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Research Article

The Effect of Eight Weeks of Concurrent Training on Serum Levels of Paraxonase-1, Irisin, Lipid Profile, and Insulin Resistance in Men With Metabolic Syndrome

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Abstract

Background: Irisin is a myokine suggested to exert anti-obesity benefits. On the other hand, paraxonase-1 (PON 1) is one of the most important free radical scavenging enzymes and is among the main protectors of lipoproteins against oxidizing compounds. This study aimed to evaluate the effect of 8 weeks of *concurrent* training on serum levels of irisin, PON 1, lipid profile, and insulin resistance in men with metabolic syndrome.

Methods: In this quasi-experimental study, 30 men with metabolic syndrome (aged 25-35 years and with body mass > 25 $kg.m^{-2}$) were purposefully selected and randomly divided into two groups of *concurrent* training (n = 15) and control (n = 15). Three sessions of the training program were held per week over an 8-week interval. *Concurrent* training included warm-up, resistance (20 minutes of resistance training), and endurance (25 minutes of activity on a stationary bike with an intensity of 50%-80% of maximum heart rate). Blood samples were collected before and 24 hours after exercise to measure serum levels of variables. Data were analyzed using independent and dependent t-tests.

Results: At baseline, serum levels of PON 1, irisin, and high-density lipoprotein (HDL) were higher in the *concurrent* training group. The results of the study also indicated that 8 weeks of *concurrent* training significantly reduced the levels of insulin resistance, triglycerides (TG), cholesterol, low-density lipoprotein (LDL), systolic, and diastolic blood pressure in men with metabolic syndrome.

Conclusion: Eight weeks of *concurrent* training improves the levels of irisin, insulin resistance, PON 1, and lipid profile of men with metabolic syndrome.

Keywords: *Concurrent* training, Insulin resistance, Irisin, Lipid profile, Paraxonase-1

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Background

Metabolic syndrome, or insulin resistance syndrome, is a metabolic disorder characterized by the presence of several risk factors for cardiovascular disease, including abdominal obesity, hyperlipidemia, hypertension, and insulin resistance. Metabolic syndrome and type 2 diabetes are the predominant risk factors associated with cardiovascular disease in obese people. Of course, the mechanisms by which metabolic syndrome develops in obese people are not well understood yet. Over the past century, researchers have sought a link between muscle contraction and metabolic changes by exercise in other organs such as the liver and adipose tissue. Accordingly, for the last decade, muscle cells have been identified as cells with a high secretory capacity. Muscle cells have a high capacity to produce several hundred secretory factors (1). Adipose tissue accumulation is closely related to obesity. Adipose tissue contributes significantly to regulating energy homeostasis, insulin sensitivity, and carbohydrate and fat metabolisms. Insulin resistance, obesity, and metabolic disorders are strongly associated with increased visceral fat mass (1).

Paraoxonase-1 (PON 1) is involved in the regulation of lipid oxidation (2). PON 1 is a 345-amino acid protein with a molecular volume of 43 kDa, produced in the liver. This enzyme can play a major role in antioxidants and lipoprotein ownership, and it can also prevent the oxidation of lipoproteins and the formation of oxidized low-density lipoprotein (LDL) in vitro. Furthermore, PON 1 prevents the oxidation of high-density lipoprotein (HDL) particles, leading to an increase in serum HDL density (2). Moreover, PON 1 activity has been found to be lower in individuals with metabolic syndrome (3).

Irisin is a hormone derived from fibronectin type III domain-containing 5 (FNDC5) with 212 amino acids. This hormone controls mitochondrial biogenesis and oxidative metabolism in numerous cells and appears to play a mediating role in metabolic disorders that improve with exercise (4). Scientists have reported that this hormone converts white into brown fat, which seems to be in favor of increasing fat metabolism given that brown fat contributes to burning and producing heat. Irisin

is a type of myokine secreted into skeletal muscle and circulates in the blood immediately after physical activity (4). The effect of irisin improves the metabolic program of the tissue and increases energy consumption in the body, which can be considered a new function of irisin in the treatment of metabolic diseases (4).

Lifestyle (e.g., diet and exercise) has been found to be effective in reducing the severity of metabolic syndrome-related disorders such as fasting glucose, triglycerides (TG), waist circumference, and systolic and diastolic blood pressure (5). Ostman et al conducted a review of the literature and reported that exercise can produce beneficial changes in body composition and cardiovascular and metabolic outcomes in people with metabolic syndrome (6). Evidence demonstrates that exercise increases PON 1 levels in healthy (7, 8) and obese individuals (9, 10). Exercise also increases irisin levels in healthy (11, 12) and obese (13, 14) individuals, but little research has been conducted on people with metabolic syndrome.

