Irisin Peptide is Myokine, Anti-Obesity and Anti-Lipidemic Factor

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Abstract

Background: The relevance of the FNDC5/irisin discovery as well as its controversy and potential functions, a need to obtain additional information regarding the nature of this hormone, the irisin, and its precise role in metabolism. **The aims of this study** were designed to evaluated the role of muscles in circulating irisin participation, as myokine hormone, as well as its association to hyperlipidemia.

Subjects and Methods: The study was carried out at the Colleges of Medicine and Athletic,University of Baghdad, and at Teaching Laborateries, Baghdad Teacing Hospital, during the period from January 2013 to July 2013. Twenty-two healthy athlete men of different kinds of chronic activity and forty healthy non-athlete control men of normal activity were enrolled in this study. Investigations included serum measurements of irisin using enzyme immunosorbent assay (ELISA) technique, lipid profile parameters including total cholesterol, triglyceride (TG), Low-density lipoprotein-cholesterol (LDL-C) and high-density lipoprotein-cholesterol (HDL-C) were also measured using spectrophotometric methods.

Results: The mean (±SD) value of serum irisin in athelets men was significantly increased compared with that of non athelets cpontrol men (p=0.01). In athelets group, serum mean value of TG was significantly decreased, while that of HDL-C was significantly increased in comparison with those of non athlete control men (for both, p=0.01). Also, significant negative correlations were observed between irisin and each of

BMI values (r=0.44 ,p=0.01) and total cholersterol concentrations (r=0.4 ,p=0.05) in athlete men group.

Conclusion: Irisin myokine in facing irisin adipokine is powerful. Irisin may be a protective factor against obesity and hyperlipidemia.

Key words: Irisin, athletics, obesity, hyperlipidemia

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Introduction

Exercise provides clear beneficial effects for the prevention of numerous diseases. However, many of the molecular events responsible for the curative and protective role of exercise remain elusive. The recent discovery of FNDC5/irisin protein that is liberated by muscle tissue in response to exercise might be an important finding with regard to this unsolved mechanism. The most striking aspect of this peptide is its alleged capacity to drive brown-fat development of white fat and thermogenesis. However, the nature and secretion form of this new protein is controversial [1].

Built on these premises, Boström's [2] work reveals that exercise and PGC1α stimulates the expression of the FNDC5 gene in muscle. This gene encodes a Type I membrane protein that might be proteolytically processed to form the secreted irisin. However, these authors were unable to detect the 12 kDa soluble form of irisin in their experiments. Relevantly, they showed that treating primary subcutaneous white adipocytes during differentiation with Fndc5 induced the activation of browning and thermogenic genes such as UCP1 in vitro. Furthermore, they showed that FNDC5/irisin was significantly elevated in plasma after endurance exercise in mice and humans and that circulating increments of this myokine forced with adenoviral vectors that expressed the full length

of FNDC5 increased energy expenditure in mice with no changes in movement or food intake [3].

Given the relevance of the FNDC5/irisin discovery as well as its controversy and potential functions, a need to obtain additional information regarding the nature of this hormone and its precise role in energy homeostasis, including its participation in food-related disorders [1]; that will open wide field for research that shed light on irisin. The aims of this study was designed to evaluated the effectiveness of irisin as dipokine to myokine and its relation to hyperlipidemia.

Subjects and Methods

Forty healthy men were enrolled to matched the twenty two healthy athlete men in their age-, BMI- and fat percentage, their age range was (38- 59 years). The subjects of the first group were on normal activity range (20- 60 min/day), while those of the second group were of different kinds of regular sport of more than 180 min /day at least for three weeks daily. Exclusion criteria included those who have diabetes mellitus (DM), thyroid disorders, Cushings syndrome, renal diseases, ischemic heart disease and any other acute or chronic illness. These criteria were achieved by accurate clinical history, clinical examination and laboratory analysis including serum estimation of TSH, T4, cortisol & creatinine.

Formal consent was taken from each subject. We received ethical approval from the Scientific Committee of the Biochemistry Depatement, College of Medicine and the scientific Committee of College of Athletics, university of Baghdad, Iraq.

