Full Length Research Article
Advancements in Life Sciences – International Quarterly Journal of Biological Sciences

ARTICLE INFO

Date Received: 10/04/2019;
Date Revised: 13/05/2019;
Date Published Online: 25/05/2019;

Authors' Affiliation:
University of Qom, Iran

***Corresponding Author:**
Mohsen Akbarpour
Email:
akbarpour.mohsen@gmail.com

How to Cite:
Akbarpour M, Ebrahimzadeh ZS (2019). Effect of Spirulina supplementation and aerobic exercise on the level of cortisol and body composition in women with type 2 diabetes. Adv. Life Sci. 6(3): 116-124.

Keywords:
Aerobic Exercise; Spirulina; Cortisol; Body Combination; Type 2 Diabetes; Overweight

Open Access

Effect of Spirulina supplementation and aerobic exercise on the level of cortisol and body composition in women with type 2 diabetes

Mohsen Akbarpour*, Zahra Samari Ebrahimzadeh

Abstract

Background: Changes in the hypothalamus-pituitary-adrenal axis and obesity play an important role in the development of diabetes. Aim of this study was to investigate the effect of spirulina supplementation and aerobic exercise on serum cortisol level and body composition in women with high BMI type 2 diabetes.

Methods: In this semi-experimental study, 28 women with type 2 diabetes and overweight with mean age of 48.4 ±7 and body mass index 29.7±3.33, were randomly assigned to aerobic training groups + spirulina, aerobic training + placebo, spirulina and placebo. The aerobic training program included six weeks and running with a severity of 60-72% of maximum heart rate. The recipient groups received three 500 mg capsules of spirulina daily for six weeks before each meal. Blood samples were collected for pre-test and post-test stages in order to study the variables studied in fasting conditions. Data analysis was performed using one-way ANOVA and t-test with a significant level ($p \leq 0.05$) and using SPSS software.

Results: Serum levels of cortisol in the aerobic- Spirulina group ($p=0.02$), aerobic group ($p=0.00$), and spirulina group ($p=0.02$) showed a significant decrease from the pre-test to post-test. Also, there was a significant difference in the level of cortisol between aerobic-spirulina group and aerobic group compared to control group ($P \leq 0.05$). However, there was no difference between the groups (fat percentage, BMI, WHR) in body composition indicators ($P>0.05$).

Conclusion: Results of Cortisol Measurement and body composition showed that aerobic training along with supplementation with spirulina has a positive effect on the cortisol reduction in women with type 2 diabetes and can therefore reduce stress and improve the health of patients with type 2 diabetes and overweight.

Scan me

Introduction

Type 2 diabetes is a metabolic disease characterized by insulin resistance in the target tissue and a chronic increase in blood glucose [1]. Sweet diabetes affects millions of people around the world, and these numbers continue to rise at an alarming rate [2]. Type 2 diabetes, as the most common endocrine disorder, has several complications and is one of the major causes of mortality in human societies [3]. In this regard, behavioral and psychological factors play a vital role in managing diabetes, which is one of the most important psychological factors affecting on diabetes stress [4]. And one of the neuroendocrine systems compatible with the organism against stressful conditions is the hypothalamus-pituitary-adrenal axis [5]. In the neuromorphic or hypothalamic-pituitary axis, mental stress stimulates the parathyroid glands of the pituitary gland and causes the release of corticotropin-enhancing agent. This agent in the anterior pituitary leads to the synthesis of adrenocorticotropin and ultimately stimulates the adrenal glands and secretion of glucocorticoid hormones such as cortisol [6]. On the other hand, studies have shown that increased levels of cortisol in the bloodstream produce adverse effects in the body, including increasing insulin resistance in different cells and imbalance in blood glucose levels [7]. Glucocorticoids also increase the production of glucose in the liver by stimulating gluconeogenesis [8], increased production of glucose leads to increased insulin levels, and increased levels of insulin in the plasma are controlled by glucocorticoids, which increases blood glucose and diabetes [9]. The activity of the adrenal-pituitary-hypothalamus axis and the sympathetic system are involved in endocrine disorder such as obesity and type 2 diabetes. According to available research evidence, obesity is one of the health-promoting factors due to the association with metabolic and hormonal disorders such as lipid metabolism disorder and type 2 diabetes [10]. Obesity and overweight are the main cause of insulin resistance and impaired glucose tolerance [11] The WHO has identified obesity as a global epidemic and century-long illness. Obesity means high body fat or high fat tissue relative to body fat that is considered to be the most important inflammatory disease and its prevalence in Iran and in the world is increasing [12]. Obesity and overweight studies are a strong predictor of metabolic diseases, people with high BMIs are more likely to develop diabetes [13]. Abdominal obesity is also associated with some illnesses. For example, studies have shown that the ratio of waist circumference to hip ratio is directly related to type 2 diabetes. [14]. Obesity and insulin resistance, also referred to as metabolic syndrome, are the result of inactive lifestyles [15], and the decline in physical activity in recent decades has caused the number of people with type 2 diabetes. Therefore, considering that obesity is the most important factor in diabetes, physical activity and exercise can be considered as a very effective method for the prevention and treatment of type 2 diabetes [16] and the beneficial effects of exercise on fat loss and the improvement of metabolic factors have long been known [17] in such a way that subordinate regular aerobic activities, such as walking, running slowly and alternately, are used as a non-pharmacological method to reduce the incidence of obesity and diabetes [18]. Research has shown that a 5% reduction in body weight due to physical activity and nutritional modification can prevent 40-60% of the occurrence of type 2 diabetes [19] one of the important issues facing diabetic patients is mental illness and depression, and in this regard, the pattern of exercise, especially aerobic, is suggested as a non-pharmacological treatment to deal with psychological stress [20]. So that some studies have shown that physical activity can have a beneficial effect on the stressful process and physiological and psychological mechanisms [21]. While the results of some other studies show no association. Gilani Nejad *et al.* (2018), after 12 weeks of yoga practice, observed cortisol reduction and improved stress, anxiety and depression in older diabetic women [22]. In contrast to Ahmed *et al.* (2015), after an examination of four weeks of aerobic training, they reported no reduction in cortisol [23].