Objectives

Therefore, this study aimed to evaluate the effect of 8 weeks of *concurrent* training on PON 1, irisin, insulin resistance, and lipid profile of men with metabolic syndrome.

Materials and Methods

The statistical sample of this quasi-experimental study consisted of 30 inactive men (using software G*Power – G) with symptoms of metabolic syndrome (according to the International Diabetes Committee, the main emphasis is on abdominal obesity, which varies by race). Based on this definition, the waist size set for abdominal obesity in Caucasians is ≥94 cm for men and ≥80 cm for women, aged 25-35 years old, with a body mass index (BMI) of > 25 kg/m^2. They did not attend any regular exercise programs for at least 6 months before the start of the study and only performed daily activities. The study used the pretest-posttest design with a control group. Subjects were selected voluntarily through a questionnaire and were then randomly divided into a *concurrent* training group (n = 15) and a control group (n = 15).

Inclusion criteria included no history of cardiovascular disease, blood, liver, kidney, respiratory, and hormonal disorders, smoking or sleep disorders, no surgery in the past year, no history of specific drugs, and no prohibition of exercise as ordered by the treating physician. It should be noted that studies obtained from the Physical Activity Readiness Questionnaire revealed that the subjects were able to perform sports activities. Before starting the operational stages of the study, the subjects were provided with relative knowledge about the type of tests and the method of conducting the research. Fasting blood samples were taken from all subjects 24 hours before the first training session and 24 hours after the last training session.

After pre-test measurements, the subjects in the *concurrent* training group received the training protocol for 3 sessions per week for 8 weeks. *Concurrent* training included warm-up, resistance, and endurance. In the warm-up session, the subjects did stretching activities with an intensity of 50% to 60% of maximum heart rate for 5 minutes. In resistance training, on the first day, the subjects performed resistance training of upper body activities for 20 minutes with a barbell bar. On the second day, spinal stabilization, deep muscle, and balance exercises were performed with a gymnastic ball. On the third day, special lower body exercises were performed with a barbell. The number of repetitions of each sports activity in each set depended on the muscular strength of each person, while the equivalent of the correct number of repetitions and the number of repetitions increased systematically with increasing the muscle strength of the subjects. There was a 10- to 15-second rest between the sets of resistance activity. In the endurance session, the subjects performed activities on a treadmill for 25 minutes with an intensity of 50% to 80% of maximum heart rate and were ultimately cooled down by doing 5 minutes of low-intensity stretching and breathing exercises (15). The subjects in the control group performed their usual daily activities.

Twenty-four hours after the end of the training period, post-test blood sampling was performed in a way similar to the pre-test conditions. After blood sampling, the samples were centrifuged for 20 minutes at 3000 rpm, and the isolated serum was kept at -80°C. In addition, a 100-item food questionnaire was used during 3 even and odd days to control the diet and calorie intake of the subjects. Then, the subjects' diet was simulated according to their reports to reduce the effect on the daily calorie intake (16).

A German-made Ska gauge and a hand scale were used to measure height and weight. The formula for BMI is weight in kilograms (kg) divided by height in meters squared (m^2), which was used to calculate BMI after measuring height and weight. Further, the OMRON M7 mercury sphygmomanometer, made in China, was used to measure blood pressure. Serum levels of PON 1 were measured by the ELISA sandwich method, produced by the German company ZellBio and supplied by the Padgin Institute of Medicine. This measurement is based on the calorimetric method and has a wavelength of 412 nm. Serum levels of irisin were measured using a kit (Cusabio Human Elisa, Sensitivity 0.78 ng/mL). Measurement of fasting glucose and blood lipids (e.g., TG, total cholesterol [COL], HDL cholesterol, and LDL cholesterol) was carried out enzymatically (Hitachi, Tokyo, Japan). Radioimmunoassay (i.e., Monobind, Inc, USA) was used to measure fasting insulin. The coefficient of change inside and outside the insulin test was less than 4%. Homeostasis model evaluation was used to determine fasting insulin resistance using fasting blood glucose and insulin levels. Further, paired samples *t* test and independent samples *t* test were used for statistical analysis and comparison of

groups after confirming the normal distribution of data using the Kolmogorov-Smirnov test.

Results

Table 1 presents the descriptive information of contextual variables, including age, height, weight, and BMI.