Five millliters (ml) of blood was collected from the peripheral vein of each enrolled subject after an overnight fasting state. The collected blood was allowed to clot for 30 minute, centrifugate at 3000 rpm for 15 minute, and the separated serum was stored in aliquote at – 20 ◦ C. Serum irisin was measured using the enzyme immunosorbant assay (ELISA) according to the method reported by Young-Pearse[4] ,glucose and lipid profile parameters including total cholesterol, TG, HDL-cholesterol, LDL-cholesterol were

measured according to spectrophotometric methods stated by Burtis CA [5] Kit for serum irisin measurements was provided by Phoenix Pharmaceuticals. INC, USA, while those for serum glucose and the lipid parameters were obtained from Human Company, Germany.

We used the Statistical Package for Social Sciences (SPSS Inc., Chicago IL, USA) version 15 for all statistical studies. We used Student' s t-tests to test for statistical significance. Linear regression was utilized to test for correlation between different studied parameters, and the significance of the r-value was assessed by related t-test. P-values of less than 0.05 were considered significant.

Results

Table 1 reveals the mean (±SD) values of clinical characteristics of athletes and non athlete control men. There were no significant differences in the mean values of age, BMI and fat percentage between the athlete men group and the non-athlete control men.

Table 2 shows the mean (±SD) values of the measured biochemical parameters in both groups of men. The role of muscle in synthesis and secretion of irisin was emphasized by the comparison of the mean value of serum irisin between athlete males and age-, BMI- and fat percentage- matched healthy control men with highly significant increased in the first group than in the later one (60.37 ± 12.31 ng/ml vs. 49.83 ± 9.55 ng/ml; p=0.001).

Regarding the glucose and lipid profile parameters, the results revealed significant decrease of serum TG (130.23±35.30 mg/dl) and significant increased of HDL-cholesterol (45.88±7.2 mg/dl) in athlete men compared with non-athlete control subjects (188.26±50.32 mg/dl, 41.33±9.1 mg/dl, for both p=0.01, respectively). The mean values of serum total cholesterol and LDL-cholesterol did not differ significantly between two groups. In athlete men group, the study also revealed significant negative correlations between the serum irisin levels and each of BMI values (r=-0.44, p=0.01), total cholesterol concentrations (r=-0.40, p=0.04), and TG levels (r=-0.35, p=0.05), figures 1,2 and 3, respectively. While, in non-athlete controls group, the serum irisin levels was

significantly positively correlated with BMI values (r=0.52, p=0.01, figure 4) and total cholesterol concentrations (r=0.34, p=0.047, figure 5).

Table 1: Clinical Characteristics of Athletes and Non Athletes Men

STUDIED PARAMETERS	STUDIED GROUPS	NO.	MEAN	SD	T-TEST P-VALUE	T-TEST SIG.
AGE (YEARS)	HEALTHY MEN	40	45.03	5.64	0.60	NS
	HEALTHY ATHLETES SUBJECTS	22	43.82	12.20		
BMI (KG/M^2)	HEALTHY MEN	40	30.24	4.54	0. 70	NS
	HEALTHY ATHLETES SUBJECTS	22	29.327	4.92		
FAT PERCENTAGE	HEALTHY MEN	40	30.44	5.82	0. 23	NS
	HEALTHY ATHLETES SUBJECTS	22	28.39	6.95		

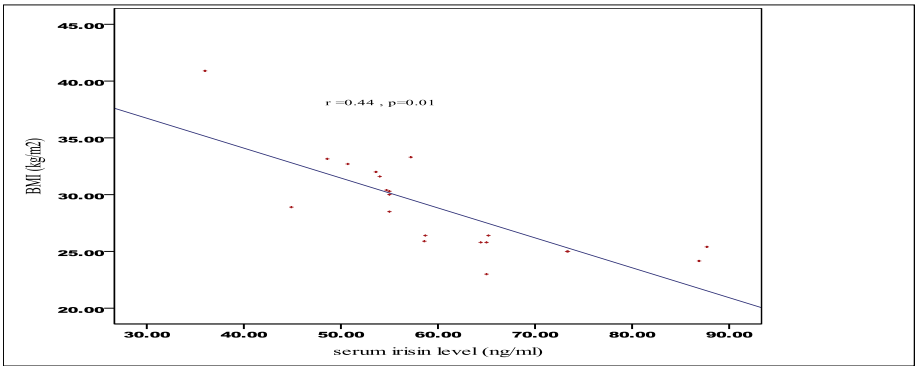

Figure (1): Correlation between serum Irisin levels (ng/ml) and BMI values in athlete men group.