On the other hand, insufficient response to some of the commonly used diabetes treatments has led to the use of complementary and alternative therapies for the treatment of diabetes in the United States, from 2 to 6.3 million people [24]. In this regard, the researchers' attention was drawn to the use of herbal supplements, including these supplements can refer to Spirulina, Spirulina is a tiny green-blue-striated algae, with spring-like filaments, photosynthesizing, and a very small size of 2 to 8 microns [25]. The algae contain high levels of protein, vitamins, minerals, essential amino acids, fatty acids and antioxidant pigments, such as beta-carotene [26] and reports suggest that spirulina has beneficial effects in treating and diseases such as obesity, type 2 diabetes, depression, weight loss, appetite inhibition, and decreased appetite for overeating [27]. Spirulina is also effective in preventing diabetes, as it contains high levels of vitamin B1 that improves the metabolism of the sugars in the body, vitamin B2, Vitamin B2 prevents obesity by burning calories, and vitamin B6, which plays a role in making insulin hormone in the body [28]. As Hoshmand and colleagues concluded in a study, the use of spirulina supplementation can improve peroxidant and antioxidant balance in people with type 2 diabetes and prevent exercise-induced oxidative stress and diabetes [29]. In another study, Lee *et al.* (2008) reported that after 12 weeks of spirulina supplementation, this supplementation affects blood lipids and inflammatory variables in patients with type 2 diabetes [30]. Therefore, considering the positive effects of spirulina algae on somebody factors in diabetic patients and the presence of psychological stress and depression in these patients and considering the controversy about the effect of training on the level of cortisol in patients with type 2 diabetes as well as the lack of adequate research on the interactions between the use of spirulina supplementation and aerobic training on the stressful process and composition of the body, the purpose of this study was to investigate the effect of supplementation of spirulina and aerobic training on serum cortisol and body composition (Percentage of body fat, WHR, BMI) in women with type 2 diabetes and overweight.

Methods

Subjects

This research was carried out with a semi-experimental randomized and four-group design with two-stage pre-test and post-test. The statistical population of this study was diabetes mellitus type 2 in Qom. Of these people, people with type 2 diabetes, our age from 30 to 55 years old, body mass index of 25 to 30 kg / m^2, blood glucose range from 160 to 300 mg / dL, Regular sports inactivity over the past 3-5 years was selected. After distributing the company's cooperation form to the research project with the presence of volunteers who were ready to participate in the research project, at the coordination meeting and after a complete description of the objectives and methods of measurement by the researcher, by completing the informed consent form and medical history questionnaires and 24-hour dietary recall were examined that among eligible candidates, 40 subjects were selected randomly as a BMI sample (So that each group has the same average BMI) and divided into 10 people in 4 groups (Aerobic-Spirulina, Aerobic-Placebo, Spirulina, and Placebo). At the end, 28 subjects completed the study period and 12 were excluded due to illness and lack of participation in the training. In this regard, none of the subjects was treated with insulin, and patients from all four groups used oral metformin glibenclamide during the study period. It should be noted that this research was registered by the Committee for Research and Ethics of the University of Qom, Faculty of Literature and Humanities, No. 7167.

