

Potential Effect of Irisin and/or Moderate Intensity Exercise on Metabolic Homeostasis in Obesity in Male Albino Rats

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Abstract

Background: Exercise may encourage myokines secretion such as irisin. Irisin is one of the myocytokines that is related to energy homeostasis and obesity.

Aim of Study: Study the effect of irisin and/or moderate intensity swimming exercise on metabolic homeostasis in high fat induced obesity in male albino rats.

Material and Methods: The present work will be carried out on 50 male albino rats, they were divided into 2 groups I: Control group 10 rats fed with normal diet and intraperitoneal injected with 150 μ g saline daily for 8 weeks II: Obese group 40 rats were fed with high fat diet they are subdivided into 4 subgroups 10 rats each IIa. Control obese IIb. Irisin treated Obese these rats are intraperitoneal injected with irisin in a dose of 100ng/ml per day for 8 weeks IIc. Exercise treated Obese the exercise groups will swim for 30min a day, 5 days a week for 8 successive weeks IId. Irisin and exercise treated obese group rats will be treated as subgroup b and c.

At the end of the experimental period, the following parameters were measured for all animals: Body Weight (BW), Body Mass Index (BMI), abdominal circumference. Blood samples were obtained to measure serum insulin, fasting blood glucose, calculate Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and, Homeostatic Model Assessment of Insulin Sensitivity (HOMA-S), measure serum Irisin, osteopontin, Total Cholesterol (TC), LDL cholesterol level, HDL cholesterol level, Triglycerides (TG), Free Fatty Acids (FFA), Nitrite/Nitrate and Malondialdehyde (MDA).

Results: Final BW in irisin and/or exercise animals are significantly decreased as compared to final BW of control obese group. Animal treated with Irisin and exercise shows insignificant change as compared to final BW in normal control group. BMI, abdominal circumference, serum insulin, fasting glucose, Homa IR, osteopontin, TC, LDL, TG, FFA, MDA are significantly increased in obese rats as compared to normal control, either Irisin injection or exercise results in significant decrease in all these parameters, when Irisin injection is combined with exercise it causes significant decrease when compared to control obese and insignificant difference with normal control group. As regard Irisin level, HOMA insulin sensitivity, HDL and Nitrite/Nitrate they are significantly decreased in obese rats as compared to normal

control, either irisin injection or exercise results in significant increase in these parameters, if Irisin injection is combined with exercise it causes significant increase in these parameters reaching the normal control level.

Conclusion: Irisin and/or moderate intensity swimming exercise initiate a novel strategy for the treatment of obesity also the potential use of irisin as a predictive marker for insulin resistance has a therapeutic potential in obese rats.

Key Words: Obesity irisin – Exercise – Osteopontin.

Introduction

SKELETAL muscle cells secrete signaling cytokines peptides referred as myokines which act in an autocrine, paracrine, and endocrine fashion in response to exercise and contribute to the immediate and chronic benefits of exercise [1]. Regular physical activity is found to play a key role in reducing the risk of obesity by increasing energy expenditure, although the detailed mechanism of which remains unclear [2] Irisin is one of the myocytokines that is related to energy homeostasis and Obesity [3]. However the effect of exercise on serum irisin level showed the contradicting results. [4-6] The contradicting results of irisin responses induced by exercise might be resulted from the difference of exercise formula either it is resistant or aerobic exercise and the metabolic state.

The purpose of this study was to evaluate the association of swimming exercise that is typically considered an aerobic exercise and provides moderate resistance exercise and/or irisin treatment with serum irisin level and other obesity-associated parameters in high-fat-diet fed Wistar rats.

Material and Methods

Animals:

The present work was carried out on 50 male Wistar rats ranging in weight between 150-200gm .

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The rats were housed in isolated animal cages (five rats in each cage) in a standard animal laboratory room and had free access to water and food all over the period of work and were kept at room temperature. Animals were obtained from animal house of Tanta University and the experiment was approved by ethical committee of Faculty of Medicine, Tanta University (2019). This study was carried out in Physiology Department Tanta University (2019).

Study design:

Animals were divided into two groups:

Group I (Control group 10 rats): Fed with a Standard chow diet: 13.5% fat, 58% carbohydrate, 28.5% protein, and this represents 336kcal/100gm till the end of the experiment [7].