Table 2: Mean (±SD) Values of Serum Irisin and Lipid Profile Parameters in Athlete and Non Athlete Men Groups

Studied parameter	Studied groups	No	Mean	SD	t-test p-value sig
Serum Irisin (ng/ml)	healthy non athlete men	40	49.83	9.55	0.001 HS
	healthy athlete men	22	60.37	12.31	
S. Total Cholesterol (mg/dl)	healthy non athlete men	40	180.0	36.7	0.08 NS
	healthy athletes men	22	162.0	35.5	
S. TG (mg/dl)	healthy non athlete men	40	188.96	50.34	0.01 HS
	healthy athletes men	22	130.23	35.3	
S.HDL-C (mg/dl)	Healthy non athlete men	40	41.33	9.1	0.01 HS
	Healthy athletes men	22	45.88	7.2	
S.LDL-C (mg/dl)	Healthy non athlete men	40	95.79	30.41	0.12 NS
	Healthy athlete men	22	85.88	31.5	

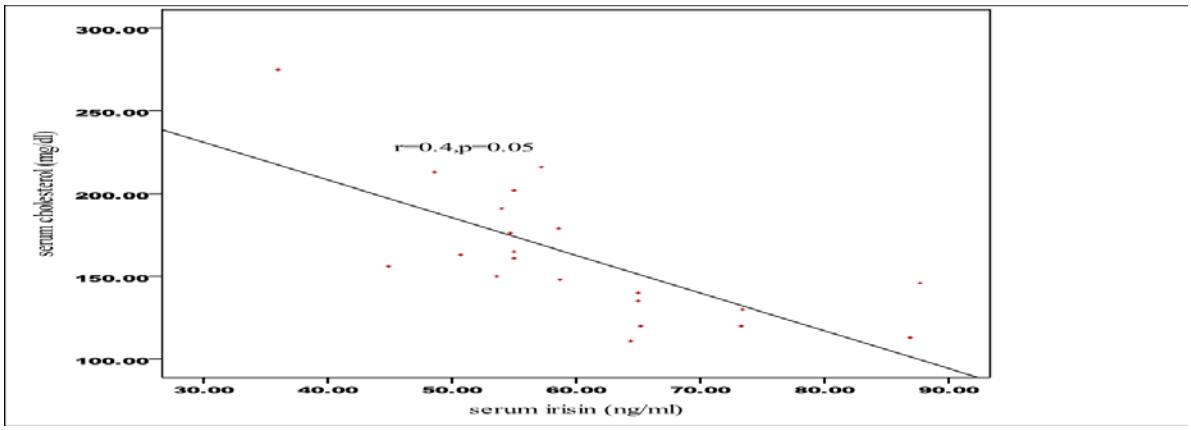

Figure (2): Correlation between serum Irisin levels (ng/ml) and total cholesterol concentrations (mg/dl) in athlete men group.

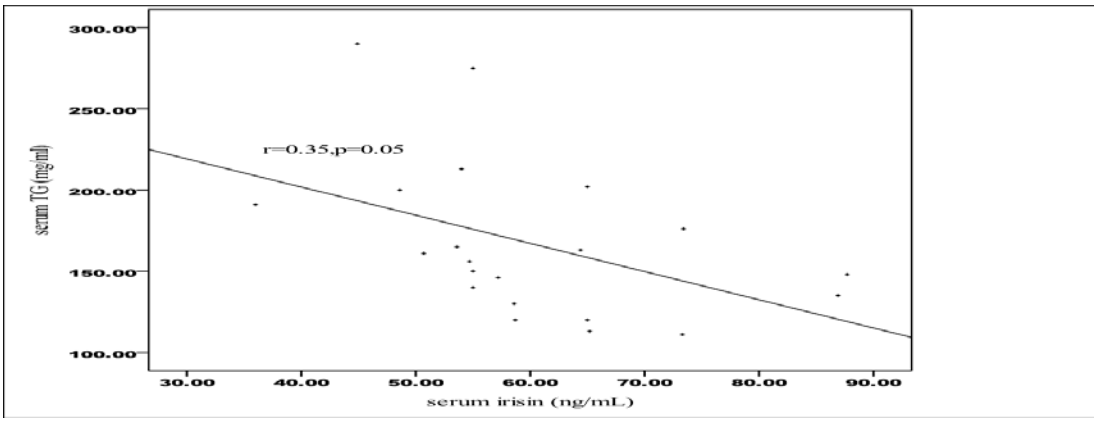

Figure3: Correlation between serum Irisin levels (ng/ml) and TG concentrations (mg/dl) in athlete men group.