Table 2 illustrates the statistical indicators related to the main research variables in the two groups of *concurrent* training and control. The results of comparing control and training groups in pre- and post-test using the independent t-test showed a significant increase in PON 1 ($P=0.041$) in the training group compared to the control group (Table 2). Moreover, the results of serum irisin level in the post test revealed a significant difference between the control and training groups, suggesting an increase in the training group ($P=0.006$).

According to the results of the in-group comparison using the dependent *t* test in Table 2, serum PON 1 levels during 8 weeks of *concurrent* training revealed a significant increase in the post-test training group compared to the pre-test ($P=0.002$). In addition, there was a significant increase in serum irisin in the exercise group in the post-test compared to the pre-test ($P=0.0001$).

Regarding insulin resistance and lipid profile, the findings of this study showed that the intragroup changes of the studied variables in the training group were significant after 8 weeks of *concurrent* training; that is, a decrease was found in insulin resistance ($P=0.001$), LDL ($P=0.021$), COL ($P=0.002$), TG ($P=0.004$), and systolic ($P=0.002$) and diastolic ($P=0.010$) blood pressure in the raining group, while there was an increase in HDL ($P=0.0001$). With regard to intergroup changes, there was a decrease in insulin resistance ($P=0.032$), LDL ($P=0.045$), COL ($P=0.026$), TG ($P=0.027$), and systolic ($P=0.046$) and diastolic blood pressure ($P=0.004$) compared with the control group, while an increase was observed in HDL ($P=0.017$).

Table 1. Individual Characteristics of the Subjects at the Basic Level

Group	*Concurrent* Training	Control	*P*
Age (y)	29.33 ± 2.94	30.26 ± 3.15	-
Height (cm)	166.33 ± 5.99	165.53 ± 5.50	-
Weight (kg)	86.13 ± 8.39	83.06 ± 5.73	0.45
BMI (kg/m^2)	31.07 ± 1.72	30.31 ± 1.53	0.35

Note. BMI: Body mass index; SD: Standard deviation; Data are presented as means ± SD; * Significant sign of difference between the two groups is $P<0.05$.

Discussion

The results of the present study indicated that 8 weeks of *concurrent* training significantly increased serum PON 1 levels in men with metabolic syndrome compared to the control group and compared to the time before training. Examining the research background, it can be said that scarce research has been conducted on the effect of combination exercises on this factor in people with a metabolic syndrome so far. Consistent with the present study, Ghorbani and Shokrollahi reported the effect of 8 weeks of rope training as contributing to significant improvement in PON 1 levels, insulin resistance, and

Table 2. Changes (Mean and SD) in Research Parameters in *Concurrent* Training and Control Groups

Variable	Group	Pre-test Mean ± SD	Post-test Mean ± SD	Intragroup Changes		Intergroup Changes	
				t	*P*	*t*	*P*
PON 1 (U/L)	*Concurrent* training	76.92 ± 14.68	92.98 ± 22.01	-3.91	0.002	2.14	0.041
	Control	79.18 ± 15.02	81.48 ± 11.84	-0.046	0.64		
Irisin (ng/mL)	*Concurrent* training	113.26 ± 17.83	120.60 ± 16.20	-5.20	0.0001	3.005	0.006
	Control	119.60 ± 12.97	119.20 ± 13.10	0.18	0.85		
Insulin resistance (HOMA-IR)	*Concurrent* training	3.75 ± 1.29	2.77 ± 1.30	4.34	0.001	-2.25	0.032
	Control	3.52 ± 1.44	3.19 ± 1.11	1.77	0.097		
LDL (mg/dL)	*Concurrent* training	92.06 ± 14.75	89.80 ± 14.95	2..58	0.021	-2.09	0.045
	Control	89.93 ± 14.49	88.13 ± 15.91	-0.85	0.40		
HDL (mg/dL)	*Concurrent* training	45.66 ± 6.47	49.666.33	-5.63	0.0001	2.52	0.017
	Control	45.869.67	46.469.60	-0.52	0.60		
COL (mg/dL)	*Concurrent* training	160.20 ± 24.2	150.53 ± 24.3	3.75	0.002	-2.34	0.026
	Control	149.4 ± 33.68	148.0 ± 31.54	0.58	0.56		
TG (mg/dL)	*Concurrent* training	173.20 ± 38.99	154.40 ± 35.53	3.43	0.004	-2.32	0.027
	Control	169.93 ± 37.22	168.26 ± 38.06	0.33	0.74		
Systolic blood pressure (mm Hg)	*Concurrent* training	14.06 ± 1.01	13.72 ± 1.26	-3.16	0.002	-1.99	0.046
	Control	13.33 ± 0.95	13.46 ± 1.04	-1.27	0.20		
Diastolic blood pressure (mm Hg)	*Concurrent* training	9.43 ± .067	8.90 ± 0.92	-2.58	0.010	-2.84	0.004
	Control	9.06 ± 0.96	9.13 ± 0.91	-0.57	0.56		

