose, announcements were installed to invite volunteers to participate in the city (parks, shopping, and entertainment centers). A total of 40 men who were non-smokers and non-alcoholics with no history of chronic disease volunteered to participate in this study. This study was approved by the Research Ethics Committee of the Islamic Azad University, Marvdasht Branch, with the code IR.IAU.M.REC.1399.050 and was registered in the Clinical Trial Center under the number IRCT20140415017288N7. All subjects eligible to take the test, one week before the start of the study, submitted a written consent form and a questionnaire and announced their readiness to begin the training program. Subjects were asked not to change their diet during the study period. It should be noted that the present study did not have a history of participating in a regular exercise program one year before the start of the study. Subjects were randomly divided into 5 groups: Control-Healthy (CN), Overweight (OW), Overweight-Training (OWAT), Overweight-Spirulina (OWSP), and Overweight-Training-Spirulina (OWATSP). During the implementation of the protocol, the control group was asked to perform their daily activities and to refrain from physical activity. Before starting the exercise, a session was dedicated to adapting people to the equipment and the correct way of doing the exercises.

Aerobic training protocol

The training groups participated in the training program for eight weeks and five sessions per week (Table 1). The training sessions were 1 hour, which included 10 minutes of warm-up and stretching, 40 minutes of aerobic training, and 10 minutes of cooling. Stretching and jogging for 10 minutes were used to warm up. The main stage of training included walking on a treadmill, stationary bike, and climbing stairs with an intensity of 65% of the maximum heart rate, which gradually increased to 85% (19).

Table 1. Aerobic exercise protocol for overweight men

Week	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Duration (minutes)	40	40	40	40	40	40	40	40
Intensity (MaxHR)	65	70	70	75	75	80	80	85

Spirulina supplementation

Spirulina tablets are purchased from Mehban Daroo Company and 2 500 mg tablets are taken daily in the morning and evening by the subjects of OWSP and OWATSP group. The placebo groups also took starch tablets at the same time (20).

Blood sampling and laboratory analysis

Two days before and after the training period (to eliminate the acute effect of the last training session) in the fasting state (12 hours), blood sampling was taken from the brachial vein while sitting. Serum levels of ICAM-1, selectin-E, ET-1, and insulin were measured by ELISA and NO by calorimetry. The insulin resistance index was calculated using the formula (HOMA-IR) as follows.

$$\text{HOMA-IR} = [(\text{Glucose mmol/L}) \times (\text{Insulin mIU/L})]/22.5$$

Data analysis procedure

The Shapiro-Wilk test was used to evaluate the normal distribution of the findings and analysis of covariance along with Tukey’s post- hoc test was used to analyze the findings (P <0.05).

Results

The descriptive characteristics of the subjects along with the statistical results of some variables are given in Table 2. The results showed that body weight and mass index in OWAT (*P* = 0.001 and *P* = 0.001) groups, OWSP (*P* = 0.004 and *P* = 0.003, respectively) and OWATSP (*P* = 0.001 and *P* = 0.001) after eight weeks of intervention, there was a significant decrease compared to the pre-test values.

Table 2. Aerobic exercise protocol for overweight men

Variable	Group	CN	OW	OWAT	OWSP	OWATSP
Age (years)	**pre-test**	56.38±5.15	56.75±4.83	55.75±5.6	58.75±4.268	58.38±4.83
Height(meters)	**pre-test**	1.73±0.05	1.69±0.07	1.7±0.06	1.69±0.05	1.7±0.07
Weight (kg)	**pre-test**	68.88±3.75	77.75±6.67	79.12±4.85	81.75±3.69	82.88±4.64
	post-test	68.75±3.32	76.94±7.19	76.31±4.79	78.81±3.7	79.69±7.47
	p	0.732	0.441	0.001*	0.004*	0.001*
BMI (kg/m2)	**pre-test**	23±1.4	27±0.99	27.36±2.14	28.59±1.86	28.58±3.22
	post-test	22.97±1.42	26.71±1.4	26.38±1.99	27.58±2.09	27.49±3.15
	p	0.781	0.427	0.001*	0.003*	0.001*

After confirming the normality of the data using the Shapiro-Wilk test, the results of the intragroup comparison showed a significant decrease in the mean of ET-1 in OWAT (P=0.011; 17.99%), OWSP (P=0.005; 16.83%), and OWATSP (*P*=0.001; 32.02%) groups (Figure 1). Data analysis using the covariance test showed that there was a significant difference in the rate of ET-1 changes between different groups (*P*=0.001, F=18.677). The results of the post hoc test showed that there was a significant increase in ET-1 in the OW group compared to the CN group (*P*=0.025). Also, a significant decrease in OWAT (*P*=0.001), OWSP (*P*=0.001), and OWATSP (*P*=0.001) groups compared to OW group; and OWATSP group was observed compared to OWSP groups (*P*=0.037) (Figure 1).