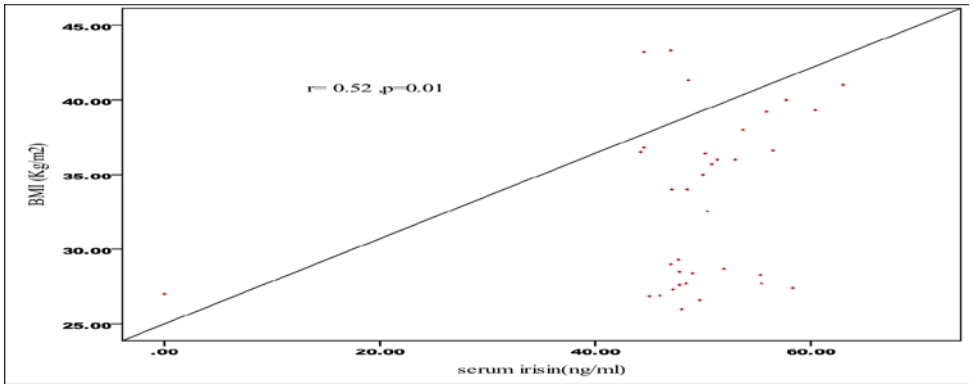

Figure (4):. Correlation between serum Irisin levels (ng/ml) and BMI (Kg/m^2) values in non athletes group.

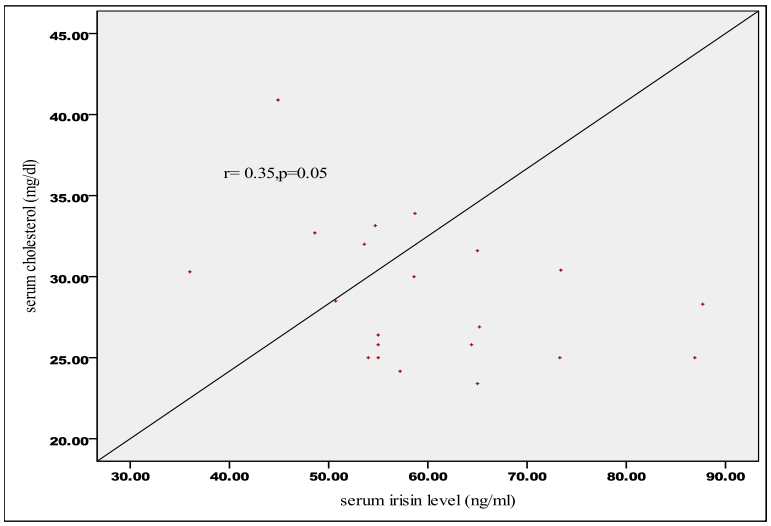

Figure (5): Correlation between serum irisin levels (ng/ml) and cholesterol concentrations (mg/dl) in non athletes group.

Discussion

Irisin has been proposed as a possible novel treatment in diabetes and obesity. Inducible brown adipocytes, named brite or beige, do not arise from the same lineage as myogenic cells and developmentally programmed brown adipocytes [6] and the cellular mechanisms underlying the browning process remain controversial. Exercise training results in adaptive structural and metabolic changes in skeletal muscle, including a change in the type of muscle fiber, mitochondrial biogenesis, and angiogenesis [7] .

Currents study's finding (Table 2) viewed the serum irisin level by muscle mass assessment in the same gender depending on physical activity, with higher serum irisin level in chronic healthy athletes men than age -, BMI -, sex- and fat percentage matching non – exercised healthy men. Laaksonen et al. [8] and Irving et al. [9] suggested that PGC-1α is strongly expressed in human skeletal muscle and can be induced by endurance training. The release of irisin from FNDC5 to the extracellular space has also been

reproduced in a number of studies, [10,11] the regulation of irisin by exercise, however, has been reproduced only in some cohorts, whereas a lack of regulation was seen in others done under different physiological and/or experimental conditions [12] .

