# The response of serum adipolin levels and insulin resistance index to high-intensity interval training in overweight men

## Respuesta de los niveles séricos de adipolina y del índice de resistencia a la insulina al entrenamiento en intervalos de alta intensidad en hombres con sobrepeso



Davar Rezaeimanesh. The department of General Courses and Basic Sciences, the College of Maritime Economics and Management, Khorramshahr University of Marine Science and Technology, Khorramshahr, Iran. Email: davarrezaee@yahoo.com
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**Abstract**

**Background**: Adipolin is mainly expressed and synthesized from fat tissue, and with its anti-inflammatory properties, while improving insulin sensitivity, it also plays a role in reducing blood glucose levels. Therefore, in this study, the response of serum adipolin levels and insulin resistance index to High-Intensity Interval Training in Overweight Men was investigated.

**Materials and Methods**: 24 overweight men (body mass index more than 25 kg/m2) were voluntarily selected and randomly divided into two groups of experimental (n=12) and control (n=12). The experimental group participated in 8 weeks of high intensity interval training (HIIT) via three sessions per week. Before and after intervention, blood sampling was performed to measure the serum levels of Adipolin, insulin, and fasting glucose. To analyze the data, independent t-test at the level of P<0.05 was used.

**Results**: The comparison between the groups indicated that the values of adipolin and insulin resistance index significant improvement in the post-test of the experimental group compared to the control group (P>0.05). Based on the results of the intra-group test, the performance of high intensity interval training causing a significant increase in adipoline and a significant decrease in glucose, insulin and insulin resistance index in the experimental group.

**Conclusion**: It seems that the implementation of high intensity interval training can have a major contribution to weight loss in overweight people by increasing adipoline and reducing the index of insulin resistance.

**Keywords:** Adipolin, Glucose, Insulin, Insulin resistance index

**Resumen**

**Antecedentes**: La adipolina se expresa y sintetiza principalmente a partir del tejido adiposo, y con sus propiedades antiinflamatorias, al tiempo que mejora la sensibilidad a la insulina, también desempeña un papel en la reducción de los niveles de glucosa en sangre. Por lo tanto, en este estudio se investigó la respuesta de los niveles séricos de adipolina y del índice de resistencia a la insulina al entrenamiento en intervalos de alta intensidad en hombres con sobrepeso.

**Materiales y métodos**: Se seleccionaron voluntariamente 24 hombres con sobrepeso (índice de masa corporal superior a 25 kg/m2) y se dividieron aleatoriamente en dos grupos: experimental (n=12) y control (n=12). El grupo experimental participó en 8 semanas de entrenamiento interválico de alta intensidad (HIIT) mediante tres sesiones semanales. Antes y después de la intervención, se tomaron muestras de sangre para medir los niveles séricos de adipolina, insulina y glucosa en ayunas. Para analizar los datos, se utilizó la prueba t independiente al nivel de P<0,05.

**Resultados**: La comparación entre los grupos indicó que los valores de adipolina e índice de resistencia a la insulina mejoraron significativamente en el post-test del grupo experimental en comparación con el grupo control (P>0,05). En base a los resultados de la prueba intragrupo, la realización del entrenamiento interválico de alta intensidad provocó un aumento significativo de la adipolina y una disminución significativa de la glucosa, la insulina y el índice de resistencia a la insulina en el grupo experimental. Conclusiones: Parece que la realización del entrenamiento interválico de alta intensidad puede tener una importante contribución a la pérdida de peso en personas con sobrepeso al aumentar la adipolina y reducir el índice de resistencia a la insulina.

**Palabras clave:** Adipolina, Glucosa, Insulina, Índice de resistencia a la insulina

The global prevalence of overweight and obesity is rapidly increasing due to a trend toward a modern lifestyle and decreased physical activity. Men have a higher prevalence of obesity and overweight than women[1]. According to the studies, obesity alters the number of adipokines and increases the number of reactive oxygen species, thereby accelerating the progression of cardiovascular diseases and atherosclerosis. Changing one's lifestyle, particularly by increasing physical activity and exercise, is one of the effective strategies that can significantly prevent overweight and obesity and, as a result, its complications[2]. Adipose tissue accumulation is the primary cause of obesity. In addition to regulating blood lipids, adipose tissue regulates energy, insulin sensitivity, and the metabolism of carbohydrates and fats. Recent research demonstrates that adipose tissue secretes numerous peptide hormones[3]. The most significant ones are leptin, resistin, vaspin, adiponectin, and visfatin. Insulin resistance, obesity, and other metabolic disorders that result in mild chronic inflammation are correlated with increased adipose tissue and adipokines secretion from this tissue[4].