Practice program

At first, the maximum heart rate was measured using formula 208-(age 0/7) for each person [31]. In this research, the training group performed a six-week aerobic exercise program. The aerobic exercise program included ten minutes of warm-up, fast walking, slow running, and tensile and smooth movements. Continuous running was performed at a severity of 60-72% of the maximum heart rate of the subjects. So that the subjects performed at the first session with 60% of maximum heart rate, and in both sessions, 2% of the intensity of the exercise was added, which increased sharply by 72% in the fifth week and was sustained at the sixth week. Also, running in the first session was fifteen minutes, both sessions were stepped up 1.5 minutes running time and increased to 26 minutes by the end of the eighteenth session. The intensity of the exercise was controlled using a pulse rate belt and at the end of each session, the cooling operation was performed with soft run, tensile and smooth movements for ten minutes.

Complementary

Spirulina consumer groups consumed three capsules of 500 mg of spirulina daily for six weeks before each meal. It should be noted that the aerobic-placebo group and the placebo group received placebo capsules that were similar to spirulina-filled capsules filled with starch and similar daily doses. The subjects in the placebo group did not have activity during the study.

The method of measuring blood variables

Blood sampling was done between 8:00 and 9:00 in the morning after 12 hours of fasting and in two stages, 24 hours before the beginning of exercise and supplementary and 48 hours after the last training session, after six weeks of aerobic training and supplementary. In the first stage, 5 cc bloods were taken from the left brachial vein of the subjects while sitting and resting. Then, the experimental group consumed supplemental supplements for six weeks and applied to regular aerobic exercise. 48 hours after completion of training and supplementation (six weeks), blood samples were taken from the subjects as first stage. After blood collection, the sera were separated by centrifugation at 3000 rpm for 10 minutes and stored until the test day in the refrigerator at -80 ° C. The samples were taken out of the freezer for 30 minutes at room temperature to melt and reach room temperature. Then the specimens were serrated five times to remove the freezing and melting concentration and the concentration of samples is homogeneous. Cortisol measurements were performed using a 2100 Stat-fax machine and ELISA method with a sensitivity of 0.25 micrograms per deciliter.

Measurement of body composition variables

Measurement of body weight was measured using a German digital scale with a precision of ± 0.1 kg without shoe with minimum dress. The height of the people was measured using a wall stadiometer 44440, manufactured by Kaveh Company with a precision of ± 0.1 cm, standing in front of the wall and without shoes, while the Scapulas were in normal conditions, and the body weight was evenly divided on both legs, and the eyes were parallel to the horizon, they were measured. In order to measure the body mass index of subjects, their height and weight were measured first, then, body mass index was obtained by dividing the weight by height squared.

In this formula, weights in kilograms and height in meters and unit of body mass index in kilograms per square meter. The percent body mass of the subjects was measured using Body Composition device. The measurement of waist to hip ratio was calculated by dividing the measurement of the smallest peripheral area of the lumbar region (the midline between the pectoral appendages of the chest and navel) on the perimeter of the largest area of the hips.

Statistical Methods

Kolmogorov-Smirnov test was used to examine the natural distribution of data and Levene's test was used to examine the homogeneity of variances. Considering the significance of the above tests to determine the effect of aerobic training course and Supplementary supplement on the serum cortisol level and body composition of women with type 2 diabetes and overweight, And considering the significance of the above tests to determine the effect of aerobic training course and spirulina supplementation on serum cortisol levels and body composition of women with type 2 diabetes mellitus and overweight, dependent T test was used to examine the differences between groups and one way analysis of variance (ANOVA) was used to examine the differences between groups. The results of the test were considered with a meaningful level ($P \leq 0.05$).

Results

The characteristics of the subjects in the research groups are shown in Table 1. According to the results of Table 1, there was no significant difference between age, height and weight indices among the research groups ($P > 0.05$). The Kolmogorov-Smirnov test also showed a normal distribution of data among the groups and a homogeneous lean test of variance in the four groups.

According to the results of this study, one-way ANOVA showed that there is a difference in the level of cortisol between the four groups of the study. Cortisol levels were significantly different between the placebo group and the spirulina-training group ($p = 0.006$) and between the placebo group and the training group ($p = 0.003$), but this difference was not significant between the placebo group and the spirulina group (table 2). At the same time, there was no difference between groups in terms of fat percentage, waist to hip ratio (WHR) and body mass index (BMI) between the four groups ($P > 0.05$).