Note. SD: Standard deviation; PON 1: Paraoxonase-1; HOMA-IR: Homeostasis model; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; COL: Total cholesterol; TG: Triglycerides.

lipid profile of inactive girls (17). Ahmadi et al, in a study, compared the effect of 8 weeks of aerobic and resistance training on the activity of PON 1, aryl esterase, and lipid profile in obese girls. The experimental groups performed aerobic exercise on a treadmill with an intensity of 60% to 75% of the stored heart rate and performed resistance training with an intensity of 55% to 75% of a maximum repetition for 8 weeks. The results showed that aerobic exercise has a significant effect on the concentrations of PON 1 and aryl esterase in obese girls (9). In contrast, Fatolahi et al found no significant changes in serum PON 1 levels in obese men after 21 days of diet and 45 minutes of aerobic exercise on a treadmill with an intensity of 70% to 85% of maximum heart rate for 60 days (18). Further, Taylor et al examined the effect of 12 weeks of endurance running training (196 ± 15 minutes/week) on serum levels of PON 1 in men and women with metabolic syndrome, finding no changes in PON levels (19). On the other hand, Tas et al observed that two methods of intermittent and continuous exercise (8 weeks, 3 sessions per week, and each session for 25-60 minutes) reduced serum PON levels in a warm environment. The discrepancies between the findings of these researchers and the findings of the present study are probably due to the influence of genetic factors, lifestyle, smoking, physical fitness, sex, and age of the subjects as well as the method, intensity, and the duration of the training (20). On the other hand, diet also affects PON 1 activity and its antioxidant levels. It is possible that the type of response and adaptation in the age groups be also influenced by physiological conditions. Age is the determining factor in PON 1 activity (21). Human studies have indicated that serum PON 1 activity is extremely low at birth and increases over time. PON 1 activity in adulthood is almost constant over time. In middle-aged people, PON 1 activity may decrease with the onset of oxidative stress conditions (22). In metabolic diseases such as diabetes, obesity, and most importantly, metabolic syndrome, the balance between antioxidants and free radicals is lost, accelerating the process of diabetes disease complications due to the increase of oxidants in the body (23). Various mechanisms have been devised to eliminate or reduce free radicals, including various proteins and enzymes that cause the degradation of free radicals. PON 1 is one of the most important free radical scavenging enzymes and is among the main proteins of lipoproteins against oxidizing compounds. The power of PON 1 has recently been found to reduce the oxidizing power of lipids in atherosclerotic lesions, thus providing protection against oxidation. Epidemiological evidence shows that decreased PON 1 activity is associated with an increased risk of cardiovascular events, which is an independent risk factor for diabetes and cardiovascular disease (7). In some studies, improvements in the antioxidant defense mechanism with regular long-term exercise have exhibited that high-intensity exercise increases the production of free radicals through high oxygen consumption for 10 to 20 minutes and reduces oxidative stress and the antioxidant defense system (24). Given the significant increase in serum PON 1 levels in the exercise group, it may be concluded that *concurrent* training may be an important factor in improving diabetes, obesity, and metabolic syndrome in individuals with metabolic syndrome and disease. The summary of research findings indicates that the type of training protocol, training intensity, and participants in the test contribute to the effect of exercise on PON 1 activity (19). However, more research is needed to elucidate the molecular mechanism of PON 1 and the changes in serum concentrations and activity of this enzyme in the body as a result of physical activity, especially *concurrent* training.