Regulating energy homeostasis requires the complex and coordinated actions of numerous organs and tissues, whose communication is regulated by hormones[5]. Biologically active proteins such as adipokines and hepatokines are secreted by adipose tissue and organs such as the liver and muscles; these biologically active proteins modulate autocrine/paracrine metabolic processes in target tissues. Disruption in hormone signaling in obesity is often associated with metabolic diseases such as type 2 diabetes[6].

Adipokines secreted by adipose tissue are regarded as the body's most essential metabolic regulators. These regulators control food consumption, glucose utilization, insulin resistance, fatty acid uptake and utilization, and inflammation. Consequently, the function of these adipokines are essential for the body's normal homeostasis, and disruption of the pathways they regulate leads to metabolic diseases such as obesity, inflammation, and type 2 diabetes[7].

Recent research has identified a group of C1q/TNF-related proteins (CTRP) that regulate metabolic and cardiovascular functions. Adipolin, also known as CTRP12, is the 12th member of the anti-inflammatory C1q/TNF family[8]. This adipocytokine, which has recently garnered the interest of researchers, is frequently synthesized and secreted by adipose tissue. Researchers found that an increase in circulating levels of adipolin decreases blood glucose levels and improves insulin sensitivity, which probably improves the body's insulin resistance by reducing adipose tissue inflammation[9].

Adipolin protein, an anti-inflammatory and insulin-sensitizing adipokine, is abundantly expressed and produced in adipose tissue. According to the findings, diabetes and obesity reduce adipolin synthesis and expression[11]. Given that obesity decreases adipolin levels, methods that increase adipolin may be useful for preventing and treating insulin resistance in type 2 diabetes patients. The results indicate that a disturbance causes metabolic disorders and cardiovascular complications in adipolin level due to increased fat mass and disruption in glucose and insulin metabolism[12].

Results indicate that in obese individuals, adipolin is negatively modulated by the vicious cycle of TNF-α, TGF-β1, and furin; therefore, any factor that can reduce the inflammatory conditions caused by obesity and affect this vicious cycle can modulate adipolin levels and provide the means to improve insulin sensitivity[13]. Physical activity is one of the most important medical and non-invasive strategies to improve insulin sensitivity and modulate insulin resistance; consequently, sports activity may contribute to improving insulin resistance by influencing insulin and glucose and improving their functions and metabolism by influencing the components of this chain. Since a sedentary (inactive) lifestyle and weight gain are associated with insulin resistance, and considering the evidence obtained regarding the importance of high-intensity interval training (HIIT) in reducing weight and improving insulin resistance, it is essential to investigate the effects of interval training on obese subjects. However, the importance of exercise in modulating metabolic disease risk factors is dependent on the intensity and volume of exercise[14]. Interval training is a suitable and effective method for controlling and reducing the risk of metabolic diseases due to the appropriate intensity and volume of exercise. According to the findings, interval training is more beneficial to health than low-intensity cardio training[15].

On the other hand, there is an increased interest in participating in a short-term exercise program that can increase physical fitness as desired. There is a growing interest in implementing interval training in this situation. Researchers have evaluated the effect of interval training under varying conditions on the ability to rapidly improve exercise capacity and skeletal muscle energy metabolism[16].

Evaluation of the effect of exercise interventions on obese and overweight individuals is of particular importance. Consequently, one of the research priorities is the development of treatment programs to prevent or treat metabolic complications associated with obesity and overweight in sedentary societies and individuals at the highest risk of contracting life-threatening diseases. The present study aims to determine whether HIIT significantly affects the serum levels of adipolin, insulin, fasting glucose, and insulin resistance in overweight individuals.

