Ann Appl Sport Sci, 11(3): e1283, 2023.
http://www.aassjournal.com; e-ISSN: 2322–4479; p-ISSN: 2476–4981. 10.61186/aassjournal.1283

ORIGINAL ARTICLE

The Effect of Eight Weeks of Circuit Resistance Training on Serum Levels of GPR119 and β-Arrestin1 in Individuals with Type 2 Diabetes

[1]Seyed Morteza Tayebi*, [1]Rasoul Eslami, [1]Irfan Iranshad, [1]Milad Golmohammadi

[1]Department of Sports Physiology, Faculty of Sports Sciences, Allameh Tabataba'i University, Tehran, Iran.

Submitted August 15, 2023; Accepted in final form November 01, 2023.

ABSTRACT

Background. The rising prevalence of diabetes has elevated its status as a significant health concern. Diabetes is a metabolic disorder characterized by elevated blood glucose levels, leading to various pathological changes such as neuropathy, nephropathy, retinopathy, gastrointestinal disorders, immune system impairment, vascular damage, and impaired tissue regeneration. **Objectives.** This study aimed to examine the effects of eight weeks of circuit resistance training (CRT) on serum levels of GPR119 and β-Arrestin1 in individuals with type 2 diabetes. **Methods.** Twenty male persons with type 2 diabetes (T2DM), who visited the diabetes clinic in Towhid Hospital and the Diabetes Association of Sanandaj city, were randomly divided into two groups: a control group (n=10) and an experimental group (n=10). CRT was conducted for eight weeks (three non-consecutive sessions per week). The exercise program consisted of gradually increasing sets, intensity, and volume, starting from 2 sets at 40% of 1RM (15 repetitions) in the initial sessions, and progressing to 4 sets at 80% of 1RM (6 repetitions) in the final sessions. Rest intervals of 20 to 30 seconds between sets and 3 minutes between rounds were implemented. GPR119 and β-Arrestin1 levels were assessed via ELISA method. **Results.** Repeated measures analysis of variance revealed that CRT significantly increased GPR119 and β-Arrestin1 levels in the experimental group (p=0.023 and p=0.032, respectively). **Conclusion.** Based on the reduction of insulin resistance (IR) in the persons with persons with T2DM in adaptation with CRT, and the roles of GPR119 and β-Arrestin1 in IR, the therapeutic implications of CRT via these proteins may be expected.

KEYWORDS: ***Resistance Training, Type 2 Diabetes, GPR119, B-Arrestin1, Insulin Resistance, Insulin Sensivity.***

INTRODUCTION

Type 2 diabetes mellitus (T2DM), a metabolic disease characterized by elevated blood glucose levels, gives rise to various complications such as retinopathy, neuropathy, and nephropathy (1). T2DM is also known as insulin-dependent diabetes, which signifies inadequate regulation of blood glucose levels (2). This disease can be classified by either insufficient insulin secretion or insulin resistance, indicating a deficiency of adequate insulin in the body or the body's inability to utilize insulin, respectively (3).

Insulin serves as a central hormone that regulates cellular energy and nutrient balance, directing anabolic processes. It plays a crucial role in facilitating the intracellular transport of glucose to insulin-responsive tissues such as muscle and adipose tissue. In muscle cells, the entry of glucose stimulates glycogen production and storage (4).

Recently, G-protein coupled receptors (GPCRs) have emerged as a family of membrane receptors responsible for recognizing a wide range

*. Corresponding Author:
Seyed Morteza Taybi, Associate Professor.
E-mail: tayebism@atu.ac.ir