The results of intra-group t-test showed a significant reduction in the cortisol index from the pre-test to post-test in the spirulina-training group (p = 0.0**0**2), placebo-training group ($p = 0.00$) and spirulina group (p = 0.02**8**). Also, an intra-group evaluation of anthropometric indices showed that percentage of fat, waist to hip ratio (WHR) and body mass index (BMI) were reduced in all three groups: spirulina-training, placebo-training, and spirulina, which was not

Group	Placebo	spirulina	Placebo-training	spirulina-training	The significance level
Variable	**mean ± s.d.**	**mean ± s.d.**	**mean ± s.d.**	**mean ± s.d.**	
Age (years)	47.16±7.44	46.28±6.21	49.57±5.76	50.87±8.60	**0.59**
Height (cm)	159.16±5.87	152±3.40	154.14±4.74	154.87±5.35	**0.13**
Weight (kg)	74.38±7.56	67.25±6.20	68.45±8.99	69.62±9.08	**0.44**

Table 1: Comparison of anthropometric indices in four groups. There was no difference between the groups (one-way ANOVA test, meaningful level ($P \leq 0.05$)

Variable	Groups	Measure time			Change	**P between groups
		Pre-test	Post-test	* P within group		
Cortisol	Spirulina-Training	15.13±1.66	12.35±3.12	0.002	2.78±1.70	**0.001**
	Placebo-Training	14.98±2.67	11.74±3.40	0.00	3.24±1.13	
	Spirulina	14.80±2.14	17.07±2.95	0.02	-2.27±2.07	
	Placebo	17.10±2.50	16.98±2.29	0.88	0.11±1.81	
WHR	Spirulina-Training	0.85±0.06	0.84±0.05	1.00	0.01±0.02	**0.38**
	Placebo-Training	0.86±0.05	0.83±0.02	0.17	0.03±0.04	
	Spirulina	0.89±0.04	0.88±0.04	0.84	0.01±0.05	
	Placebo	0.86±0.03	0.87±0.04	0.58	-0.01±0.02	
BMI	Spirulina-Training	29.77±3.19	29.08±3.37	0.18	0.68±1.33	**0.99**
	Placebo-Training	29.14±2.34	29.01±2.37	0.30	0.12±0.30	
	Spirulina	31.01±5.18	29.41±3.64	0.26	1.60±3.46	
	Placebo	28.91±2.62	29.00±2.84	0.59	-0.08±0.36	
Fat Percentage	Spirulina-Training	39.85±3.23	38.32±3.26	0.10	1.52±2.29	**0.85**
	Placebo-Training	39.88±3.32	39.21±2.28	0.19	0.67±1.21	
	Spirulina	38.41±5.12	37.70±4.81	0.20	0.71±1.32	
	Placebo	37.66±3.01	37.88±3.20	0.52	-0.21±0.77	

Table 2: Comparison of cortisol levels and body composition of participants in the four groups after six weeks of training (Information is shown as mean ± standard deviation)

significant ($P > 0.05$).