The results of the present study suggested that 8 weeks of *concurrent* training increased irisin. The findings are consistent with the findings of Reisi (25), Khodadadi et al (14), and Boström et al (26). On the other hand, they are not consistent with the results of research by Norheim et al (27). This inconsistency may be due to the type of exercise, the intensity of the exercise, the sex of the subjects, and the physiological adaptations to long-term exercise (25). In their study on the effect of resistance training on plasma irisin protein in male rats, Reisi (25) concluded that plasma irisin protein increased significantly after 32 sessions of resistance training. Resistance training may improve body composition by increasing the conversion of white to brown fats through secreting myokines such as irisin. Irisin is one of the myokines which was found to increase following the exercise. Hence, after exercise and physical activity, peroxisome proliferator-activated receptor gamma coactivator-1 alpha expression increases as a transcriptional activating molecule, stimulating the expression of FNDC5 membrane protein in muscle cells. The FNDC5 molecule released from the membrane of muscle cells is broken down, and a part of it enters the bloodstream called irisin. The irisin molecule produces binds to peroxisome proliferator-activated receptor alpha receptors on the surface of white adipose tissue and converts white adipose tissue to brown adipose tissue by increasing the expression of these receptors. On the other hand, the irisin molecule can increase the mitochondrial content of white adipose tissue and increase its conversion to brown adipose tissue by enhancing the expression of the uncoupling protein 1 molecule on the surface of white adipose tissue. This function of irisin is associated with increased metabolic activity and energy consumption in the body, which is considered a new function of irisin in the treatment of metabolic diseases (28). Irisin can also lead to the browning of adipose tissue by inhibiting phosphoinositide 3-kinase senzyme signaling and increasing the expression of phosphatase and tensin homologmolecules (29). Depending on the type of exercise and the activated signaling pathways, the myokines associated with those targets regulate processes within the skeletal muscle and other tissues.

Moreover, the importance of the regulatory role of irisin in the insulin resistance index and the lack of available data on the response of irisin to short-term exercise is recognized (14).

Furthermore, the results of the present study revealed that 8 weeks of *concurrent* training reduced insulin resistance, which are consistent with the findings of Monteiro et al (30) and Aminilari et al (31). However, this result is inconsistent with the results of Zarei et al (32) and Jeon et al (33). This discrepancy may be due to the intensity of training, the type of subjects, the type of exercise, and the sex or age of the subjects. Jeon et al (33) evaluated the effect of 12 weeks of aerobic and resistance training with a controlled diet on 30 overweight men and concluded that insulin resistance in both aerobic and resistance groups was significantly higher than that in the diet-only group. Previous research has proved that insulin secretion is inhibited due to increased levels of norepinephrine resulting from exercise. It is also possible that the decrease in insulin due to exercise is associated with the saving of glucose consumption, which limits the consumption of blood glucose by the muscles, making blood glucose more available to the brain. Among the possible causes of decreased insulin resistance due to activity, we can mention insulin-independent mechanisms such as increasing the amount of glucose transporter type 4 because of muscle contractions (34). Mann et al (34) found that both intensity and duration of exercise were effective so that the improvement in insulin sensitivity occurred when applied exercise was at its highest level. Therefore, according to the characteristics of the subjects in the present study, probably 3 training sessions per week for 8 weeks were sufficient to achieve a significant change in insulin and insulin resistance index. Insulin resistance and impaired glucose metabolism are generally gradual processes that begin with overweight and obesity. Studies demonstrated that exercise improves glucose homeostasis and increases insulin sensitivity. Mann et al (34) found that mechanisms that can increase insulin action after exercise include increased signaling of insulin receptors, higher levels of glucose transporter protein, greater glycogen storage capacity due to increased glycogen synthetase and hexokinase activity, more glucose release from blood to muscle because of increased muscle capillaries and changes in muscle composition to enhance glucose uptake, and decreased release and increased clearance of free fatty acids (34).

In addition, the results of the present study suggested that performing 8 weeks of *concurrent* training (resistance-endurance) decreased LDL, TG, and cholesterol while increasing HDL compared to the control group. So far, many studies have investigated the effect of different exercises on lipid profiles. The results of the present study are consistent with the results of the study by Hajinia et al (35) and Hosseini Kakhk et al (36) but do not agree with the results of Abedi et al (37) and Haghighi et al (38). This discrepancy can be attributed to the physiological characteristics of the subjects, the intensity and type of exercise, and the subjects' genetic characteristics. Jamali et al (39) examined the effects of eight weeks of resistance training on obese and overweight boys aged 13-14 years, finding that these exercises had no effects on cholesterol, LDL, and TG levels. Another study by Haghighi et al (38) showed that 8-week aerobic training and green tea supplementation on body fat percentage and serum lipid profiles have no significant effects on low-density lipoprotein levels in obese and overweight women. On the other hand, the results of the present study are consistent with the results of the studies conducted by Ghasemnian et al (40) and Calders et al (41). Ghasemnian et al (40) reported that 8 weeks of *concurrent* training reduced plasma TG. In another study, Calders et al (41) found that *concurrent* training lowered cholesterol and LDL. Exercise generally increases plasma volume, which may increase the absolute amount of high-density lipoprotein, while its concentration may not change or may even decrease. In terms of age, some studies have revealed that the mismatching of training intensity led to poor adaptations in blood lipid profiles. High- and low-intensity exercise has been reported to increase low-density lipoprotein levels in untrained adolescents. Since plasma fats are expressed in terms of their concentration (milligrams of fat per deciliter of blood), any change in plasma volume, regardless of the change in total fat, affects its plasma concentration (33). In addition, plasma fat levels are highly dependent on changes in body weight. Therefore, the independent effects of body weight change on plasma fats should also be considered when evaluating the effects of exercise (33).