## Materials and methods

The current semi-experimental research has a pre-test post-test design including a control group. The statistical population included overweight men aged 19 to 25 years who were chosen voluntarily based on the criteria for entering the research. For this purpose, 24 volunters were randomly divided into two experimental and control groups. All subjects participated in the orientation session where the research procedures and exercise protocols were explained to them in detail. Afterwards, they signed a written consent to participate in the research after knowing the aim of the research as well as how to perform the workout. In the two steps of pre-test and post-test, height, weight (using calipers and scales), and body mass index (divided by weight to the square of height in meters) were measured. After that, all subjects were asked not to change their diet until the end of the research protocol so that they could continue their normal diet as before. In the two steps of pre-test and post-test, height, weight (using calipers and scales), and body mass index (divided by weight to the square of height in meters) and Peak oxygen consumption (VO2peak) using the Rockport One Mile Walk Test, were measured. After that, all subjects were asked not to change their diet until the end of the research protocol so that they could continue their normal diet as before. According to the schedule, 24 hours prior to the first training session and following 12 hours of overnight fasting, the subjects were referred to the laboratory between 8 and 11 AM for initial blood sampling.

The inclusion criterion was overweight individuals (body mass index of over 25 kg/m$^2$). Exclusion criteria included a history of cardiovascular, thyroid, respiratory, diabetes, musculoskeletal disorders, hyperlipidemia, smoking, or being on a weight-loss diet.

### The training protocol

The experimental group was referred to the training hall one day after blood collection to implement the protocol. The subjects warmed up for ten minutes, including three minutes of stretching and two minutes of running, and then an interval training protocol was administered. The exercise program included running for one minute at 85-88% of maximum heart rate followed by a two-minute active rest interval at 50-55% of maximum heart rate, which was performed six times in the first session and ten times by the eighth week[17]. After implementing the protocol for eight weeks and 48 hours after the final training session, blood sampling was conducted under pretest conditions.

### Measurement of biochemical variables

In the pretest phase, blood samples were taken after 12 hours of overnight fasting, and in the post-test phase, 48 hours after the last training session. Next, 5 cc of blood was taken from the subjects' arm veins by a specialist, following the hygiene principles. Blood samples were poured into tubes containing anticoagulant Ethylene Diamine Tetra Acetic Acid (EDTA). After that, the blood samples were centrifuged at 3000 rpm for 15m. Following centrifugation and plasma separation, they were frozen at -80°C and used to measure the research variables. The serum levels of adipolin were analyzed biochemically and measured using the ELISA method and a Chinese Cuza-bio commercial kit. Based on the kit's sensitivity, the serum's minimum detectable dose of adipolin was less than 7.8 (pg/ml). Fasting blood sugar was measured using a Hitachi 902 Analyzer made in Japan and a Glucose kit (Pars Azmoon) made in Iran. Furthermore, insulin was assessed through the ELISA method and using a special kit from Monobind Inc, USA, with a sensitivity of 0.75 ($\mu$IU/ml) and intra-group variation coefficient of 6.3%. The insulin resistance index was calculated as follows:

HOMA-IR = Fasting insulin (µU/mL) × Fasting glucose (mmol/L)/22/5.

### Statistical method

The results of the Kolmogorov-Smirnov test indicated that the data distribution was normal. According to the independent t-test, there was no statistically significant difference between the groups' pretest variables (P>0.05).

## Results

The results of the Klomogrof-Smirnov test indicated the normality of the data distribution. The results of the independent t-test, the variables in the pre-test showed no significant difference of any of the variables between the groups (P>0.05).

Table 1 displays the subjects' body composition and physical fitness results. Post-test independent t-test results indicated a significant difference between the experimental and control groups regarding BMI and $VO_2$max (P<0.05). According to the paired t-test, implementing a high-intensity interval training course significantly decreased weight and BMI and increased $VO_2$max, respectively, in the experimental group (P<0.05).