of extracellular signals (5). GPCRs are among the most abundant groups of cell signaling receptors, with approximately 2% of the human genome exclusively encoding GPCRs (6). These receptors encompass a vast spectrum of physiological functions, with their involvement in metabolic disorders, particularly diabetes, being among the most significant (7). It has recently been demonstrated that the G-protein-coupled receptor 2 (GPCR2 or GPR119) is a GPCR predominantly expressed in the gastric antrum (B-cells) and the gastrointestinal tract (enteroendocrine cells) in humans. Studies have suggested that the expression of GPR119 in B-cells of the pancreatic islets leads to the hypothesis that this receptor may play a role in insulin modulation (8). Furthermore, activation of GPR119 has been shown to increase intracellular AMPK accumulation, resulting in increased glucose-dependent insulin secretion from pancreatic β-cells. Additionally, GPR119 may influence the secretory activity and survival of β-cells, leading to improved glucose homeostasis in patients with type 2 diabetes mellitus (T2DM) (2). Moreover, GPR119 is expressed in some enteroendocrine cells (L and K cells) in the small intestine and by β-cells in the islets of Langerhans in the gastric antrum. In all three cell types, GPR119, upon agonist binding, activates adenylate cyclase and increases AMPK. This leads to the secretion of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) or insulin from L, K, and β-cells. Additionally, both GLP-1 and GIP can interact with their respective receptors on β-cells to stimulate insulin secretion. Therefore, GPR119 agonists can increase insulin secretion through both mechanisms. Given that GLP-1 (and possibly GIP) promotes β-cell survival, GPR119 agonists may also affect both secretory activity and survival of β-cells, leading to improved glucose homeostasis in patients with T2DM (2). Stimulation of GPR119 appears to be a completely novel and undiscovered approach for the treatment of T2DM, resulting in increased glucose-dependent insulin secretion through specific mechanisms (2). GPR119 may offer an attractive therapeutic target for T2DM treatment, and its agonists may represent potential insulin secretagogues without the risk of inducing hypoglycemia.

On the other hand, β-arrestins are also multifunctional proteins that play various roles within the large family of GPCRs (9). Multiple studies have demonstrated that β-arrestins terminate GPCR-mediated cellular signaling. Moreover, β-arrestins interact with GPCRs through a process known as receptor desensitization and act as scaffold proteins, creating a scaffold-independent signaling pathway by recruiting other proteins that regulate a wide range of physiological processes, including diabetes-related metabolism. Studies have also shown that β-arrestin mediates insulin secretion in the gastric antrum and β-cells through glucose-dependent mechanisms and can contribute to the effective improvement of blood glucose profiles (9). Due to the anti-diabetic functions of β-arrestins in modulating insulin signaling, inflammatory pathways, and insulin secretion, β-arrestins can become a potential therapeutic target. Ultimately, the discussed studies here indicate that β-arrestins are crucial for proper cellular signaling regulation involved in T2DM. It is also worth mentioning that all members of the large GPCR family have a positive role in controlling and improving the condition of patients with T2DM (9).

Nowadays, in addition to dietary and medication interventions, exercise is recommended as one of the primary components in the treatment of diabetes (10-13). Studies have shown that physical activity leads to a reduction in blood glucose and body fat, as well as protection against cardiovascular complications. Regular exercise reduces dyslipidemia and increases insulin sensitivity. By increasing the concentration of the GLUT4 receptor on the plasma membrane or sarcoplasmic reticulum, insulin resistance improves positively through increased glucose uptake into cells. Resistance training has also been proposed as an effective therapeutic tool in the management of chronic diseases such as type 2 diabetes. Based on conducted studies, resistance exercises can improve strength and muscle volume, making them a beneficial medical intervention for individuals with type 2 diabetes. Resistance exercise can increase insulin sensitivity and daily energy expenditure. Additionally, muscular hypertrophy resulting from resistance training is associated with lower levels of inflammatory markers, cytokines, and other factors involved in diabetes. Regarding the effects of exercise on GPR119 and β-Arrestin1, no specific research has been conducted. Therefore, this study aims to answer the question of how circuit resistance training affects GPR119 and β-Arrestin1

in individuals with type 2 diabetes. This effect may have therapeutic implications for type 2 diabetes and its related complications in individuals with this condition.

MATERIALS AND METHODS

Research Method. This study was conducted in a field setting using a semi-experimental design with two groups: control and experimental. The measurement of variables was carried out using pre-and post-test assessments.