Another aspect that remains to be clarified is the timing of irisin increase after exercise; since the above studies have tested irisin in different time before and after exercise the possibility exists that irisin increases for a finite period of time after exercise but its levels do not stay elevated for a prolonged period of time [2,14]. Another study conducted by Handschin and Spiegelman [15] and Wenz et al. [16] showed the positive beneficial effect of exercise in muscle on PGC-1α induction which in turn stimulates mitochondrial biogenesis, angiogenesis, and fiber-type switching. It also provides resistance to muscular dystrophy and the health benefits of elevated muscle expression of PGC-1α may go beyond the muscle itself. PGC-1α stimulates the secretion of factors from skeletal muscle that affect the function of other tissues via stimulating the expression of several muscle gene products including FNDC5-irisin. Irisin is induced in exercise and it activates profound changes in subcutaneous adipose tissue stimulating browning and UCP1 expression. The negative correlation in athlete men between irisin and BMI along with positive one in non- athlete controls may pointed to protective positive effect of exercise on production of irisin and answer the mastery that link the exercise and weight loss. The significant increased of HDL-C and significant decreased of TG in athlete men group along with significant negative correlations between irisin and each of cholesterol and TG (figures 2 and 3) may arise a new aspect of irisin as anti-lipidemic factor and be considered as protective against ischemic heart disease. Although, the mean value of BMI of both groups did not differ significantly, the significant negative correlation that observed between irisin and BMI values in athletes group (figure 1) beside the positive one in non athletes group (figure 4) may solve the unexplained link between the prolonged regular exercise and the weight loss, means that irisin peptide is the miss circle in this link.

In conclusion the present study revealed the muscle origin of circulated irisin and its appeared as a myokine peptide factor. The study also suggested the anti-obesity and anti-lipidemic effect of irisin, but these need for future studies.

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References

1. Erickson HP :"Irisin and FNDC5 in retrospect: An exercise hormone or a transmembrane receptor?".Adipocyte.2013,2 (4): 289–293.
2. Bostrom P, Wu J, Jedrychowski MP, et al. A PGC-1- alpha-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012; 481: 463–468.
3. Reynolds G. "Exercise Hormone May Fight Obesity and Diabetes". Well . Nature .2012,418,463 -468 .
4. Young-Pearse TL, Bai J, Chang R, Zheng JB, LoTurco JJ, Selkoe DJ. "A critical function for beta-amyloid precursor protein in neuronal migration revealed by in utero RNA interference". J Neurosci 2007; 27(52): 14459-69.Burtis CA,Ashwood ER, Bruns DE.Fundamentals of clinical chemistry". Sixth edition, 2008; 401-402.
5. Burtis CA, Ashwood ER, Bruns DE.Fundamentals of clinical chemistry". Sixth edition, 2008; 401-402.
6. Soyal SM, Felder TK, Auer S, Hahne P, Oberkofler H, Witting A, Paulmichl M, Landwehrmeyer GB, Weydt P, Patsch W. A greatly extended PPARGC1A genomic locus encodes several new brain specific isoforms and influences Huntington Disease age-of-onset. Hum Mol Genet. 2012; 21:3461-3473.
7. Berger J, Moller DE . "The mechanisms of action of PPARs". Annu. Rev. Med. 2002,200253: 409–35.

8. Laaksonen DE, Lindstrom J, Lakka TA, et al. Medicine. Irisin, light my fire. Science 2012; 336: 42–43.
9. Irving BA, Robinson MM, Nair KS. Age effect on myocellular remodeling: response to exercise and nutrition in humans. Ageing Res Rev 2012; 11: 374–389.
10. Wen MS, Wang, CY, Lin SL, et al. Decrease in irisin in patients with chronic kidney disease. PLoS One 2013; 8(5): e64025 http://dx.doi.org/ 10.1371/journal.pone.0064025.
11. Moreno-Navarrete JM, Ortega F, Serrano M, et al. Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. J Clin Endocrinol Metab 2013; 98: E769–E778.
12. Sanchis-Gomar F, Lippi G, Mayero G, et al. Irisin: Anew potential hormonal target for the treatment of obesity and type 2 diabetes. J. Diabetes 2012; 4(196).
13. Bostrom P, Wu J, Jedrychowski MP, et al. A PGC-1- alpha-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature. 2012; 481: 463–468.
14. Benton CR, Holloway GP, Han X-X, et al. Increased levels of peroxisome proliferator-activated receptor gamma, co-activator 1- alpha (PGC- 1α) improve lipid utilization, insulin signalling and glucose transport in skeletal muscle of lean and insulin-resistant obese Zucker rats. Diabetologia 2010; 53: 2008–2019.
15. Handschin C, Spiegelman BM. The role of exercise and PGC-1-alpha in inflammation and chronic disease. Nature 2008; 454: 463-469.40.
16. Wenz T, Rossi SG, Rotundo RL, et al. Increased muscle PGC-1alpha expression protects from sarcopenia and metabolic disease during aging. Proc. Natl. Acad. Sci. 2009; 106: 20405–20410.