**Table 1. Investigation of inter- and intra-group changes in general characteristics in two groups.**

| Variables | Group | Pre-test Mean and SD | Post-test Mean and SD | In-group t | In-group P | Intergroup t | Intergroup P |
|---|---|---|---|---|---|---|---|
| Weight (kg) | experimental | 88.4±8.7 | 80.1±6.5 | 6.35 | *0.0001 | 1.06 | 0.298 |
| | control | 83.5±6.5 | 82.8±6.1 | 1.75 | 0.108 | | |
| BMI (kg/m²) | experimental | 27.95±1.71 | 15.35±1.74 | 6.57 | *0.001 | 2.10 | ¥0.047 |
| | control | 27.06±1.85 | 26.82±1.66 | 1.78 | 0.101 | | |
| $VO_2$max (ml.kg/min) | experimental | 34.58±4.8 | 39.6±7.3 | 4.38 | *0.001 | 2.09 | ¥0.048 |
| | control | 34.1±4.5 | 34.4±4.3 | 1.30 | 0.220 | | |

*In-group Statistical significance; ¥ intergroup Statistical significance

**Figure 1. Mean (±Standard error) of Adipolin before and after training in groups. ¥ intergroup Statistical significance**

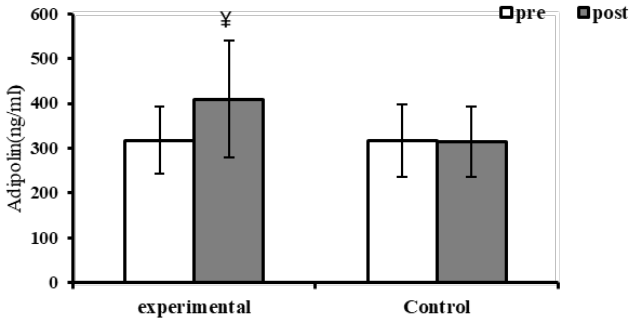
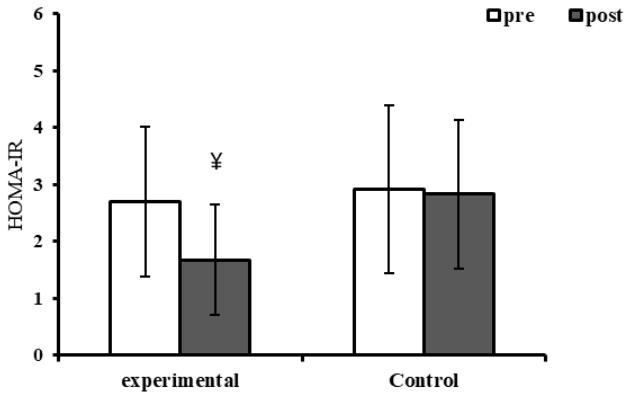



**Figure 2. Mean (±Standard error) of HOMA-IR before and after training in groups. ¥ intergroup Statistical significance**




The post-test intergroup test revealed a significant difference (P<0.05) between the experimental and control groups in adipolin level (Figure 1) and insulin resistance index (Figure 2) between the experimental and control groups. The intragroup test revealed that the implementation of HIIT significantly increased adipolin and decreased glucose, insulin, and insulin resistance index in the experimental group (P<0.05).

## Discussion and Conclusion

The objective of the present study was to examine the effect of HIIT on the serum levels of adipolin and the insulin resistance index in obese men. According to the findings, HIIT led to a significant increase in adipolin levels and a decrease in the insulin resistance index. The experimental group's weight, BMI, glucose, and insulin levels also decreased significantly, while $VO_2$max increased.

Some studies have shown that gene expression and serum levels of adipolin decrease in overweight, obese, and diabetic individuals due to the stress associated with obesity[12]. A negative regulator of adipolin, TNF-α is one of the pro-inflammatory adipocytokines derived from adipose tissue.

Inducing TNF-α and endoplasmic reticulum stress in the adipocyte culture medium reduces adipolin gene expression. On the other hand, aerobic training (cardio) and weight loss have been approved for lowering adipolin levels[18].