Discussion

Aerobic exercise training has always been considered as a non-pharmacological strategy to reduce the complications of obesity and diabetes, and the diet of type 2 diabetes patients is also very important. Therefore, this study was conducted with the aim of evaluating the effect of aerobic training and supplementation of spirulina on serum cortisol and body composition of women with type 2 diabetes and overweight. The results of this study showed a significant decrease in serum cortisol levels in the spirulina-training group and the training group compared to placebo group. The results of this study were consistent with the findings of Shirvani *et al.*, Delakerda *et al.*, [32,33]. But it is not consistent with the findings of Piry *et al.*, and Sadr al-Ashrafi *et al.*, [34,35]. Shirvani *et al.*, investigated the effect of 8 weeks aerobic training, Bruce & Stage Test (three sessions per week, with intensity 45-85% of maximum heart rate) on thyroid hormones and cortisol in 20 women and concluded that thyroid hormones increased and cortisol levels decreased significantly [32]. Delkerda *et al.*, also examined the effect of 8 weeks of aerobic training on patients with depression and decreased symptoms of anxiety and stress [33]. On the other hand, Pierre *et al.*, who studied the effect of 8 weeks of aerobic training (Three sessions per week, each session 30 minutes and an intensity of 65-85% of the maximum heart rate) on cortisol and leptin levels in obese and lean men, showed a significant increase in serum cortisol levels [34]. Sadr al-Sharra *et al.*, also investigated the effect of aerobic rhythmic exercises (For 8 weeks, each session with an intensity of 120 blows of the metronome) on cortisol and testosterone concentration in inactive women, and concluded that the concentration of resting levels after cortisol activity was significantly increased [35]. The reason for the difference in findings may be attributed to different subjects in research that were diabetic, depressed, obese or inactive, also, these differences can be correlated with a different training program, including volume, intensity, repetition, rest rate and type of exercise program, or differences in the examination of plasma or serum levels, and also the time taken for blood (Immediately or after recovery) affects the response of cortisol to exercise. Physical stress or tissue damage is first transmitted through the brain stem and eventually go to the midline in the hypothalamus, where the CRF is secreted into the pituitary port system and within a few minutes, the entire control steps will release a large amount of cortisol into the bloodstream. Subjective stress also increases the rate of ACTH secretion and ultimately cortisol by increasing the activity of the limbic system in the amygdala and the hippocampus and sending the message to the posterior hypothalamus [36]. Regarding this, it can be concluded that stress control is the most important factor in reducing cortisol, probably the most important mechanism of the effect of aerobic training on the reduction of cortisol due to the increase of endorphins in the patients, which leads to the improvement of stress [37]. Also, aerobic physical activity in women increases the amount of progesterone and this increase reduces psychological symptoms such as stress, anxiety and depression. Deep breathing and diaphragm also cause stress control in aerobic exercises, thereby reducing the sympathetic nerve stimulation, which is useful in improving many symptoms of anxiety [38]. The cause of cortisol reduction in this study may be related to the time of blood sampling. The post-test blood collection was performed 48 hours after the last training session and after returning to the initial state. One of the factors that increases cortisol in some studies is that cortisol is an anti-inflammatory hormone, any kind of exercise, stress, stroke, decreased or elevated body temperature and inflammation lead to increased cortisol secretion after exercise [39]. As well as rising levels of cortisol immediately after exercise, it is attributed to a decrease in insulin levels, in other words, there is an inverse relationship between insulin and cortisol levels [40]. Also, the results of this study showed a significant reduction of cortisol in the spirulina group from pre-test to post-test. This finding was consistent with Anzer Alam *et al.*, who reported using Spirulina supplementation for 45 days on 40 patients with type 2 diabetes, to reduce mental parameters such as stress and fatigue in people with type 2 diabetes [41]. Reducing levels of cortisol in the spirulina group can be explained as follows: The cortisol hormone secretion is largely controlled by the Adreno Cortico Trophic Hormone (ACTH) from the hypothalamic-pituitary axis [36], and since the activity of the adrenal-hypophyseal-hypothalamic axis and the central sympathetic system contribute to endocrine disorders such as increased blood glucose and type 2 diabetes [10], and spirulina is also the richest source of niacin, pantothenic acid, biotin, folic acid and inositol, one of the essential ingredients for energy release in the body and better working of the sympathetic nervous system, it can inhibit the activity of the adrenal-hypophyseal-hypothalamic (HPA) axis and reduce cortisol [42]. In the context of body composition indices, the present study showed a decrease in fat percentage, waist to hip ratio (WHR) and body mass index (BMI) in aerobic-spirulina group and aerobic group, which was not significant. These results are consistent with the findings of Jorg *et al.*, and Ibanez *et al.*, [43,44]. However, it was inconsistent with the findings of al-Kardar *et al.*, and Fenicha *et al.*, [45,46]. Jorg *et al.*, investigated the effect of three months of aerobic and resistance training on type 2 diabetic patients and reported no significant change in anthropometric indices in both aerobic and resistance groups [43]. Eybenz *et al.*, in a study of 9 men with type 2 diabetes, concluded that there was no significant reduction in body composition after 4 weeks of progression [44]. Alkard *et al.*, showed a significant change in body composition indices in patients with type 2 diabetes, with the effect of three months of aerobic training (with an intensity of 60-80% of maximum heart rate) and resistance training (with intensity 60-80% of one maximum repetition) [45]. Fenicha *et al.*, examined 41 obese women with type 2 diabetes and concluded that 16 weeks of resistance training significantly reduced BMI, waist circumference and body mass in these patients [46]. There are various reasons for the difference between the research results and this research. The most important reason for this can be the type of activity, but the interference of different variables, such as the length of time the subjects went to work, nutrition, daily activity of subjects, as well as the training program, could be different from other reasons. Probably a long-term exercise program, and a higher volume or reduced diet may have more beneficial effects on the body's composition. Increasing blood flow in adipose tissue, increasing the activity of important lipolytic enzymes such as hormone-sensitive lipase and lipoprotein lipase, which increases the entry of fatty acids into the bloodstream and, as a result of increased fat oxidation, is a mechanism for reducing fat percentage and body mass index through exercise [47]. Visceral fat is metabolically active in the tissue and plays a major role in regulating insulin sensitivity and other metabolic processes, hence abdominal obesity predicts insulin resistance [48]. Reducing body fat also indicates a decrease in visceral fat, and interventions such as exercise with a steady-state ratio will reduce visceral fat. As shown, visceral fat loss response to exercise is faster than total body fat, and a 10% reduction in weight reduces visceral fat by 35%. And the reason for the decrease in visceral fat due to exercise is the visceral sensitivity of the visceral adipocytes to stimulate the lipolytic process that occurs in response to the catecholamines released by the exercise, which reduces the waist to hip ratio [49]. The results of this study showed a decrease in the body composition indices in the spirulina group, which was not significant, and this result is in agreement with the findings of Sharifi *et al*, Mir Fayyzi and colleague [50,51]. Sharifi *et al.*, studying the effect of 10 weeks of resistance training (3 sessions per week with intensity of 16-81% of one maximal repeat) with supplemental supplementation on the body composition of 31 women with type 2 diabetes did not show a significant decrease in fat percentage and body mass index [50]. Mir Faezi *et al.*, did not report a significant decrease in body mass index by examining the effect of 90 days of consumption of cranberry (1 g / day) [51]. On the other hand, according to Houshmand *et al.*, the effect of eight weeks of cumin (daily 2 pills 25 mg) supplementation on body composition indices showed that 40 overweight men had a significant decrease in weight, fat percentage and body mass index [52]. The most important reason for the difference in the findings is related to the type of supplement and the duration of supplementation. Given that the spirulina supplement contains the essential unsaturated fatty acid called gammalinoleic acid (GLA) and a low protein-rich protein source, low calorie and no cholesterol, this is one of the mechanisms that can reduce inflammation and obesity after taking spirulina supplementation [42]. Possibly, the low number of subjects in the different groups of the present study has affected the results of statistical tests and differences with the results of other studies. The present study was a semi-experimental one in the overweight type II diabetic population, so the control of all effective factors such as genetic factors or other factors independent of obesity and diabetes was beyond the control of the researchers, and these factors could affect the outcomes.