Participants/Patients. The study population consisted of men with type 2 diabetes who were attending the diabetes clinic of Towhid Hospital and the Diabetes Association of Sanandaj. Among them, 20 eligible volunteers were randomly assigned to two groups: a control group and an experimental group, each consisting of 10 individuals. The inclusion criteria for participation in the study were age between 45-55 years, fasting blood glucose levels between 100 and 250 mg/dL, oral medication with metformin, and a history of diabetes for more than five years. The exclusion criteria included complications related to type 2 diabetes (such as neuropathy, nephropathy, retinopathy, cardiovascular complications, joint discomfort, and diabetic foot ulcers), a history of hypoglycemia in the past two months, depression, smoking and alcohol consumption, insulin injections, changes in antidiabetic medications, blood pressure higher than 160/95 mm Hg, and regular participation in any form of exercise training in the past six months. The selection process of participants was supervised by a specialist diabetes physician. It is also worth mentioning that no changes were made to the patient's medication, including antidiabetic drugs, during the eight-week exercise period. After explaining the study protocol and relevant procedures, the participants provided written consent to participate in the research. During the exercise period, the participants were asked to refrain from engaging in other physical activities and to control their diet according to recommendations. In the end, three individuals from both groups decided to withdraw from the study. The present study was conducted under the ethical guidelines of the 1975 Helsinki Declaration and was registered and approved by the Ethics Committee of Allameh Tabataba'i University (Code: IR.ATU.REC.009).

Measurements. Determination of anthropometric indices and of maximal strength (1RM) was conducted one week before the initiation of the exercise program in three separate non-consecutive sessions. The measurement of anthropometric indices, including weight, height, and BMI, was performed. Weight was measured using a digital scale with minimal clothing, barefoot, and with an empty bladder. Height measurement was taken in a standing position without shoes using a wall-mounted stadiometer. BMI (Kg/m^2) was calculated using the formula "weight divided by height squared." The participants' maximal strength (1RM) determined using the Brzycki formula (Equation 1):

Equation 1: $$\mathbf{1RM} = \frac{weight\ lifted}{1.0278-(0.0278\times rep)}$$

Measurement of blood variables was performed 48 hours before the first- and 48 hours after and last-exercise sessions. The participants arrived at the laboratory in a 12-hour overnight fasting state, and under laboratory conditions, 10 ml of blood was taken from the antecubital vein in a seated position. After centrifugation and separation of serum samples, they were stored at a temperature of -20°C for future assessments. The serum levels of GPR119 and β-arrestin1 were measured using an enzyme-linked immunosorbent assay (ELISA) method with GPR119 and β-arrestin1 kits (Zelbio, Germany, sensitivity = 0.06 ng/ml).

Exercise protocol and implementation method. Before the start of the training program, during familiarization sessions, the participants were fully instructed on the resistance exercise machines, proper performing of each exercise, correct breathing during exercises, and how to increase or decrease weights on each machine.

The CRT used in this study was conducted for eight weeks, with three non-consecutive sessions per week. Each training session lasted an average of 60 minutes, consisting of a 10-minute warm-up period (including light jogging and stretching exercises), 40 minutes of resistance training using weight machines, and a 10-minute cool-down period (including stretching exercises). The CRT program included exercises with 10 machines (bench press, seated leg press, seated shoulder press, lying leg curl, bicep curl, calf raise, seated row, lat pulldown, spinal extension, triceps pushdown) performed in a circuit. Initial sessions started with 2 circuits and increased to 4 circuits in the final sessions. The training intensity (volume) started at 40% of 1RM (15 repetitions) in the initial sessions and ended at 80% of 1RM

(6 repetitions) in the final sessions. A rest period of 20 to 30 seconds was taken between each exercise, and a rest period of 3 minutes was given between each circuit (Table 1).

Table 1. Protocol of 8 weeks of circuit resistance training

	Week 1			Week 2			Week 3			Week 4			Week 5			Week 6			Week 7			Week 8		
Session	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Intensity	40%	40%	45%	45%	50%	50%	55%	55%	60%	60%	60%	65%	65%	65%	70%	70%	70%	75%	75%	75%	80%	80%	80%	80%
Repetition	15			12			10			10			8			8			6			6		
Set	2			2			3			3			3			4			4			4		

Statistical Analysis. Mean plus/minus standard error of mean was used as descriptive statistics. Inferential statistical analysis using repeated measures-analysis of variance (ANOVA). The LSD test was used to test the main effects of the interaction effect of GROUP×TIME. The acceptable significance level was less than 0.05 ($p<0.05$). SPSS software was used to analyze the data.