Group II (obese group 40 rats): Rats of this group were fed with high fat diet (50.10% fat mainly saturated; 33.60% carbohydrate; 16.30% protein; and this represents 493kcal/100g) for 8 weeks [8] after the 8 weeks this group was subdivided into 4 equal Subgroups 10 rats each.

Subgroup IIa: Control obese group: Rats were treated by intraperitoneal injection of 150 μ saline daily for 8 weeks.

Subgroup IIb: Irisin treated obese group: Rats were treated by intraperitoneal injection of 150 μ of prepared irisin solution (100ng/ml) daily for 8 weeks, the solution was prepared by dissolving irisin powder in saline solution [9].

Subgroup IIc: Exercise treated obese group: Rats were treated by moderate intensity swimming exercise. It was performed without a load in a barrel filled with water at 33-35°C to a depth of 40-50cm, which allowed free swimming [10]. The duration of the first swimming exercise was limited to 15min then increased by 5min daily up to 30min. Rats in the exercise groups swam for 30min a day, 5 days a week for 8 successive weeks [11].

Subgroup IId: Irisin and exercise treated obese group: Rats were treated by intraperitoneal injection of 150 μ of prepared irisin solution (100ng/ml) daily for 8 weeks [9] in addition to exercise treatment as in subgroup IIc [11].

Anthropometric measures:

- 1- Body weight was measured at the start and the end of the experiment to evaluate the initial and final body weight using electronic scale.
- 2- BMI is calculated at the start (data not shown) and the end of the experimental period body

mass index (BMI) = Weight in grams/nose to anus length in cm [12].

- 3- Abdominal circumference were measured for all animals the biggest region of the rat's abdomen using soft ruler at the end of the experimental period.

Samples collection and biochemical analysis:

Blood samples were obtained from retro-orbital venous plexus 24 hours from the last exercise and animals allowed for fasting overnight. Serum was separated by centrifugation of blood at 3000rpm for 15 minutes and the separated sera were then stored in aliquots at -30°C till used for estimation of the following parameters:

Fasting serum insulin by radioimmunoassay procedure using insulin ELISA kit [13] fasting serum glucose level by enzymatic colorimetric methods [14]. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) [15] Homeostatic model assessment of insulin sensitivity [15] are calculated, Serum Irisin [16], osteopontin [17] total cholesterol level [18], LDL cholesterol level [19], HDL cholesterol level was measured according to method of Grove [20]. Triglycerides level was measured by GPO enzymatic method [21], free fatty acids [22], Nitrite/Nitrate level [23]. Malondialdehyde (MDA) [24] levels were measured.

Statistical analysis:

All values were expressed as mean \pm Standard Deviation (SD). Data were statistically analyzed using one way ANOVA for multiple group comparisons, followed by scheffe (F) for comparison between individual group. Significance was set at ($p \leq 0.05$).

Results

As shown in (Table 1) final BW in irisin ttt or exercise ttt animals are significantly decreased as compared to final BW of control obese group. Animal treated with Irisin and exercise show significant decrease in final BW compared to control obese rats, also they show insignificant change compared to either initial or final BW in normal control group, as regard BMI and Abdominal circumference both are significantly increased in control obese rats as compared to normal control group, either Irisin injection or exercise results in significant decrease in them as compared to control obese group, when Irisin injection is combined with exercise it causes significant decrease and improvement in these parameters reaching the normal control level.

Table (2) showed that osteopontin and Malondialdehyde are significantly increased in control obese rats as compared to normal control group, either Irisin injection or exercise results in significant decrease in all these parameters as compared to control obese group, when Irisin injection is combined with exercise it causes significant decrease and improvement in these parameters reaching the normal control level. As regard irisin level and nitrite/nitrate level they are significantly decreased in control obese rats as compared to normal control either irisin injection or exercise results in significant increase these parameters as compared to control obese group, if Irisin injection is combined with exercise it causes significant increase in these parameters reaching the normal control level.

Table (3) showed significant increase in Serum insulin, fasting glucose, Homa IR, total cholesterol, LDL, Triglyceride, FFA, in obese control rats as compared to normal control group either irisin injection or exercise results in significant decrease these parameters as compared to control obese group, if Irisin injection is combined with exercise it causes significant decrease in these parameters reaching the normal control level. On the other hand it showed significant decrease in HOMA-IS and HDL in obese control rats as compared to normal control group either irisin injection or exercise results in significant increase these parameters as compared to control obese group, if Irisin injection is combined with exercise it causes significant decrease in these parameters reaching the normal control level.