In general, six weeks aerobic training, supplementation of spirulina and aerobic training significantly reduced serum levels of cortisol in all three groups of spirulina-training, placebo-training, and spirulina. Anthropometric indices were also reduced, which was not significant. In other words, both of the two factors are complementary to spirulina and aerobic exercise, and have positive and beneficial effects on cortisol and stress in women with type 2 diabetes and are effective in improving the health of type 2 diabetic patients and overweight through different mechanisms. However, in order to achieve accurate results, further research has to be done regarding the effect of exercise and the use of spirulina supplementation in overweight type 2 diabetic patients.

Conflict of Interest Statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

Acknowledgements

Thanks and gratitude to the efforts of all the patients who patiently and diligently helped us with this research, as well as from the company of Setareye Shakhab Qeshm who supported the research in providing the supplements needed.

References

1. Snowling, NJ, Hopkins, W. G. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients a meta-analysis. Diabetes care. (2016); 29(11): 2518-2527.
2. DW, LeRoith D. The worldwide diabetes epidemic. Current Opinion in Endocrinology, Diabetes and Obesity. (2012); 19(2): 6-93.
3. Klein OL, Krishnan JA, Glick S, Smith LJ,, Systematic review of the association between lung function and Type 2 diabetes mellitus, Diabetic Medicine (2010); 27(9): 977-987.
4. Snoek FJ. Management of diabetes: Psychological aspects of diabetes management. Tucson: The Medicine Publisher; (2002) 2:56-63.
5. Fries E, Dettenborn L, Kirschbaum C. The cortisol awakening response (CAR): facts and future directions. International Journal of Psychophysiology. 2009; 72(1): 67-73.
6. Stephens I. Medical Yoga Therapy Children, (2017); 4(12): 1-20.