RESULTS

Descriptive statistics for the morphological profile of the samples are summarized in Table 2.

GPR119. There was a significant interaction effect of time×group ($F=361.6$, $p=0.023$, $\eta^2=0.3$). In other words, while GPR119 in the control group (pre = 0.66 ± 0.06 and post = 0.70 ± 0.04) did not significantly change over the time, its level increased significantly in the experimental group (pre = 0.30 ± 0.06 and post = 0.71 ± 0.03) as a result of 8 weeks of CRT (Graph 1).

β-Arrestin1. There was a significant interaction effect of time×group ($F=507.5$, $p=0.032$, $\eta^2=0.3$). β-Arrestin1 in the control group (pre = 0.66 ± 0.06 and post = 0.70 ± 0.04) did not significantly change over time, but its level increased significantly in the experimental group (pre = 0.30 ± 0.06 and post = 0.71 ± 0.03) due to 8 weeks of CRT (Graph 2).

DISCUSSION

The present study aimed to investigate the effect of an eight-week CRT on the serum levels of GPR119 and β-Arrestin1 in individuals with type 2 diabetes. The findings demonstrated a significant increase in GPR119 and β-Arrestin1 levels. On the other hand, in the previous published data from this study, the experimental group showed a significant decrease in fasting blood sugar (FBS) compared to the control group; insignificant change in insulin levels; and a significant reduction in IR (3). Furthermore, the research findings indicated that body weight and BMI had a significant decrease in experimental group compared to the control group (3).

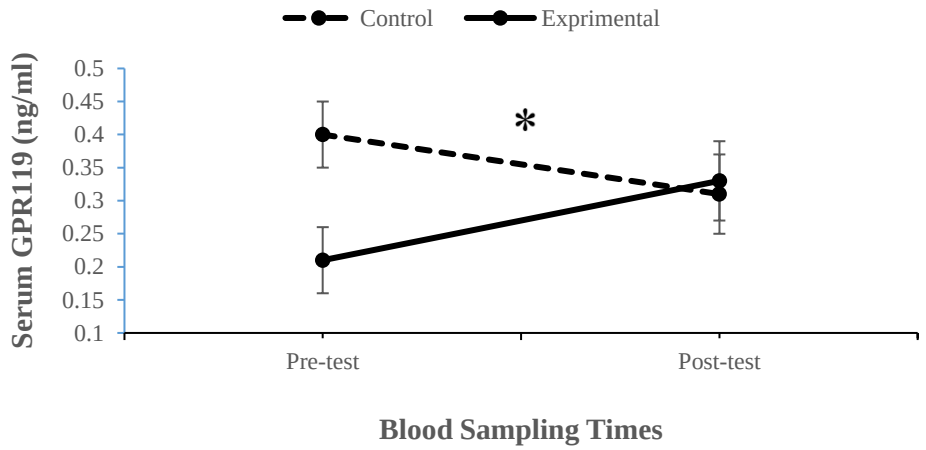
Considering the scarcity of research on the relationship between GPR119, β-Arrestin1, and exercise, although existing studies have not measured these variables, they have referred to their potential role. In this regard, Schonke et al. demonstrated that the expression of GPR119 and cannabinoid receptor 2 (CB2R) increases in response to acute aerobic or resistance exercise (14). This, in turn, can increase glucose uptake and insulin secretion, making it a therapeutic target in individuals with type 2 diabetes (15). In another study, Fujiwara et al. showed the role of several GPRs, including GPR119, as major sensors for fatty acids, and their involvement in the release of glucagon-like peptide-1 (GLP-1) concerning diet and exercise in individuals with type 2 diabetes (16). Since GLP-1 is a peptide hormone that affects insulin secretion from pancreatic beta cells, it regulates and reduces blood glucose levels in individuals with type 2 diabetes (17), Lan et al. demonstrated that activation of GPR119 receptors in GLUTag cells enhances GLP-1 secretion in the presence or absence of glucose, thereby affecting insulin secretion, indicating a close relationship between GPR119 and GLP-1 (18). Furthermore, GPR119 in another study, was found to activate adenylyl cyclase (AC) and increase AMPK, leading to the secretion of GLP-1 (2). In terms of exercise and GLP-1, studies have shown that eight weeks of resistance training can increase GLP-1 levels and improve blood glucose levels and insulin secretion in individuals with type 2 diabetes (19). Another study demonstrated that a twelve-week combined exercise regimen resulted in increased GLP-1 levels, decreased insulin resistance, and ultimately improved FBS in individuals with type 2 diabetes (20). Therefore, the evidence suggests