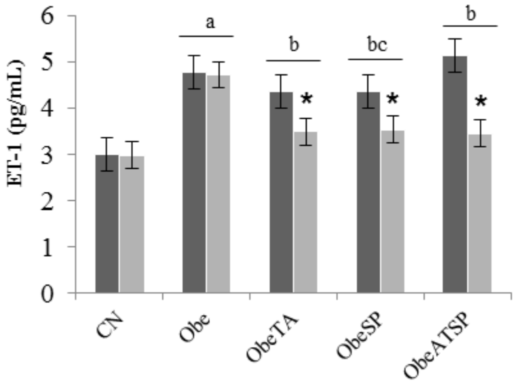

Figure 1. Changes in serum ET-1 levels in different groups using t-test and analysis of covariance (level of *P* <0.05).
* Difference with pretest, a difference with CN group, b difference with OW group, c difference with OWATSP group.
Control-Normal (CN), Overweight (OW), Overweight-Training (OWAT), Overweight-Spirulina (OWSP), and Overweight-Training-Spirulina (OWATSP).

The results of the intragroup comparison showed a significant decrease in the mean levels of ICAM-1 in OWAT (*P*=0.001, F=9.21), OWSP (*P*=0.001, F=6.32), and OWATSP (*P*=0.001, F=13.57) groups (Figure 2). Data analysis using the covariance test showed that there was a significant difference in the rate of ICAM-1 changes between different groups (*P*=0.001, F=10.034). The results of the post hoc test showed that there was a significant increase in ICAM-1 in the OW group compared to the CN group (*P*=0.011). Also, a significant decrease in OWAT (*P*=0.001), OWSP (*P*=0.045), and OWATSP (*P*=0.001) groups compared to OW group; and OWATSP group was observed compared to OWSP groups (*P*=0.047) (Figure 2).

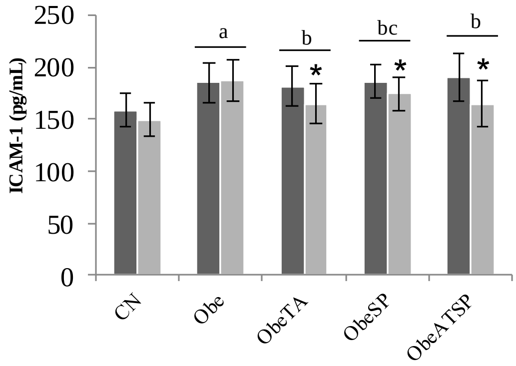

Figure 2. Changes in serum ICAM-1 levels in different groups using t-test and analysis of covariance (level of *P* <0.05).
* Difference with pretest, a difference with CN group, b difference with OW group, c difference with OWATSP group.
Control-Normal (CN), overweight (OW), overweight-training (OWAT), overweight-spirulina (OWSP), and overweight-training-spirulina (OWATSP).

In addition, the results of the intragroup comparison showed a significant increase in the mean levels of selectin-E in the OWAT (*P*=0.001; 19.30%), OWSP (P=0.008; 11.84%), and OWATSP (*P*=0.000; 23.27%) groups (Figure 3). Data analysis using the covariance test showed that there was a significant difference in the amount of selectin-E changes between different groups (*P*=0.000, F=14.468). The test results showed that there was a significant increase in selectin-E in the OW group compared to the CN group (*P*=0.035). Also, a significant decrease in OWAT (*P*=0.001), OWSP (*P*=0.033), and OWATSP (*P*=0.000) groups compared to the OW group; and OWATSP group was observed compared to OWSP groups (*P*=0.011) (Figure 3).