**Table 2. Investigation of inter- and intra-group changes in variables in two groups.**

| Variables | Group | Pre-test Mean and SD | Post-test Mean and SD | In-group t | In-group P | Intergroup t | Intergroup P |
|---|---|---|---|---|---|---|---|
| Adipolin (ng/L) | experimental | 317.4±76.4 | 409.5±130.1 | 2.96 | *0.013 | 2.16 | ¥0.041 |
| | control | 316.5±80.1 | 314.8±77.8 | 1.42 | 0.183 | | |
| glucose (mg/dl) | experimental | 101.2±21.6 | 86.3±21.4 | 3.04 | *0.011 | 1.43 | 0.166 |
| | control | 97.7±17.5 | 96.7±16.3 | 1.64 | 0.129 | | |
| Insulin (IU/ml) | experimental | 10.85±5.14 | 7.84±4.07 | 3.17 | *0.009 | 1.96 | 0.062 |
| | control | 11.84±5.04 | 11.61±4.61 | 0.852 | 0.413 | | |
| Insulin resistance (HOMA) | experimental | 2.69±1.32 | 1.67±0.97 | 3.18 | *0.009 | 2.39 | ¥0.025 |
| | control | 2.92±1.48 | 2.83±1.31 | 1.20 | 0.255 | | |

*In-group Statistical significance; ¥ intergroup Statistical significance

Endoplasmic reticulum stress is another inflammatory factor closely associated with obesity. According to the findings, endoplasmic reticulum stress results in the spread of inflammation, apoptosis of pancreatic β-cells, disruption of insulin synthesis, and the development of insulin resistance. This stress can also inhibit the expression of adipolin in cultured adipocytes (fat cells). Insulin can also play a role in regulating adipolin levels[19]. Rehmat Elahi et al. reported that eight weeks of low-intensity, continuous training could increase plasma adipolin in rats and modulate the amount of fat and subsequent obesity. These modifications confirm that weight loss significantly affects the elevated levels of adipolin in circulation[20]. It is anticipated that training volume will play a significant role in how adipolin responds. Therefore, long-term physical activity with low to moderate training volume (intensity, duration, and frequency) affects the adipolin plasma concentration. Suri et al. reported that 10-week cardio training has no significant effect on the serum levels of adipolin in obese men and that adipolin levels decrease following low-intensity continuous training as weight loss occurs. These contradictory findings in the conducted research are likely attributable to differences in the protocol's duration and intensity, as well as the subjects' level of physical fitness[21].

Reducing the amount of inflammatory adipocytokines appears to require a reduction in fat mass. Therefore, by decreasing the content of adipose tissue and the volume of fat cells due to a decrease in macrophage penetration into adipose tissue, the synthesis, and secretion of TNF-α are also reduced[20].

In addition, the results demonstrated a significant reduction in insulin resistance in obese individuals due to high-intensity interval training. Physical activity likely reduces blood glucose and increases insulin action through an increase in insulin receptor signaling and an increase in the translocation of glucose transporter to the plasma membrane. A decrease in the release of free fatty acids, an increase in the activity of glycogen synthase and hexokinase enzymes, an increase in the recruitment of muscle capillaries, and a change in the composition of the muscle to harvest glucose are also possible strategies[22].

Changing muscle composition, increasing glucose delivery to muscle, and decreasing the release of free fatty acids modulate insulin resistance and increase glucose uptake sensitivity to insulin. Given the existence of an inverse relationship between insulin/glucose and adipolin, it can be suggested that a significant change in insulin and glucose may be one of the causes of the increase in adipolin levels after high-intensity interval training[23].

TNF-α increases the expression of pro-inflammatory cytokines and decreases the expression of adipolin in fat cells by activating JNK in adipocytes[18], according to the findings of some studies. Decreased expression of adipolin worsens adipose tissue's inflammatory conditions and, as a result, increases insulin resistance. Endoplasmic reticulum stress is overactivated in numerous tissues, increasing inflammation, apoptosis of pancreatic β-cells, disruption of insulin synthesis, and the development of insulin resistance[22].

Physical activity is a recommended therapeutic strategy for reducing inflammation and preventing and treating obesity and obesity-related metabolic disorders such as type 2 diabetes and insulin resistance[19]. Several studies aimed at identifying the molecular mechanisms induced by physical activity and exercise have investigated the reduction of metabolic disorder-related factors.