a close and positive relationship between GPR119 and exercise, which can serve as a therapeutic target for IR, and improvement of FBS in individuals with type 2 diabetes. In the present study, CRT was able to increase the serum levels of GPR119 and improve IR, and glucose uptake in individuals with type 2 diabetes.

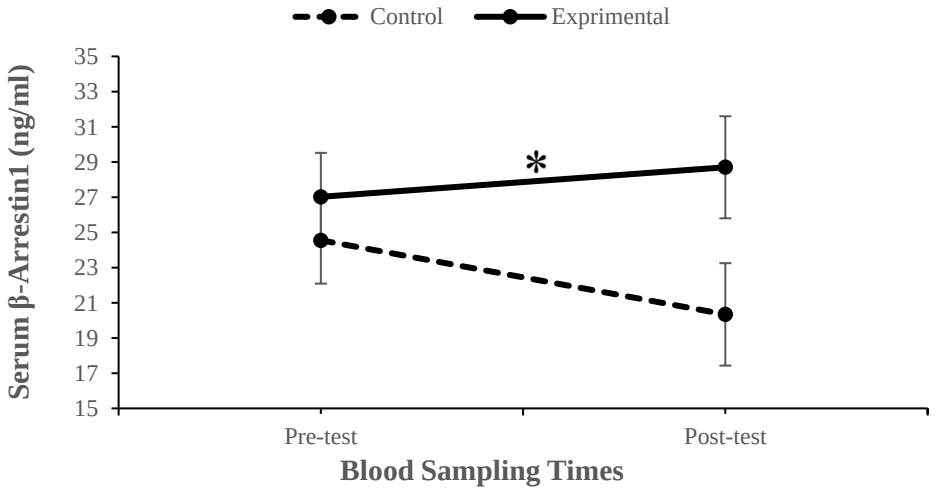
Table 2. Characteristics of participants

Groups	Age (year)	Body Height (cm)	Body Mass (kg)	BMI (kg/m^2)
Control (n=8)	51 ± 1	174 ± 2	83.56 ± 4.01	27.43 ± 0.98
Experimental (n=9)	50 ± 1	166 ± 2	83.96 ± 3.78	30.12 ± 0.92

BMI: Body mass index. Mean ± SEM.



Graph 1. Serum GPR119 in adaptation with eight-week circuit resistance training (CRT) in men with type 2 diabetes. *: a significant effect of CRT at $p < 0.05$.



Graph 2. Serum β-Arrestin1 in adaptation with eight-week circuit resistance training (CRT) in men with type 2 diabetes. *: a significant effect of CRT at $p < 0.05$.

On the other hand, when serum levels of b-Arrestin1 in the control group had a significant decrease over time, its level increased in the experimental group as a result of the 8-week CRT program. However, there haven't been many studies conducted on the relationship between b-Arrestin1 and exercise. Since b-Arrestin1 acts as a mediator of insulin secretion in the gastric mucosa and beta cells, inhibiting b-Arrestin1 leads to insulin signal degradation and increased insulin resistance in