Table (1A): Initial and final body weight in all groups studied (mean ± SD).

Parameters	Normal control		Obese							
	Initial	Final	Control		Irisin ttt		Exercise ttt		Irisin & exercise ttt	
			Initial	Final	Initial	Final	Initial	Final	Initial	Final
Body weight (gm)	191±24.3	274.7a±38.0	288a±30.3	437.4bc±43.2	288a±30.3	310.5bde±29.8	288a±30.3	315.7bdg±25.1	288a±30.3	269.9dfh±41.5

p-value >0.05.

a: Sig vs. initial normal control.
 b: Sig vs. final normal control.
 c: Sign vs. initial control obese.
 d: Sign vs. final control obese.

e: Sig vs. initial irisin treated obese.
 f: Sig vs. final irisin treated obese.
 g: Sig vs. initial exercise treated obese.
 h: Sig vs. final exercise treated obese.

Table (1B): BMI, abdominal circumference, in all studied groups (mean values ± SD).

Parameters	Normal control	Obese			
		Control	Irisin ttt	Exercise ttt	Irisin & exercise ttt
BMI (gm/cm ²)	0.596±0.106	0.950a±0.140	0.667b±0.141	0.681b±0.142	0.579b±0.141
Abdominal circumference (cm)	14.47±1.428	21.73a±2.428	16.91a ¹ b±1.226	17.04a ¹ b±0.888	14.53b,c,d±1.21

p-value >0.05

a: Sig vs. normal control.
 b: Sig vs. control obese.
 c: Sign vs. Irisin treated obese.
 d: Sign vs. exercise ttt.

Table (2): Serum irisin, osteopontin, Nitrite/Nitrate, Malondialdehyde in all studied groups (mean values ± SD).

Parameters	Normal control	Obese			
		Control	Irisin ttt	Exercise ttt	Irisin & exercise ttt
Serum irisin (ng/ml)	37.9±3.089	28.83a±3.418	69.71a ¹ b±4.403	72.96a ¹ b±4.684	84.65a ¹ b ¹ c ¹ d±4.638
Serum osteopontin (ng/ml)	36±3.4	76.5a±4.4	63.7a ¹ b±5.9	66.7a ¹ b±5.5	38.1b ¹ c ¹ d±3.8
Nitrite/Nitrate (µmol/L)	15.90±1.921	9.35a±1.23	11.53a ¹ b±1.56	11.12a ¹ b±1.32	15.42b,c,d±1.77
Malondialdehyde (µmol/L)	1.36±0.20	2.74a±0.35	1.9a ¹ b±0.09	1.94a ¹ b±0.13	1.43b,c,d±0.17

p-value >0.05

a: Sig vs. normal control.
 b: Sig vs. control obese.
 c: Sign vs. Irisin treated obese.
 d: Sign vs. Exercise ttt.

Table (3): Serum fasting glucose, insulin, HOMA-IR, (HOMA-S) in all studied groups (mean values \pm SD).

Parameters	Normal control	Obese			
		Control	Irisin ttt	Exercise ttt	Irisin & exercise ttt
Serum fasting glucose (mg/dl)	88.41 \pm 8.19	148.7a \pm 10.17	106.49a ^a b \pm 14.57	110.3a ^a b \pm 12.33	83.90b ^b c ^c d \pm 8.408
Serum insulin (μ U/ml)	12.24 \pm 1.788	18.66a \pm 2.095	13.98a ^a b \pm 1.24	14.06a ^a b \pm 1.362	12.40b ^b c ^c d \pm 1.902
HOMA-IR	2.65 \pm 0.287	6.84a \pm 0.861	3.77a ^a b \pm 0.384	3.79a ^a b \pm 0.309	2.55b ^b c ^c d \pm 0.365
(HOMA-S)	0.329 \pm 0.005	0.290a \pm 0.004	0.315a ^a b \pm 0.007	0.313a ^a b \pm 0.003	0.331b ^b c ^c d \pm 0.008

a: Sig vs. normal control.

b: Sig vs. control obese.

c: Sign vs. Irisin treated obese.

d: Sign vs. exercise ttt.