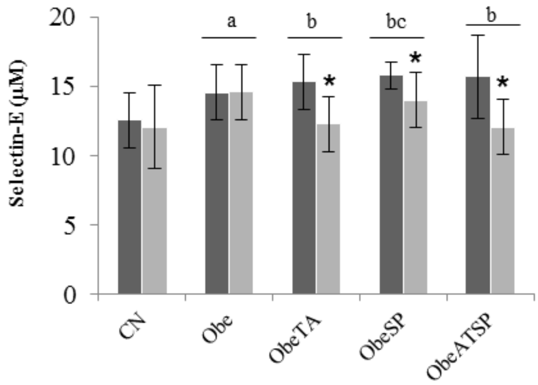

Figure 3. Changes in serum Selectin-E levels in different groups using t-test and analysis of covariance (level of *P* <0.05).
* Difference with pretest, a difference with CN group, b difference with OW group, c difference with OWATSP group.
Control-Normal (CN), overweight (OW), overweight-training (OWAT), overweight-spirulina (OWSP), and overweight-training-spirulina (OWATSP).

Another result of this study using the intragroup test was a significant increase in the mean levels of nitric oxide in OWAT (*P*=0.005; 8.49%), OWSP (*P*=0.001; 10.75%), and OWATSP

(*P*=0.001; 18.0257 groups (Figure 4). Data analysis using the covariance test showed that there was a significant difference in the number of nitric oxide changes between different groups (*P*=0.001, F=8.717). The results of the post hoc test showed that there was a significant decrease in nitric oxide levels in the OW group compared to the CN group (*P*=0.013). Also, a significant decrease was observed in OWAT (*P* = 0.026), OWSP (*P*=0.010), and OWATSP (*P*=0.001) groups compared to the OW group (Figure 4).

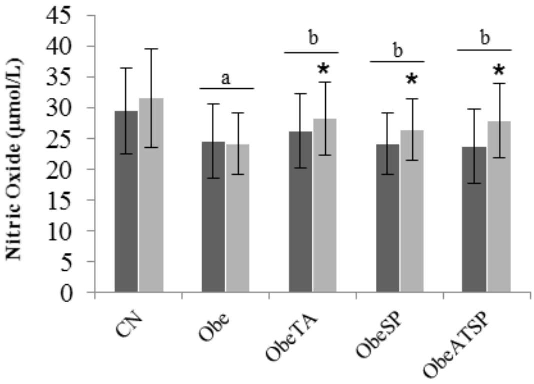

Figure 4. Changes in serum Nitric Oxide levels in different groups using t-test and analysis of covariance (level of *P* <0.05).
* Difference with pretest, a difference with CN group, b difference with OW group, c difference with OWATSP group.
Control-Normal (CN), overweight (OW), overweight-training (OWAT), overweight-spirulina (OWSP), and overweight-training-spirulina (OWATSP).

The results of the intragroup comparison showed a significant decrease in the mean HOMA-IR levels in the OWAT (*P*=0.021; 17.37%), OWSP (*P*=0.017; 8.31%), and OWATSP (*P*=0.001; 39.35%) groups (Figure 5). Data analysis using the covariance test showed that there was a significant difference in the amount of HOMA-IR changes between different groups (*P*=0.001, F=23.073). The results of the post hoc test showed that there was a significant increase in HOMA-IR in the OW group compared to the CN group (*P*= 0.001). Also, a significant decrease in OWAT (*P*=0.001), OWSP (*P*=0.001), and OWATSP (*P*=0.001) groups compared to OW group; and OWATSP group was observed compared to OWAT (*P*=0.022) and OWSP (*P*=0.001) groups (Figure 5).

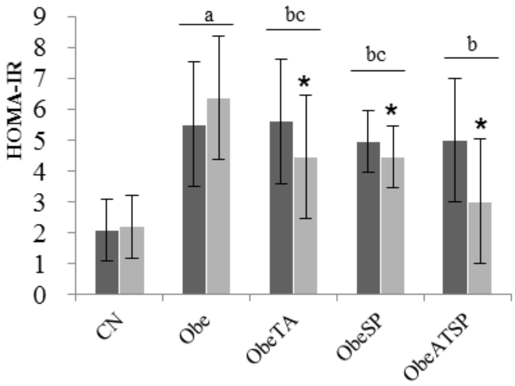

Figure 5. Changes in serum HOMA-IR levels in different groups using t-test and analysis of covariance (level of *P* <0.05).
* Difference with pretest, a difference with CN group, b difference with OW group, c difference with OWATSP group.
Control-Normal (CN), overweight (OW), overweight-training (OWAT), overweight-spirulina (OWSP), and overweight-training-spirulina (OWATSP).