individuals with type 2 diabetes (21). On the other hand, GLP-1 is a polypeptide hormone secreted by enteroendocrine L cells and enhances glucose-dependent insulin secretion in pancreatic beta cells, and it has also been studied for its anti-diabetic effects (21). It has been shown that b-Arrestin1 and GLP-1 are related. In one example, Sonoda et al. demonstrated in a study that widespread inhibition and suppression of b-Arrestin1 significantly reduce GLP-1 signaling, leading to decreased activation of ERK and CREB, decreased expression of IRS-2, decreased AMPK levels, and disrupted insulin secretion (21). Furthermore, studies have shown that eight weeks of resistance training lead to increased GLP-1 hormone levels, improved blood glucose levels, and insulin secretion in individuals with type 2 diabetes (19). In another study, it was shown that twelve weeks of combined exercise had a positive effect on GLP-1 and insulin resistance in individuals with type 2 diabetes, resulting in increased GLP-1 levels, decreased insulin resistance, and ultimately improved blood glucose levels (20). These findings indicate a close and positive relationship between b-Arrestin1 and exercise, which can serve as a therapeutic mechanism in diabetes, IR, and improved FBS in individuals with type 2 diabetes.

CONCLUSION

The findings of the present study demonstrated that an eight-week CRT (3 sessions/week) with intensities of 40%-80% of 1RM and 15-6 repetitions/exercise resulted in increased resting levels of GPR119 and β-Arrestin1 of men with type 2 diabetes. This may potentially resulting in a reduction in insulin resistance through improved insulin signaling performance.

APPLICABLE REMARKS

- Circuit resistance training (at least 8 weeks, 3 sessions/week) with low to moderate intensity prescribed for the reduction of fasting blood glucose and insulin resistance of men with T2DM and without retinopathy, neuropathy, nephropathy, and etc.

AUTHORS' CONTRIBUTIONS

Study concept and design: Seyed Morteza Taybi. Acquisition of data: Milad Golmohammadi. Analysis and interpretation of data: Seyed Morteza Taybi, Milad Golmohammadi. Drafting the manuscript: Seyed Morteza Taybi, Milad Golmohammadi. Critical revision of the manuscript for important intellectual content: Rasoul Eslami, Irfan Iranshad. Statistical analysis: Seyed Morteza Taybi. Administrative, technical, and material support: Seyed Morteza Taybi, Irfan Iranshad. Study supervision: Seyed Morteza Taybi, Rasoul Eslami.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Teixeira-Lemos E, Nunes S, Teixeira F, Reis F. Regular physical exercise training assists in preventing type 2 diabetes development: focus on its antioxidant and anti-inflammatory properties. Cardiovasc Diabetol. 2011;10(1):12. [DOI:10.1186/1475-2840-10-12] [PMID:21276212]
2. Zhu X, Huang W, Qian H. GPR119 agonists: a novel strategy for type 2 diabetes treatment. Diabetes mellitus–insights perspectives. 2013. [DOI:10.5772/48444]
3. Tayebi SM, Golmohammadi M, Eslami R, Shakiba N, Costa PB. The Effects of Eight Weeks of Circuit Resistance Training on Serum METRNL Levels and Insulin Resistance in Individuals with Type 2 Diabetes. Journal of Diabetes & Metabolic Disorders. 2023. [DOI:10.1007/s40200-023-01225-1]
4. Wilcox G. Insulin and insulin resistance. Clin Biochem Rev. 2005;26(2):19-39.
5. Kobilka BK. G protein coupled receptor structure and activation. Biochim Biophys Acta. 2007;1768(4):794-807. [DOI:10.1016/j.bbamem.2006.10.021] [PMID:17188232]
6. Lagerstrom MC, Schioth HB. Structural diversity of G protein-coupled receptors and significance for drug discovery. Nat Rev Drug Discov. 2008;7(4):339-57. [DOI:10.1038/nrd2518] [PMID:18382464]
7. Hauser AS, Attwood MM, Rask-Andersen M, Schioth HB, Gloriam DE. Trends in GPCR drug discovery: new agents, targets and indications. Nat Rev Drug Discov. 2017;16(12):829-42. [DOI:10.1038/nrd.2017.178] [PMID:29075003]
8. Overton HA, Fyfe MC, Reynet C. GPR119, a novel G protein-coupled receptor target for the treatment of type 2 diabetes and obesity. Br J Pharmacol. 2008;153 Suppl 1(Suppl 1):S76-81. [DOI:10.1038/sj.bjp.0707529] [PMID:18037923]