Conclusion

Overall, the findings of the present study indicated that 8 weeks of *concurrent* training through the secretion of myokines such as irisin increased PON 1 while decreasing insulin resistance and lipid profile in men with metabolic syndrome. Therefore, it can be useful and valuable to prevent or reduce metabolic syndrome and promote men's health.

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Author Contributions

Conceptualization [SAHDH]; Methodology [BA]; Investigation [MV]; Writing and Original Draft [SAHDH]; Writing, Reviewing, and Editing [All Authors]; Funding Acquisition [All Authors]; Resources [All Authors]; Supervision [BA].

Conflict of Interests

The authors declare that they have no conflict of interests.

Ethical Approval

The present study was approved by the Ethics Organization in

Biomedical Research of Mahallat Islamic Azad University (code: 20021404972002). All ethical principles were considered in this study. The participants were informed of the purpose of the study and its stages, and informed consent was obtained from all subjects. They were also assured of the confidentiality of their information. Moreover, the subjects were free to withdraw from the study at any stage. They were also informed that they would be provided with the results of the research.

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References

1. Azarpazhooh MR, Najafi F, Darbandi M, Kiarasi S, Oduyemi T, Spence JD. Triglyceride/high-density lipoprotein cholesterol ratio: a clue to metabolic syndrome, insulin resistance, and severe atherosclerosis. Lipids. 2021;56(4):405-12. doi: 10.1002/lipd.12302.
2. Esmaeilnejad B, Dalir-Naghadeh B, Tavassoli M, Asri-Rezaei S, Mahmoudi S, Rajabi S, et al. Assessment of hepatic oxidative damage, paraoxonase-1 activity, and lipid profile in cattle naturally infected with *Babesia bigemina*. Trop Anim Health Prod. 2021;53(2):219. doi: 10.1007/s11250-021-02662-x.
3. Meneses MJ, Silvestre R, Sousa-Lima I, Macedo MP. Paraoxonase-1 as a regulator of glucose and lipid homeostasis: impact on the onset and progression of metabolic disorders. Int J Mol Sci. 2019;20(16):4049. doi: 10.3390/ijms20164049.
4. De Sousa RAL, Improta-Caria AC, de Freitas Souza BS. Exercise-linked irisin: consequences on mental and cardiovascular health in type 2 diabetes. Int J Mol Sci. 2021;22(4):2199. doi: 10.3390/ijms22042199.
5. Yamaoka K, Tango T. Effects of lifestyle modification on metabolic syndrome: a systematic review and meta-analysis. BMC Med. 2012;10:138. doi: 10.1186/1741-7015-10-138.
6. Ostman C, Smart NA, Morcos D, Duller A, Ridley W, Jewiss D. The effect of exercise training on clinical outcomes in patients with the metabolic syndrome: a systematic review and meta-analysis. Cardiovasc Diabetol. 2017;16(1):110. doi: 10.1186/s12933-017-0590-y.
7. Taheri Chadorneshin H, Abtahi-Eivary S, Cheragh-Birjandi S, Yaghoubi A, Ajam-Zibad M. The effect of exercise training type on paraoxonase-1 and lipid profile in rats. Shiraz E Med J. 2017;18(7):e46131. doi: 10.5812/semj.46131.
8. Turgay F, Ongun A, Çolakoğlu M. Effects of long-term training, periods of detraining and retraining on paraoxonase 1 activity in child swimmers. Turkiye Klinikleri J Sports Sci. 2018 Oct 1;10(3):130-8. doi: 10.5336/sportsci.2018-61534.
9. Ahmadi M, Abbassi Daloii A, Behbudi L. Comparison between the effects of eight weeks of aerobic and resistance training on paraoxonase-1, arylesterase activity and lipid profile in obese girls. Sci J Kurd Univ Med Sci. 2016;21(4):83-93. [Persian].
10. Roberts CK, Ng C, Hama S, Eliseo AJ, Barnard RJ. Effect of a short-term diet and exercise intervention on inflammatory/anti-inflammatory properties of HDL in overweight/obese men with cardiovascular risk factors. J Appl Physiol (1985). 2006;101(6):1727-32. doi: 10.1152/japplphysiol.00345.2006.