Discussion

The results of the present study showed that the serum levels of ET-1, ICAM-1, and selectin-E as well as HOMA-IR index in the Obe group were higher than the CN group. Also, the NO level was lower in the Obe group than CN. Studies have shown that obesity is associated with increased inflammation and endothelial dysfunction (1). Factors that enhance atherogenesis following obesity include Angiotensin-2, oxLDL, and hyperglycemia, which activate NF-κB and AMPK in arteries, followed by stimulation of proinflammatory cytokines and chemokines, increase ICAM-1 and VCAM-1 synthesis, and iNOS activation (21). Clinical studies have shown that in obese people, NO levels are reduced, leading to impaired endothelial-dependent vasodilation. These studies have shown that decreased endothelial expression of Nitric Oxide Synthase (eNOS), the enzyme responsible for NO production in the endothelium, is a major cause of endothelial dysfunction following obesity (22).

The results of the present study showed that exercise training reduced serum levels of ET-1, ICAM-1, and selectin-E as well as HOMA-IR index in overweight adult men. Regulation of endothelial function through exercise is one of the most important mechanisms of exercise to improve cardiovascular disease (23). In line with the present study, Zaho et al. (2021) in a study showed that 12 weeks of exercise significantly reduced VCAM-1, ICAM-1, and selectin-E levels in obese children and adolescents and improved anthropometric indices (24). Ghodrati et al. (2017) in a study on overweight inactive men showed that ICAM-1 and selectin-E levels decreased after aerobic continuous and high interval intensity training, although selectin-E decreased in the intermittent exercise group. The high intensity was not significant (25). Also, Kasımay et al. (2010) in a study showed that aerobic exercise was associated with a significant decrease in body mass index, body fat content, systolic and diastolic blood pressure. NO, and ET-1 concentrations decreased significantly after 12 weeks of regular aerobic exercise and diet. These changes were also associated with improved glucose homeostasis in patients with impaired glucose tolerance (26). However, Tenório et al. (2018) stated that low-intensity aerobic exercise had no significant effect on ICAM-1, VCAM-1, and HOMA-IR in obese adolescents (27). Nikbakht et al. (2016) also stated in a study on overweight men that endurance training, despite a significant reduction in serum ICAM-1, did not have a significant effect on VCAM-1 and selectin-E (28). The difference in findings may be due to age, body composition, and type of exercise used. Exercise seems to improve endothelial damage indicators through various pathways such as weight loss, fat reduction, antioxidant effects, and inflammation. It has been shown that there is a correlation between ICAM-1 and selectin-E with obesity (29). Adipose tissue is also responsible for the secretion of some inflammatory cytokines. Exercise training appears to reduce ICAM-1 by reducing inflammatory markers such as NFκβ. (30). Another mechanism may be due to the antioxidant effects of aerobic exercise. Since ROS increases ICAM-1, aerobic exercise activity reduces adhesion molecules by enhancing antioxidant defense as well as reducing free radicals (31). Excessive ROS, such as superoxide, reduces the production and availability of NO in the arteries. In the present study, it was shown that NO levels increased significantly following aerobic exercise. Moccia et al. (2020) have shown that intracellular Ca2 + signaling plays an important role in modulating the function of endothelial cells such as NO emission, ROS production, and adhesion molecule secretion (32). Although the present study did not examine possible changes in Ca2+ signaling, a previous study showed that exercise could increase Ca2 + signaling activity (33) and thus affect NO and subsequently the levels of ET-1, ICAM-1, and selectin-E.