Insulin is considered one of the factors whose changes following physical activity and exercise regulate adipolin levels effectively. Insulin is the primary hormone that regulates glucose homeostasis and carbohydrate metabolism. Translocation of GLUT4 to the plasma membrane and transverse tubules, as well as cellular glucose uptake, are enhanced by insulin binding to subunits of insulin receptors and activation of insulin signaling pathways[23]. An increase in available insulin receptors and a decrease in the release of free fatty acids[24] can be an additional mechanism for reducing insulin resistance following physical activity. The effect of muscle contraction on the translocation of GLUT4 to the plasma membrane likely explains these findings. Activated by AMPK, this physiological process is mediated by protein kinase or the increased cytoplasmic calcium concentration resulting from membrane depolarization[25]. During the current study, high-intensity interval training increased glucose reabsorption by skeletal muscle and decreased insulin resistance by increasing glucose transport into muscles or decreasing fatty acid synthesis.

HIIT-induced weight loss reduces the volume and number of adipocytes and the number of macrophages and endothelial cells. The increased production of anti-inflammatory mediators by adipocytes, the production of fibrinogen in the liver, and the production of other anti-inflammatory mediators are additional effects of sports on weight loss. Due to the inverse relationship between insulin and adipolin in obesity and overweight, any factor that can reduce insulin levels to normal values can improve the function of adipolin by increasing its functional isoform.

Overall, implementing an 8-week high-intensity interval training increased adipolin levels and reduced insulin resistance in overweight individuals. Performing HIIT seems to be effective in improving adipolin. Since there are no sufficient findings on the effect of exercise and physical activity protocols on adipolin levels, even though there is insufficient information in this field, additional research is required to help understand the molecular mechanisms involved in regulating adipolin after exercise.

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## References



1. Yoo HJ, Choi KM. Adipokines as a novel link between obesity and atherosclerosis. World J Diabetes. 2014 15;5(3):357-63.

2. Rezaeian, N.et al. Effect of Resistance Training on Serum Levels of Adipolin and Insulin Resistance in Obese Women. Journal of Sport Biosciences. 2020; 12(1), 1-16.

3. Lopes WA, Leite N, da Silva LR, Brunelli DT, Gáspari AF, Radominski RB, et al. Effects of 12 weeks of combined training without caloric restriction on inflammatory markers in overweight girls. J Sports Sci. 2016;34(20):1902-12

4. Bouchard, D.R.; Soucy, L.; Sénéchal, M.; Dionne, I.J and Brochu, M."Impact of resistance training with or without caloric restriction on physical capacity in obese older women". Menopause. 2009;16(1):66-72.

5. Stefan N, Häring HU. The role of hepatokines in metabolism. Nat Rev Endocrinol. 2013;9(3):144-52.

6. Tan SY, Lei X, Little HC, Rodriguez S, Sarver DC, Cao X, et al. CTRP12 ablation differentially affects energy expenditure, body weight, and insulin sensitivity in male and female mice. Am J Physiol Endocrinol Metab. 2020 1;319(1):E146-E162.

7. Choi HY, Park JW, Lee N, Hwang SY, Cho GJ, Hong HC, et al. Effects of a combined aerobic and resistance exercise program on C1q/TNF-related protein-3 (CTRP-3) and CTRP-5 levels. Diabetes Care. 2013;36(10):3321-7.

8. Fadaei R, Moradi N, Kazemi T, Chamani E, Azdaki N, Moezibady SA, et al. Decreased serum levels of CTRP12/adipolin in patients with coronary artery disease in relation to inflammatory cytokines and insulin resistance. Cytokine. 2019;113:326-31. [ Persian]

9. Aslani MR, Amani M, Moghadas F, Ghobadi H. Adipolin and IL-6 Serum Levels in Chronic Obstructive Pulmonary Disease. Advances in Respiratory Medicine. 2022; 90(5):391-398.

10. Wei Z, Peterson JM, Lei X, Cebotaru L, Wolfgang MJ, Baldeviano GC, Wong GW. C1q/TNF-related protein-12 (CTRP12), a novel adipokine that improves insulin sensitivity and glycemic control in mouse models of obesity and diabetes. Journal of Biological Chemistry 2012; 287(13): 10301-10315.