Table (4): Lipid profile in all studied groups (mean values \pm SD).

Parameters	Normal control	Obese			
		Control	Irisin ttt	Exercise ttt	Irisin & exercise ttt
Serum total cholesterol (mg/dl)	104.2 \pm 7.192	163.7a \pm 46.54	122.9a,b \pm 9.43	127.4a ^a b \pm 10.79	102.4b ^b c ^c d \pm 16.87
Serum LDL cholesterol (mg/dl)	49.15 \pm 4.51	73.97a \pm 4.84	56.02a ^a b \pm 5.35	54.30a ^a b \pm 4.90	48.01b ^b c ^c d \pm 4.90
Serum HDL cholesterol (mg/dl)	41.12 \pm 4.09	24.03a \pm 4.16	34.93a ^a b \pm 4.20	36.45a ^a b \pm 4.15	41.70b ^b c ^c d \pm 3.94
Serum triglycerides (mg/dl)	137.5 \pm 7.587	176.7a \pm 9.851	147.3a ^a b \pm 9.891	145.3a ^a b \pm 7.377	134.3b,c,d \pm 7.704
Serum free fatty acids (mmol/ml)	86.3 \pm 6.56	189.9a \pm 10.53	157a ^a b \pm 10.49	163.2a ^a b \pm 14.97	87.5b ^b c ^c d \pm 9.7

p-value >0.05

a: Sig vs. normal control.

b: Sig vs. control obese.

c: Sign vs. Irisin treated obese.

d: Sign vs. exercise ttt.

Discussion

It is evident from the results of the present work the beneficial effect of either irisin or exercise on body weight as it significantly decreased final BW in irisin ttt or exercise ttt animal. In addition, animal treated with both Irisin & exercise show significant decrease in BW compared to final BW in control obese animals, irisin ttt group and exercise ttt group and with insignificant difference from final BW of normal control. This indicate that combination of irisin and exercise treatment are more potent in reducing body weight in obese animal.

Body weight, BMI, abdominal circumference are significantly decreased due to conversion of white adipocytes to brown one by irisin leads to increase energy expenditure and thermogenesis with decrease in these anthropometric parameters [25], negative association between circulating irisin with body weight, BMI and abdominal circumference has been previously reported [26].

Results of present work denote that irisin is significantly decreased in obese rats Irisin is secreted from skeletal muscle into circulation by proteolytical cleavage of Fibronectin type III domain-containing protein5 (FNDC5) [27], the precursor of irisin. In obesity, FNDC5 expression, and consequently secretion of irisin from adipocytes is decreased [26]. This results are in accordance with previous results that show reduction of irisin

in obese Chinese adults [28]. Lower levels of circulating irisin in obese group could be explained by impaired peroxisome proliferator activated receptor-gamma coactivator 1 alpha (PGC-1 α) expression and functions in the muscle and adipose tissue PGC-1 α is a master regulator of irisin secretion. Moreno-Navarrete et al., reported a decreased circulating irisin concentration and FNDC5 gene expression in adipose tissue and muscle from obese with a subsequent reduction in mitochondrial biogenesis and thus depression of irisin-the PGC-1 α -dependent myokines. [29] But the significant increase in glucose, insulin, HOMA IR in obese rats observed in this study could be a cause of decrease PGC-1 α activity and decrease of irisin [30].

Kurdiova et al., suggest that chronic hyperglycemia and hyperlipidemia are possible causes for decreased FNDC5 gene expression [31]. The low irisin concentrations in obese could be also explained by hyperlipidemia but the Potential associations between irisin concentration and lipid profile are poorly understood [32]. Gouni-Berthold identified higher probabilities of raised lipid levels in subjects with low irisin concentrations as in obese with inverse associations between irisin concentrations and total, LDL cholesterol as well as triglycerides [33].

Additional decrease in irisin secretion from adipose tissue as a result of the inflammatory processes and oxidative stress observed in obesity

cannot be excluded [34]. Obesity is characterized by low-grade chronic inflammation and it induces elevated oxidative stress. Increased production of ROS impairs cellular structures together with decreased antioxidant defense system [35].

Malondialdehyde (MDA) a marker of oxidative stress was significantly increased in control obese animals this reflects in vivo oxidative damage to lipids and increased plasma lipid peroxidation.