11. Leal LG, Lopes MA, Batista ML Jr. Physical exercise-induced myokines and muscle-adipose tissue crosstalk: a review of current knowledge and the implications for health and metabolic diseases. Front Physiol. 2018;9:1307. doi: 10.3389/fphys.2018.01307.
12. Huh JY, Siopi A, Mougios V, Park KH, Mantzoros CS. Irisin in response to exercise in humans with and without metabolic syndrome. J Clin Endocrinol Metab. 2015;100(3):E453-7. doi: 10.1210/jc.2014-2416.
13. Abedi B, Akhlaghi R, Saremi A. Plasma irisin increases after acute endurance exercise in obese and normal weight women. Complementary Medicine Journal. 2017;2(23):1887-96. [Persian].
14. Khodadadi H, Rajabi H, Attarzadeh Hosseini SR, Abbasian S. The Effect of high intensity interval training (HIIT) and pilates on levels of irisin and insulin resistance in overweight women. Iran J Endocrinol Metab. 2014;16(3):190-6. [Persian].
15. Skrypnik D, Bogdański P, Mądry E, Karolkiewicz J, Ratajczak M, Kryściak J, et al. Effects of endurance and endurance strength training on body composition and physical capacity in women with abdominal obesity. Obes Facts. 2015;8(3):175-87. doi: 10.1159/000431002.
16. Potischman N, Carroll RJ, Iturria SJ, Mittl B, Curtin J, Thompson FE, et al. Comparison of the 60- and 100-item NCI-block questionnaires with validation data. Nutr Cancer. 1999;34(1):70-5. doi: 10.1207/s15327914nc340110.
17. Ghorbanian B, Shokrollahi F. The effects of rope training on paraoxonase-1 enzyme, insulin resistance and lipid profiles in inactive girls. Tehran Univ Med J. 2017;75(4):307-15. [Persian].
18. Fatolahi H, Azarbayjani MA, Peeri M, Matin Homaee H. The effect of exercise on paraoxonase-1 activity and lipid profile in obesity and insulin resistance conditions. Iran J Diabetes Obes. 2017;9(1):82-93. [Persian].
19. Taylor JK, Carpio-Rivera E, Chacón-Araya Y, Grandjean PW, Moncada-Jiménez J. The effects of acute and chronic exercise on paraoxonase-1 (PON1): a systematic review with meta-analysis. Res Q Exerc Sport. 2022;93(1):130-43. doi: 10.1080/02701367.2020.1812493.
20. Taş M, Zorba E, Yaman M. Comparison of the effects of different training methods on arylesterase activity and paraoxonase activity levels in hot environment. TOJRAS: The Online Journal of Recreation and Sport. 2012;1(1):1-8.
21. Otocka-Kmiecik A, Bortnik K, Szkudlarek U, Nowak D, Orłowska-Majdak M. Effect of exercise on plasma paraoxonase1 activity in rugby players: dependance on training experience. Redox Rep. 2013;18(3):113-9. doi: 10.1179/1351000213y.0000000047.
22. Korkmaz A, Venojärvi M, Wasenius N, Manderoos S, Deruisseau KC, Gidlund EK, et al. Plasma irisin is increased following 12 weeks of Nordic walking and associates with glucose homoeostasis in overweight/obese men with impaired glucose regulation. Eur J Sport Sci. 2019;19(2):258-66. doi: 10.1080/17461391.2018.1506504.
23. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. J Clin Invest. 2004;114(12):1752-61. doi: 10.1172/jci21625.
24. Taherkhani S, Valaei K, Arazi H, Suzuki K. An overview of physical exercise and antioxidant supplementation influences on skeletal muscle oxidative stress. Antioxidants (Basel). 2021;10(10):1528. doi: 10.3390/antiox10101528.
25. Reisi J. Effect of 8 weeks resistance training on plasma irisin protein level and muscle FNDC5 and adipose tissue UCP1 genes expression in male rats. Sport Physiol. 2016;7(28):117-30. [Persian].
26. Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, et al. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012;481(7382):463-8. doi: 10.1038/nature10777.
27. Norheim F, Langleite TM, Hjorth M, Holen T, Kielland A, Stadheim HK, et al. The effects of acute and chronic exercise on PGC-1α, irisin and browning of subcutaneous adipose tissue in humans. Febs j. 2014;281(3):739-49. doi: 10.1111/