The results of the present study showed a significant decrease in serum levels of ET-1, ICAM-1, and selectin-E as well as HOMA-IR index with the use of spirulina. NO levels also increased significantly. Clinical studies have shown that obesity is associated with endothelial dysfunction (1) and an increase in adhesion molecules, as well as an increase in the HOMA-IR index (6). However, the use of spirulina was able to reverse this trend. In this regard, Heo et al. (2017) stated that spirulina reduces iNOS and ET-1 and inhibits ROS (17). In an animal study, Martínez et al. (2018) showed that spirulina consumption decreased levels of sVCAM-1, selectin-E, and ET-1 and increased glutathione peroxidase and glutathione oxidase levels in hypertensive mice (18). Changes in endothelial injury indices can be explained by the following: (1) Decreased endothelial oxidative stress stimuli due to antioxidant compounds in spirulina and thus reduced expression of cell adhesion molecules, (2) Increased NO concentration due to increased expression of endothelial nitric oxide synthase gene and thus decreased vascular wall resistance by reducing mechanical stress to blood vessels, and (3) inhibition of an angiotensin-converting enzyme by bioactive peptides, which leads to a decrease in AT-II receptor ligand (angiotensin-II) and thus a reduction in intracellular signaling cascades associated with cell damage. In addition, angiotensin-induced mechanical stress reduction can be effective (18).

In the present study, serum levels of ET-1, ICA, M-1, and selectin-E in the ObeATSP group were significantly reduced compared to Obe and ObeSP groups and also HOMA-IR index in the ObeATSP group was significantly reduced compared to Obe, ObeTA, and ObeSP. According to the researchers, a study that examined the simultaneous effect of aerobic exercise and blue-algae spirulina on endothelial injury indices was not observed. However, Kasraei et al. (2017) in a study showed that combined exercise and diet significantly reduced CRP, ICAM-1, and TNF-α in adult patients with type 2 diabetes, and the effect of interaction between exercise and diet was more than each alone (34). Exercise and curcumin have also been shown to improve endothelial function in adults (31). It seems that in the present study, exercise and supplementation with their synergistic effect caused more effect of each alone. One of the limitations of the present study is the lack of study of oxidative stress in obese people due to costs. According to the points mentioned in the text, the endothelial function seems to be strongly affected by oxidative pressure. Also, the length of the research period was another limitation of the present study that could not show the long-term effects of lifestyle changes such as changes in the level of physical activity or the use of some supplements in the long run.

Conclusion

AT and SP can improve endothelial function in overweight adult people by affecting the levels of ET-1, ICAM-1, and selectin-E and NO. However, the simultaneous effect of AT with SP on these indices was better. Improvement in endothelial function also appears to be associated with improvements in insulin resistance index. However, the cellular mechanism of these changes needs further investigation.

Acknowledge

This research was conducted in the form of a doctoral dissertation (162323353) at the personal expense of the Islamic Azad University, Ayatollah Amoli Branch. The authors hereby express their gratitude to the participants in this study.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Meyers MR, Gokce N. Endothelial dysfunction in obesity: etiological role in atherosclerosis. Current Opinion in Endocrinology, Diabetes and Obesity. 2007; 14(5):365-9. [view at publisher] [DOI] [PMID] [Google Scholar]

2. Kolettis TM, Barton M, Langleben D, Matsumura Y. Endothelin in coronary artery disease and myocardial infarction. Cardiology in review. 2013; 21(5):249-56. [view at publisher] [DOI] [PMID] [Google Scholar]

3. Ghosh A, Gao L, Thakur A, Siu PM, Lai CW. Role of free fatty acids in endothelial dysfunction.

Journal of biomedical science. 2017; 24(1):1-15. [DOI] [PMID] [PMCID] [Google Scholar]

4. Best PJ, Lerman A. Endothelin in cardiovascular disease: from atherosclerosis to heart failure. Journal of cardiovascular pharmacology. 2000; 35:S61-S3. [view at publisher] [DOI] [PMID] [Google Scholar]

5. Chien Y, Lai YH, Kwok CF, Ho LT. Endothelin-1 suppresses long-chain fatty acid uptake and glucose uptake via distinct mechanisms in 3T3-L1 adipocytes. Obesity. 2011; 19(1):6-12. [view at publisher] [DOI] [PMID] [Google Scholar]

6. Olausson J, Daka B, Hellgren MI, Larsson CA, Petzold M, Lindblad U, et al. Endothelin-1 as a predictor of impaired glucose tolerance and type 2 diabetes-A longitudinal study in the Vara-Skövde Cohort. Diabetes research and clinical practice. 2016; 113:33-7. [view at publisher] [DOI] [PMID] [Google Scholar]

7. Valipoor F, Khadem Ansari Mh, Valizadeh N, Rasmi Y. Endothelial function biomarkers and lipid profile in women and men with metabolic syndrome. Studies in Medical Sciences. 2011; 22(5):474-9. [view at publisher] [Google Scholar]