It is clear that the level of osteopontin is significantly increase in obese rats Osteopontin, is an extracellular matrix protein may play a key role in linking obesity to the development of insulin resistance by promoting inflammation and the accumulation of macrophages in adipose tissue with subsequent decrease in irisin in these animals [36].

Nitrite/Nitrate are significantly reduced in obese rats. Piva et al., reported negative associations between nitrite/nitrate levels and obesity which were mediated by inflammation [37]. Impaired NO metabolism, especially reduced NO production and bioavailability, has been recognized as a risk factor for development of obesity [38].

Physical exercise increases endogenous irisin, reduced adiposity and improved energy balance and subclinical inflammation [39]. It is evident from our results that after exercise irisin concentrations increase significantly. Varela-Rodríguez et al., correlated the relation of Irisin mRNA levels in muscle tissue and irisin levels in the blood plasma [40].

Aerobic exercise increases serum irisin level and prompt uncoupling protein 1 (UCP1) mRNA expression in inguinal white adipose tissue, on the other hand injection of an anti-irisin antibody proceeding to exercise prevent this increase in UCP1. This suggests that irisin is an important stimulus to white adipose tissue to increase UCP1 expression after exercise [27]. However Fain et al., observed that serum irisin levels increase only in familial hypercholesterolemic animals not in normal metabolic states after aerobic exercise [41]. Huh et al., found that serum irisin increases after 30 minutes of exercise [42]. Similarly, Kraemer et al., found increase in serum irisin levels in the first 54 minutes of treadmill [43]. Sharma et al., reported a positive feedback loop whereby increased circulating irisin increases PGC 1 α levels, which in turn induces further irisin secretion. PGC1 α is in fact the master regulator capable of increasing UCP1 protein in brown adipose tissue [44].

In the present study, 8 weeks of moderate intensity swimming exercise or exogenous administration of irisin to obese rats, significantly improved all metabolic profile, oxidative and inflammatory parameters as compared to control obese group, on the other hand all parameters studied are returned to normal control level in group treated both irisin and exercise. Irisin reduces oxidative stress as proved by significant decrease in MDA, it has been previously reported that Irisin prevent oxidative stress in the liver through the inhibition of protein arginine methyltransferase-3 [45] Wang et al., established that Irisin treatment reduces I/R-induced oxidative stress as it increases SOD activity [46].

Furthermore, irisin significantly increases NO level, it has been previously reported that swimming exercise increases eNOS expression at the protein level [47].

Also irisin itself increased NO production and phosphorylation of endothelial nitric oxide synthase (eNOS) in endothelial cells [48].

Combination of irisin administration and/or induction of endogenous irisin release by exercise reduce fasting blood glucose and increase insulin sensitivity. This improvement in glucose and lipid profile was achieved by increase glucose uptake combined with reduce gluconeogenesis in the liver [49]. Exercise induced overexpression of Fndc5 in obese animals reduced hyperglycemia and hyperinsulinemia [50].

Irisin prevent glucose/lipid metabolic dearangement, improve insulin resistance and increase energy expenditure via enhance lipolysis and uncoupling of oxidative phosphorylation [51].

Irisin is insulin-regeneration hormone and can accelerate the generation of beta cell it has an antiapoptotic action on pancreatic beta cells stimulate their proliferation and insulin biosynthesis and secretion [52] it has a potent antioxidant, anti-inflammatory activities especially under condition of exercise [53].

Conclusion:

Swimming exercise that represent aerobic and resistant exercise in the same time increase irisin secretion in abnormal metabolic state. Irisin either endogenous or exogenous initiate a novel strategy for the treatment of obesity and its complications even in absence of caloric restriction through ameliorating oxidative stress, increasing NO production reducing osteopontin that is new indicator for insulin resistance associated with metabolic syndrome.

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التأثير المحتمل للايريزين و/أو التدريب الرياضى معتدل الشده على التوازن الأيضى فى السمنة على الجرزان البيض

الخلفية: التمرين قد يشجع إفراز الميوكين مثل الايريزين وهو مرتبط بتوازن الطاقة والسمنة.