9. Feng X, Wang W, Liu J, Liu Y. beta-Arrestins: multifunctional signaling adaptors in type 2 diabetes. Mol Biol Rep. 2011;38(4):2517-28. [DOI:10.1007/s11033-010-0389-3] [PMID:21086182]
10. Saeidi A, Hackney AC, Tayebi SM, Ahmadian M, Zouhal H. Diabetes, Insulin Resistance, Fetuin-B and Exercise Training. Annals of Applied Sport Science. 2019;7(2):1-2. [DOI:10.29252/aassjournal.7.2.1] [PMID:31321377]
11. Saeidi A, Tayebi SM, Khosravi A, Malekian F, Khodamoradi A, Sellami M, et al. Effects of exercise training on type 2-diabetes: the role of Meteorin-like protein. Health Promot Perspect. 2019;9(2):89-91. [DOI:10.15171/hpp.2019.12] [PMID:31249794]
12. Saeidi A, Tayebi SM, Khosravi A, Razi O, Sellami M, Abderrahman AB, Zouhal H. Obesity, Fat Mass, Osteopontin and Exercise Training. International Journal of Applied Exercise Physiology. 2019;8(1):177-9.
13. Tayebi SM, Ghanbari-Niaki A, Saeidi A, Hackney AC. Exercise Training, Neuregulin 4 and Obesity. Ann Appl Sport Sci. 2017;5(2):1-2. [DOI:10.18869/acadpub.aassjournal.5.2.1] [PMID:30899900]
14. Schönke M, Martinez-Tellez B, Rensen PC. Role of the endocannabinoid system in the regulation of the skeletal muscle response to exercise. Curr Opin Pharmacol. 2020;52:52-60. [DOI:10.1016/j.coph.2020.05.003] [PMID:32619926]
15. Rensen PC. Role of the endocannabinoid system in the regulation of the skeletal muscle response to exercise. Current Opinion in Pharmacology. 2020;52:1-9. [DOI:10.1016/j.coph.2020.05.003] [PMID:32619926]
16. Fujiwara Y, Eguchi S, Murayama H, Takahashi Y, Toda M, Imai K, Tsuda K. Relationship between diet/exercise and pharmacotherapy to enhance the GLP-1 levels in type 2 diabetes. Endocrinology, Diabetes Metabolism. 2019;2(3):e00068. [DOI:10.1002/edm2.68] [PMID:31294084]
17. Drucker DJ, Jin T, Asa SL, Young TA, Brubaker PL. Activation of proglucagon gene transcription by protein kinase-A in a novel mouse enteroendocrine cell line. Mol Endocrinol. 1994;8(12):1646-55. [DOI:10.1210/mend.8.12.7535893] [PMID:7535893]
18. Lan H, Lin H, Wang C, Wright M, Xu S, Kang L, et al. Agonists at GPR119 mediate secretion of GLP-1 from mouse enteroendocrine cells through glucose-independent pathways. Br J Pharmacol. 2012;165(8):2799-807. [DOI:10.1111/j.1476-5381.2011.01754.x] [PMID:22029751]
19. Akbarpour M, Fathollahi Shoorabeh F, Mardani M, Amini Majd F. Effects of Eight Weeks of Resistance Training and Consumption of Pomegranate on GLP-1, DPP-4 and Glycemic Statuses in Women with Type 2 Diabetes: A Randomized Controlled Trial. Nutrition Food Sciences Research. 2021;8(1):5-10.
20. Nejati R, Attarzadeh Hosseini SR, Bijeh N, Raouf Saeb A. The effects of twelve weeks of combined exercises on GLP-1 and insulin resistance in women with type 2 diabetes. Journal of Shahid Sadoughi University of Medical Sciences. 2019;27(1):1187-201. [DOI:10.18502/ssu.v27i1.877]
21. Sonoda N, Imamura T, Yoshizaki T, Babendure JL, Lu JC, Olefsky JM. Beta-Arrestin-1 mediates glucagon-like peptide-1 signaling to insulin secretion in cultured pancreatic beta cells. Proc Natl Acad Sci U S A. 2008;105(18):6614-9. [DOI:10.1073/pnas.0710402105] [PMID:18445652]