11. Sargolzaei J, Chamani E, Kazemi T, Fallah S, Soori H. The role of adiponectin and adipolin as anti-inflammatory adipokines in the formation of macrophage foam cells and their association with cardiovascular diseases. Clin Biochem. 2018;54:1-10.

12. Kelly AS, Steinberger J, Olson TP, Dengel DR. In the absence of weight loss, exercise training does not improve adipokines or oxidative stress in overweight children. Metabolism. 2007 Jul;56(7):1005-9.

13. Wang G, Chen JJ, Deng WY, Ren K, Yin SH, Yu XH. CTRP12 ameliorates atherosclerosis by promoting cholesterol efflux and inhibiting inflammatory response via the miR-155-5p/LXRα pathway. Cell Death Dis. 2021;12(3):254.

14. Liu JX, Zhu L, Li PJ, Li N, Xu YB. Effectiveness of high-intensity interval training on glycemic control and cardiorespiratory fitness in patients with type 2 diabetes: a systematic review and meta-analysis. Aging Clin Exp Res. 2019;31(5):575-593.

15. Ellingsen Ø, Halle M, Conraads V, Støylen A, Dalen H, Delagardelle C, et al. High-intensity interval training in patients with heart failure with reduced ejection fraction. Circulation. 2017;135(9):839-49.

16. Gibala MJ, Little JP, Van Essen M, Wilkin GP, Burgomaster KA, Safdar A, et al. Short-term sprint interval versus traditional endurance training: similar initial adaptations in human skeletal muscle and exercise performance. The Journal of physiology. 2006 Sep 15;575(3):901-11.

17. 17- Francois ME, Little JP. Effectiveness and safety of high-intensity interval training in patients with type 2 diabetes. Diabetes spectrum: a publication of the American Diabetes Association. 2015 Jan;28(1):39.

18. Enomoto T, Ohashi K, Shibata R, Higuchi A, Maruyama S, Izumiya Y, et al. Adipolin/C1qdc2/CTRP12 protein functions as an adipokine that improves glucose metabolism. Journal of Biological Chemistry. 2011 Oct 7;286(40):34552-8.

19. Mohammad M, Karim D, Mehdi M, Marziyeh S, Hadi S, Shila N. The Combinatory Effect of Spirulina Supplementation and Resistance Exercise on Plasma Contents of Adipolin, Apelin, Ghrelin, and Glucose in Overweight and Obese Men. Mediators Inflamm. 2022; 13;2022:9539286.

20. Rahmatollahi M, Ravasi A, Soori R. Effect of 8 Weeks of Low-Intensity Continuous Training on Plasma Adipolin, Insulin Resistance, and Weight of Fatty FatFilled Rats. Adv Obes Weight Manag Control. 2017; 7(5): 00211.[ Persian]

21. Galdavi, R., Mogharnasi, M., Nayebifar, S. The effect of continuous training on plasma levels of adipolin, insulin sensitivity and body fat percent in overweight and obese women. Journal of Practical Studies of Biosciences in

Sport, 2022; 10(21): 42-52.

22. 22 Babapour B, Doustkami H, Avesta L, Moradi A, Saadat S, Piralaei K, et al. Correlation of Serum Adipolin with Epicardial Fat Thickness and Severity of Coronary Artery Diseases in Acute Myocardial Infarction and Stable Angina Pectoris Patients. Med Princ Pract. 2021;30(1):52-61.

23. Balducci S, Zanuso S, Nicolucci A, Fernando F, Cavallo S, Cardelli P, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. Nutrition, Metabolism and Cardiovascular Diseases. 2010 ;20(8):608-17.

24. Inoue DS, De Mello MT, Foschini D, Lira FS, Ganen AD, Campos RM, et al. Linear and undulating periodized strength plus aerobic training promote similar benefits and lead to improvement of insulin resistance on obese adolescents. Journal of Diabetes and its Complications. 2015 ;29(2):258-64.

25. Santos JM, Ribeiro SB, Gaya AR, Appell HJ, Duarte JA. Skeletal muscle pathways of contraction-enhanced glucose uptake. International journal of sports medicine. 2008; 29(10):785-94.