7. K. Karlsson M, Nordqvist A, Karlsson C. Physical activity, muscle function, falls and fractures. Food & nutrition research. 2008;52(1):1920.
8. Lundgren M, Burén J, Ruge T, Myrnas T, Eriksson JW. Glucocorticoids down-regulate glucose uptake capacity and insulin-signaling proteins in omental but not subcutaneous human adipocytes. The Journal of Clinical Endocrinology & Metabolism. 2004;89(6):2989-97.
9. Plat L, Byrne MM, Sturis J, Polonsky KS, Mockel J, Fery F, *et al*. Effects of morning cortisol elevation on insulin secretion and glucose regulation in humans. American Journal of Physiology-Endocrinology and Metabolism. 1996;270(1):E36-E42.
10. Rosmond R, Björntorp P. The hypothalamic–pituitary–adrenal axis activity as a predictor of cardiovascular disease, type 2 diabetes and stroke. Journal of internal medicine. 2000; 247(2): 188-97.
11. Tahrani AA, Bailey CJ, Del Prato S, Barnett AH. Management of type 2 diabetes: new and future developments in treatment. The Lancet. 2011;378(9786):182-97.
12. Woo JG, Guerrero ML, Ruiz-Palacios GM, Peng Y-m, Herbers PM, *et al*. Specific Infant Feeding Practices Do Not Consistently Explain Variation in Anthropometry at Age 1 Year in Urban United States, Mexico, and China Cohorts. J Nutr, (2013); 143(2):166-174.
13. Gower BA, Munoz J, Desmond R, Hilario-Hailey R, Jiao X. Changes in intraabdominal fat in early postmenopausal women: Effects of hormone use, Obesity;(2006); 14:1046-1055.
14. Wee CC, Huskey KW, Ngo LH, Fowler-Brown A, Leveille SG, Mittlemen MA, *et al*. Obesity, Race, and Risk for Death or Functional Decline Among Medicare Beneficiaries A Cohort Study. Annals Inter Med, (2011); 154(10):645-655.
15. Yavari, A. the effect of various exercise training on glycemic control and cardio vascular risk factors. (2013), Dissertation of Philosophy Doctor. Azarbaijan national academy of science institute of physiology N.A.A.I. Karaev.
16. Larijani B. Diabetes and exercise. Institute of Endocrinology and Metabolism Tehran, Iran, (2011); 4-15.
17. Razavi Majd, Zainab, Nasali, Parvaneh, Hanachi, *et al*. Investigating the Effect of One on Respiratory Indices in Patients with Asthma, D Aerobic Exercises and Vitamin Supplementation Journal of Qom University of Medical Sciences,(2012); 6::48-74.
18. Lin X, Eaton CB, Manson JE, Liu S. the Genetics of Physical Activity. Current Cardiology Reports, (2017); 19(12): 119.
19. Wang Y, Xue H, Huang Y, Huang L, Zhang D. A Systematic Review of Application and Effectiveness of Health Interventions for Obesity and Diabetes Treatment and Self-Management: Advances in Nutrition. AnInternational Review Journal, (2017); 8(3): 449-62.
20. Rashidi P. Comparison of occupational stress, basal plasma levels of cardiovascular risk factor fibriogen, reactive protein, cortisol, vital vitality and aerobic power in three groups of Malayer female teachers. Thesis, Bu Ali Sina University. (2002) 4; 14-21.
21. Koch SC, Morlinghaus K, Fuchs T. The joy dance: Specific effects of a single dance intervention on psychiatric patients with depression. The Arts in Psychotherapy. 2007;34(4):340-9.
22. Nazari Gilani Nezhad Tayyebeh, Guayani Abasali, Foroughi Abbas, Omidi Nahid. Comparison of the effect of Hotayoga training and aerobic training on serum cortisol levels and stress, anxiety and depression in women with type 2 diabetes." Razi Journal of Medical Sciences, (2017); 24 (15).
23. Alghadir AH, Gabr SA, Aly FA. The effects of four weeks aerobic training on saliva cortisol and testosterone in young healthy persons". Journal of Physical Therapy Science, (2015); 27(7):2029-33.
24. Ogbera AO, Dada O, Adeyeye F, Jewo PI. Complementary and alternative medicine use in diabetes mellitus. West African Journal of Medicine (2011); 29 (3): 158 - 62.
25. Belay, A. New Scientific Developments in the Health Benefits of Spirulina (A1't11rosp1'ra) 1Phycocyanin and its Potential Health Benefits. Nutritional Sciences. (2004); 7(3): 165-173.
26. James Raja, Vasudhevan, Iyyadurai, Sampath, Kunchitam. Interaction of Spirulina with Different Levels of Vitamin E on Growth, Reproduction, and Coloration in Goldfish (Carassius auratus). (2009); 61(4).
27. Choonawala BB (2007). Spirulina production in brine effluent from cooling towers. (M.Tech.:Biotechnology)-Dept. of Biotechnology, Durban University of Technology, 185 leaves.
28. Karkos P, Leong S, Karkos C, Sivaji N, Assimakopoulos D. Spirulina in clinical practice: evidence-based human applications. Evidence-based complementary and alternative medicine. 2011; 3: 4-12.
29. Ravi M, De SL, Azharuddin S, Paul SF. The beneficial effects of Spirulina focusing on its immunomodulatory and antioxidant properties. Nutrition & Dietetics Suppl. 2010;2:73-83.
30. Lee EH, Park J-E, Choi Y-J, Huh K-B, Kim W-Y. A randomized study to establish the effects of spirulina in type 2 diabetes mellitus patients. Nutrition Research and Practice. 2008;2(4):295-300.
31. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. Journal of the american college of cardiology. 2001;37(1):153-6.
32. Hackney AC, Kraemer WJ, Hooper DR. Hormonal Changes Associated with Physical Activity and Exercise Training. Exercise and Human Reproduction: Springer; 2016. p. 125-43.
33. De la Cerda P, Cervello E, Cocca A, Viciana J. Effect of an aerobic training program as complementary therapy in patients with moderate depression. Perceptual and Motor Skills. (2011); 112(3):9 -761.
34. Hayes LD, Grace FM, Sculthorpe N, Herbert P, Ratcliffe JW, Kilduff LP, *et al*. The effects of a formal exercise training programme on salivary hormone concentrations and body composition in previously sedentary aging men. Springerplus. 2013; 2(1): 18.
35. Anderson T, Wideman L. Exercise and the cortisol awakening response: a systematic review. Sports medicine-open. 2017;3(1):3
36. Drust B, Waterhouse J, Atkinson G, Edwards B, Reilly T. Circadian rhythms in sports performance—an update. Chronobiology international. 2005;22(1):21-44.
37. Rutjes AW, Di Nisio M.24 weeks of Pilatesaerobic and educative training to improve body fat mass in elderly Serbian women. Clinical Interventions in Aging. (2014); 28(9): 741-2.
38. Miyamoto GC, Costa LOP, Galvanin T, Cabral CMN. Efficacy of the addition of modified pilates exercises to a minimal intervention in patients with chronic low back pain: a randomized controlled trial. Brazilian Journal of Physical Therapy. (2013); 93(3): 310-20.