febs.12619.
28. Castillo-Quan JI. From white to brown fat through the PGC-1α-dependent myokine irisin: implications for diabetes and obesity. Dis Model Mech. 2012;5(3):293-5. doi: 10.1242/dmm.009894.
29. Jaffari H, Abedi B, Fatolah H. The effect of 8 weeks of carob supplementation and resistance training on lipid profile and irisin in obese men. Int J Sport Exc Health Res. 2020;4(2):91-5. doi: 10.31254/sportmed.4212.
30. Monteiro PA, Chen KY, Lira FS, Saraiva BT, Antunes BM, Campos EZ, et al. Concurrent and aerobic exercise training promote similar benefits in body composition and metabolic profiles in obese adolescents. Lipids Health Dis. 2015;14:153. doi: 10.1186/s12944-015-0152-9.
31. AminiLari Z, Fararouei M, Amanat S, Sinaei E, Dianatinasab S, AminiLari M, et al. The effect of 12 weeks aerobic, resistance, and combined exercises on omentin-1 levels and insulin resistance among type 2 diabetic middle-aged women. Diabetes Metab J. 2017;41(3):205-12. doi: 10.4093/dmj.2017.41.3.205.
32. Zarei M, Beheshti Nasr SM, Hamedinia M, Taheri Chadorneshin H, Askari Majdabadi H. Effects of 12 weeks of combined aerobic-resistance exercise training on levels of chemerin, omentin and insulin resistance in men with type 2 diabetes. Koomesh. 2020;22(1):155-63. doi: 10.29252/koomesh.22.1.155. [Persian].
33. Jeon YK, Kim SS, Kim JH, Kim HJ, Kim HJ, Park JJ, et al. Combined aerobic and resistance exercise training reduces circulating apolipoprotein J levels and improves insulin resistance in postmenopausal diabetic women. Diabetes Metab J. 2020;44(1):103-12. doi: 10.4093/dmj.2018.0160.
34. Mann S, Beedie C, Balducci S, Zanuso S, Allgrove J, Bertiato F, et al. Changes in insulin sensitivity in response to different modalities of exercise: a review of the evidence. Diabetes Metab Res Rev. 2014;30(4):257-68. doi: 10.1002/dmrr.2488.
35. Hajinia M, Haghighi A, Askari R.The effect of high-intensity interval training and high-intensity resistance training on the lipid profile and body composition in overweight and obese men. JTorbat Heydariyeh Univ Med Sci. 2020;8(3):61-74. [Persian].
36. Hosseini Kakhk SA, Khaleghzadeh H, Nematy M, Hamedinia M. The effect of combined aerobic- resistance training on lipid profile and liver enzymes in patients with non-alcoholic fatty liver under nutrition diet. Sport Physiol. 2015;7(27):65-84. [Persian].
37. Abedi B, Poorfakhimi Abarghu J, Ghadami A, Amini Rarani S. The effects of resistance training and green tea supplementation on lipid profile and insulin resistance in obese and overweight men. Complementary Medicine Journal. 2017;7(1):1767-76. [Persian].
38. Haghighi AH, Yaghoubi M, Hosseini Kakhk SA. The effect of eight weeks aerobic training and green tea supplementation on body fat percentage and serum lipid profiles in obese and overweight women. Med J Mashhad Univ Med Sci. 2013;56(4):211-8. doi: 10.22038/mjms.2013.1757. [Persian].
39. Jamali E, Asad MR, Rassouli A. Effect of eight-week endurance exercise on resistin gene expression in visceral adipose tissues in obese rats. J Shahid Sadoughi Univ Med Sci. 2017;25(1):20-31. [Persian].
40. Ghasemnian AA, Ghorbanian B, Gorzi A. The effects of 8 weeks ofintervalcombinedexercise trainingon risk factorsof asthma, insulin resistanceand some of the major physiological indices in overweight and obese adolescents. Sci J Kurd Univ Med Sci. 2014;19(1):67-77. doi: 10.22102/19.1.67. [Persian].
41. Calders P, Elmahgoub S, Roman de Mettelinge T, Vandenbroeck C, Dewandele I, Rombaut L, et al. Effect of combined exercise training on physical and metabolic fitness in adults with intellectual disability: a controlled trial. Clin Rehabil. 2011;25(12):1097-108. doi: 10.1177/0269215511407221.