الهدف: دراسة تأثير الايريزين و/أو ممارسة السباحة ذات الكثافة المعتدلة على التوازن الأيضى فى السمنة عالية الدهون المستحثة فى الفئران الذكور البيضاء

المواد والأساليب: سيتم تنفيذ العمل الحالى على ٥٠ الفئران البيضاء الذكور، وتنقسم إلى مجموعتين: مجموعة التحكم (I): ١٠ فئران تغذى النظام الغذائى العادى وحقق داخل الصفاق مع ١٥٠ ميكرو لتر مطول المالح يومياً لمدة ٨ أسابيع.

ثانياً: مجموعة البدناء (II) تم تغذية ٤٠ من الفئران نظام غذائى عالى الدسم انها تنقسم إلى ٤ مجموعات فرعية ١٠ من الفئران فى كل مجموعة: (IIa) السمنة المتحكمة. (IIb) الفئران البدينة المعالجة بالايريسين مع حقن الايريزين داخل الصفاق فى جرعة of 100ng/ml يومياً لمدة ٨ أسابيع. (IIc) مجموعة السمنة مع ممارسة الرياضة ستسبح مجموعات التمارين لمدة ٣٠ دقيقة فى اليوم، ٥ أيام فى الأسبوع لمدة ٨ أسابيع متتالية. (IId) مجموعة السمنة الفئران المعالجة بالايريسين والرياضة معا يتم التعامل معها مثل الفئة الفرعية b و c فى نهاية الفترة التجريبية تم قياس المعلمات التالية لجميع الفئران: وزن الجسم (BW) مؤشر كتلة الجسم (BMI)، محيط البطن. تم الحصول على عينات الدم لقياس الأنسولين المصل، والجلوكوز الصيام فى الدم. احسب تقييم نموذج التماثل لمقاومة الأنسولين (هوما-IR)، وتقييم نموذج التماثل لحساسية الأنسولين (هوما-S)، قياس المصل الايريسين، اوستيوبونتين، الكوليسترول الكلى (TC)، مستوى الكوليسترول LDL، مستوى الكوليسترول الحميد، الدهون الثلاثية (TG)، الأحماض الدهنية الحرة، نيتريت/نترات ومالونداهيد.

النتائج: انخفض الوزن النهائى فى المجموعة المعالجة بالايريزين و/أو ممارسة الرياضة بشكل كبير ذات دلالة إحصائية بالمقارنة مع الوزن النهائى للمجموعة السمنة المتحكمة. المجموعة المعالجة بالايريسين وممارسة الرياضة معا لا يظهر تغيير بالمقارنة مع Irisin النهائى فى مجموعة التحكم العادية. مؤشر كتلة الجسم، المحيط البطنى، مصل BW، الأحماض TG، LDL، TC، اوستيوبونتين، IR الأنسولين، الجلوكوز الصيام، هوما- أظهرت زيادة كبيرة ذات دلالة إحصائية فى الفئران البدناء بالمقارنة MDA الدهنية الحرة، أو ممارسة الرياضة ادى إلى انخفاض Irisin مع المجموعة السيطرة العادية. اما حقن مع Irisin كبير ذات دلالة إحصائية فى جميع هذه النتائج. عندما يتم الجمع بين حقن ممارسة الرياضة انه يسبب انخفاضاً كبيراً ذات دلالة إحصائية بالمقارنة مع مجموعة السمنة المسيطرة والفرق ليس له دلالة إحصائية مع مجموعة التحكم العادية. وفيما يتعلق، والكوليسترول الحميد، نيتريت/نترات S بمستوى ايراسين، وحساسية الأنسولين فى هوما، فانها تنخفض بشكل ملحوظ ذات دلالة إحصائية فى الفئران البدينة مقارنة بالتحكم أو ممارسة الرياضة ادى إلى زيادة ذات دلالة إحصائية فى Irisin العادية، اما حقن مع ممارسة الرياضة فانه يسبب زيادة كبيرة Irisin هذه المعلمات. ذا تم الجمع بين حقن ذات دلالة إحصائية فى المعلمات الوصول إلى مستوى التحكم العادى.

الاستنتاج: و/أو ممارسة السباحة كثافة معتدلة بدء استراتيجية جديدة لعلاج السمنة أيضا Irisin كعلامة التنبؤيه لمقارنة الأنسولين لديه إمكانات علاجية فى Irisin الاستخدام المحتمل للسمنة.

الكلمات الرئيسية: السمنة ايريسين، ممارسة الرياضة، اوستيوبونتين.