8. Santulli G, Iaccarino G. Pinpointing beta adrenergic receptor in ageing pathophysiology: victim or executioner? Evidence from crime scenes. Immunity & Ageing. 2013; 10(1):1-13. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

9. Taddei S, Galetta F, Virdis A, Ghiadoni L, Salvetti G, Franzoni F, et al. Physical activity prevents age-related impairment in nitric oxide availability in elderly athletes. Circulation. 2000; 101(25):2896-901. [view at publisher] [DOI] [PMID] [Google Scholar]

10. Sena CM, Pereira AM, Seiça R. Endothelial dysfunction-a major mediator of diabetic vascular disease. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease. 2013; 1832(12):2216-31. [view at publisher] [DOI] [PMID] [Google Scholar]

11. Lerman A, Zeiher AM. Endothelial function: cardiac events. Circulation. 2005; 111(3):363-8. [view at publisher] [DOI] [PMID] [Google Scholar]

12. Lakatta EG. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part III: cellular and molecular clues to heart and arterial aging. Circulation. 2003; 107(3):490-7 [view at publisher] [DOI] [PMID] [Google Scholar]

13. Miyaki A, Maeda S, Yoshizawa M, Misono M, Saito Y, Sasai H, et al. Effect of habitual aerobic exercise on body weight and arterial function in overweight and obese men. The American journal of cardiology. 2009; 104(6):823-8. [view at publisher] [DOI] [PMID] [Google Scholar]

14. Metkus Jr TS, Baughman KL, Thompson PD. Exercise prescription and primary prevention of cardiovascular disease. Circulation. 2010; 121(23):2601-4. [view at publisher] [DOI] [PMID] [Google Scholar]

15. Delp M, Laughlin M. Regulation of skeletal muscle perfusion during exercise. Acta Physiologica Scandinavica. 1998; 162(3):411-9. [view at publisher] [DOI] [PMID] [Google Scholar]

16. Samuels R, Mani U, Iyer U, Nayak U. Hypocholesterolemic effect of Spirulina in patients with hyperlipidemic nephrotic syndrome. Journal of medicinal food. 2002; 5(2):91-6. [view at publisher] [DOI] [PMID] [Google Scholar]

17. Heo S-Y, Ko S-C, Kim CS, Oh G-W, Ryu B, Qian ZJ, et al. A heptameric peptide purified from Spirulina sp. gastrointestinal hydrolysate inhibits angiotensin I-converting enzyme-and angiotensin II-induced vascular dysfunction in human endothelial cells. International journal of molecular medicine. 2017; 39(5):1072-82. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

18. Martínez-Sámano J, Torres-Montes de Oca A, Luqueño-Bocardo OI, Torres-Durán PV, Juárez-Oropeza MA. Spirulina maxima decreases endothelial damage and oxidative stress indicators

in patients with systemic arterial hypertension: Results from exploratory controlled clinical trial. Marine drugs. 2018; 16(12):496. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

19. Villareal DT, Aguirre L, Gurney AB, Waters DL, Sinacore DR, Colombo E, et al. Aerobic or resistance exercise, or both, in dieting obese older adults. New England Journal of Medicine. 2017; 376(20):1943-55. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

20. Eskandari M, Pournemati P, Hooshmand Moghadam B, norouzi j. The Interactive Effect of Aerobic Exercise and Supplementation of Blue-Algae (Spirulina) on Anthropometric Indexes and Cardiovascular Risk Factors in Diabetic Men. Sadra Medical Journal. 2019; 8(1):51-62. [view at publisher] [Google Scholar]

21. Xia F, Wang C, Jin Y, Liu Q, Meng Q, Liu K, et al. Luteolin protects HUVECs from TNF-α-induced oxidative stress and inflammation via its effects on the Nox4/ROS-NF-κB and MAPK pathways. Journal of atherosclerosis and thrombosis. 2014:23697. [view at publisher] [DOI] [PMID] [Google Scholar]

22. Avogaro A, de Kreutzenberg SV. Mechanisms of endothelial dysfunction in obesity. Clinica chimica acta. 2005; 360(1-2):9-26. [view at publisher] [DOI] [PMID] [Google Scholar]