39. Del Corral P, Howley ET, Hartsell M, Ashraf M, Younger MS. Metabolic effects of low cortisol during exercise in humans. Journal of Applied Physiology. 1998;84(3):939-47.
40. Viru, A. Mechanism of general adaptation. Med Hypothsis. (1992); 38(4) :296-300.
41. Alam, A., *et al*. "Efficacy of Spirulina (Tahlab) in Patients of Type 2 Diabetes Mellitus (Ziabetus Shakri)-A Randomized Controlled Trial".journal of diabetes & metabolism.issn, J Diabetes Metab,(2016); 7(10): 6155-6156.
42. Kulshreshtha A, Jarouliya U, Bhadauriya P, Prasad G, Bisen P. Spirulina in health care management. Current pharmaceutical biotechnology. 2008; 9(5): 400-5.
43. Jorge MLMP, de Oliveira VN, Resende NM, Paraiso LF, Calixto A, Diniz ALD, *et al*. The effects of aerobic, resistance, and combined exercise on metabolic control, inflammatory markers, adipocytokines, and muscle insulin signaling in patients with type 2 diabetes mellitus. Metabolism. 2011;60(9):1244-52.
44. Ibañez J, Izquierdo M, Argüelles I, Forga L, Larrión JL, García-Unciti M, *et al*. Twice-weekly progressive resistance training decreases abdominal fat and improves insulin sensitivity in older men with type 2 diabetes. Diabetes care. 2005;28(3):662-7.
45. Abd E-Kader, Sh. Aerobic versus resistance exercise training in modulation of insulin resistance, adipocytokines and inflammatory cytokine levels in obese type 2 diabetic patients. Journal of Advanced research, (2011); 2: 179 -183.
46. Fenicchia L, Kanaley J, Azevedo Jr J ,Miller C, Weinstock R, *et al*. (2114). Influence of resistance exercise training on glucose control in women with type 2 diabetes. Metabolism, 53(3):284-9.
47. Venables MC, Achten J, Jeukendrup AE. Determinants of fat oxidation during exercise in healthy men and women: a cross-sectional study. Journal of applied physiology. 2005; 98(1): 160-7.
48. Turgeon JL, Carr MC, Maki PM, Mendelsohn ME, Wise PM. Complex Actions of Sex Steroids in Adipose Tissue, the Cardiovascular System, and Brain: Insights from Basic Science and Clinical Studies. Endocrine Reviews: (2006); 27: 575–605.
49. Giannopoulou I, Ploutz-Snyder LL, Carhart R, Weinstock RS, Fernhall B, *et al*. Exercise is required for visceral fat loss in postmenopausal women with type 2 diabetes. The Journal of Clinical Endocrinology & Metabolism, (2005); 90: 1511–1518.
50. Calle M, Fernandez M. Inflammation and type 2 diabetes. Diabetes & metabolism. 2012; 38(3): 183-91.
51. Mirfiyzy, Mani. Mehdi Zadeh Toursani, Zahra. Asghari Jafar Abadi, Mohammad. Rezvani, Hamid Reza Mirfiyyya, Seyyedeh Zahra. Cranberry fruit effect on blood glucose and lipids control in type II diabetic patients. Scientific Journal of the Army Medical Sciences Academy of the Islamic Republic of Iran, (2009); (9):221-294.
52. Hooshmand B. SHabkhiz. F. Medical Journal of Mashhad University of Medical Sciences, (2008); 61(2): 900-910.