23. Adams V, Reich B, Uhlemann M, Niebauer J. Molecular effects of exercise training in patients with cardiovascular disease: focus on skeletal muscle, endothelium, and myocardium. American Journal of Physiology-Heart and Circulatory Physiology. 2017; 313(1):H72-H88. [view at publisher] [DOI] [PMID] [Google Scholar]

24. Zhao W, Yin Y, Cao H, Wang Y. Exercise Improves Endothelial Function via the lncRNA MALAT1/miR-320a Axis in Obese Children and Adolescents. Cardiology Research and Practice. 2021; 2021:8840698. [view at publisher] [DOI] [PMID] [PMCID] [Google Scholar]

25. Ghodrati K, Mirzaei B, Tadibi V. Comparison of The Chronic and Acute Effects of Aerobic Continuous and High Interval Intensity Training (HIIT) on Vascular Inflammation Indices (ICAM-1, E-Selectin) in Sedentary Overweight Men. Journal of Applied Health Studies in Sport Physiology. 2019; 6(1):53-9. [view at publisher] [Google Scholar]

26. Kasımay Ö, Ergen N, Bilsel S, Kaçar Ö, Deyneli O, Gogas D, et al. Diet-supported aerobic exercise reduces blood endothelin-1 and nitric oxide levels in individuals with impaired glucose tolerance. Journal of clinical lipidology. 2010; 4(5):427-34. [view at publisher] [DOI] [PMID] [Google Scholar]

27. Tenório TR, Balagopal PB, Andersen LB, Ritti-Dias RM, Hill JO, Lofrano-Prado MC, et al. Effect of low-versus high-intensity exercise training on biomarkers of inflammation and endothelial dysfunction in adolescents with obesity: A 6-month randomized exercise intervention study. Pediatric exercise science. 2018; 30(1):96-105. [view at publisher] [DOI] [PMID] [Google Scholar]

28. Nikbakht H, Gaeini A, Mohammadzadeh Salamat K. The effect of endurance training on serum adhesion molecules in overweight men. Scientific Journal of Kurdistan University of Medical Sciences. 2016; 21(3):79-88. [view at publisher] [Google Scholar]

29. Ito H, Ohshima A, Inoue M, Ohto N, Nakasuga K, Kaji Y, et al. Weight reduction decreases soluble cellular adhesion molecules in obese women. Clinical and Experimental Pharmacology and Physiology. 2002; 29(5-6):399-404. [view at publisher] [DOI] [PMID] [Google Scholar]

30. Ding Y-H, Young CN, Luan X, Li J, Rafols JA, Clark JC, et al. Exercise preconditioning ameliorates inflammatory injury in ischemic rats during reperfusion. Acta neuropathologica. 2005; 109(3):237-46. [view at publisher] [DOI] [PMID] [Google Scholar]

31. Akazawa N, Choi Y, Miyaki A, Tanabe Y, Sugawara J, Ajisaka R, et al. Curcumin ingestion and exercise training improve vascular endothelial function in postmenopausal women. Nutrition

research. 2012; 32(10):795-9. [view at publisher] [DOI] [PMID] [Google Scholar]

32. Moccia F, Negri S, Faris P, Berra-Romani R. Targeting the endothelial Ca2+ toolkit to rescue endothelial dysfunction in obesity associated-hypertension. Current medicinal chemistry. 2020; 27(2):240-57. [view at publisher] [DOI] [PMID] [Google Scholar]

33. Rode B, Shi J, Endesh N, Drinkhill MJ, Webster PJ, Lotteau SJ, et al. Piezo1 channels sense whole body physical activity to reset cardiovascular homeostasis and enhance performance. Nature communications. 2017; 8(1):1-11. [DOI] [PMID] [PMCID]

34. Kasraei H, Kargaefard M, Nazarali P, Nobari H, Zare A. The effect of combined exercise with and without diet restriction on weight loss on some inflammatory markers (CRP, TNF-α and ICAM-1) in elderly men with type 2 diabetes. Iranian Journal of Diabetes and Lipid Disorders. 2019; 18(4):207-20. [view at publisher] [Google Scholar]

How to cite:

Raoufi Sangachin A, Abdi A, Barari A. Protective Effect of Aerobic Training with Blue-Algae Spirulina Supplementation on Endothelial Dysfunction and Insulin Resistance in Overweight Adults Men. *Jorjani Biomedicine Journal*. 2022; 10(1):22-32.