

Research Article

Effects of concurrent training and fenugreek supplementation on myokines and lipid profiles in overweight women

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Abstract

Exercise induced myokines play an important role in metabolic regulation and inter organ communication. This study investigated the effects of concurrent training and fenugreek supplementation, separately and in combination, on circulating myokines and lipid profile in overweight women. Forty overweight women (BMI $\geq$ 25 kg/m²) were randomly assigned to four groups: concurrent training (CT), fenugreek supplementation (FG), combined concurrent training plus fenugreek (CT+FG), and control (CON). The intervention lasted 6 weeks (3 sessions per week). The concurrent training protocol consisted of circuit based resistance exercises (50–70% 1RM) followed by aerobic training at 55–70% HRmax. Participants in the supplementation groups consumed fenugreek extract capsules (670 mg/day; two 335 mg capsules taken after breakfast and dinner). Fasting blood samples were collected before the intervention and 48 hours after the final training session. Concurrent training significantly improved lipid profile by reducing triglycerides (TG) and low density lipoprotein (LDL) and increasing high density lipoprotein (HDL) ($p < 0.05$). Training interventions also significantly increased circulating irisin and Myonectin levels ($p < 0.05$). Fenugreek supplementation alone improved HDL levels but showed no significant effect on myokine concentrations. The combined CT+FG group demonstrated the greatest improvements in lipid profile and myokine responses compared with the other groups. Concurrent training appears to be an effective strategy for improving lipid profile and increasing circulating myokines in overweight women. Fenugreek supplementation may provide additional benefits for lipid profile when combined with exercise; however, its direct effects on myokines remain unclear. Further studies with larger sample sizes are warranted to clarify the potential synergistic effects of exercise and fenugreek supplementation.

Key Words: Concurrent training, Fenugreek, Irisin, Myonectin, Lipid profile, Overweight

Introduction

Obesity or overweight, a chronic metabolic disease, is considered one of the main challenges of public health worldwide (Bhupathiraju et al., 2016), and despite global warnings and increasing awareness of the complications and harms of this phenomenon, a significant increase in the prevalence of this disease is still observed worldwide (Bastien et al., 2014). Today, most people become overweight with increasing age, which is usually associated with a decrease in physical activity, so that the amount of overweight varies depending on lifestyle and diet. In addition to dietary counseling, behavioral support, and medications are recognized as the main factors involved in controlling overweight and obesity (Bray et al., 2016).

On the other hand, skeletal muscle has recently been recognized as an endocrine organ that not only contains important metabolic molecules whose release changes metabolism but also interacts with other tissues through the release of some hormones known as myokines (Albrecht et al., 2015). It is possible that myokines released from skeletal muscle mediate the beneficial effects of exercise in relation to health (Athanasίου et al., 2022). Therefore, muscle cells are very metabolically active and interact with other organs during training and exercise by producing and releasing myokines. Myokines have autocrine, paracrine and endocrine effects (Pedersen, 2019). Irisin and Myonectin are two myokines that are produced in exercising skeletal muscles and then enter the bloodstream. Moreover, irisin is a 112-amino acid myokine (the secreted form of the transmembrane protein fibronectin type III domain-containing 5, FNDC5) (Tari et al., 2019) that was discovered in 2012. Irisin is likely a bridge between the interaction between skeletal muscle and other tissues involved in homeostasis and energy metabolism, including fat tissue. More specifically, irisin is a hormone stimulated by exercise that is secreted by skeletal muscle in white mice and humans (Boström et al., 2012). Therefore, irisin is a muscle-derived signal that directly interacts with fat tissue and causes browning of white fat tissue. This capacity of irisin improves the metabolic

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profile, increases the energy cost of the whole body and has antiobesity and antidiabetic effects that improve with exercise and training (Polyzos et al., 2013).

Myokines, which are regulated by skeletal muscle contraction, play a vital role in the relationship between muscle and other tissues, such as fat, liver, and pancreas (Ellingsgaard et al., 2011). On the other hand, Myonectin is now considered a myokine that was first observed in the retinal pigment epithelium before being known as a myokine (Peterson et al., 2014). Myonectin was introduced as a myokine in 2012 by Seldin et al. Myonectin, or CTRP15 (C1q/TNF-related protein isoform 15), is a newly recognized myokine whose release is affected by exercise and nutrition. It can increase plasma free fatty acid uptake by fat tissue and the liver through increasing the release of fatty acid transporters such as FATP (Fatty acid transport proteins), FATP412 (Fatty acid transport proteins412) and CD36 (Fatty acid translocase/Cluster of Differentiation 36). Myonectin acts as a myokine, which is the interface between skeletal muscle and other metabolic organs of the body, such as fat tissue and the liver, and regulates and coordinates metabolism in the whole body (Seldin et al., 2012). Considering that obesity and overweight are effective factors in changing myokines and that the amount of Myonectin in overweight people is greater than that in people with normal weight, the effects of exercise and training in this group of people may differ from those in people with normal weight (Norheim et al., 2011).

Therefore, investigating the effects of exercise and training on the amount of myokines produced by overweight people may be helpful in understanding the effective mechanisms involved in this process. Currently, all kinds of exercise and physical activities involve different energy devices and cause different adaptations, which, as one type of training method, can be referred to as concurrent training, simultaneous training of several energy-producing devices and Concurrent implementation of several types of training (such as strength and endurance exercises) (Gorzi et al., 2017). Concurrent training, which is a combination of weight training and aerobic exercise, is a key component of exercise recommendations for controlling weight, obesity, and general health (Bull et al., 2020). These types of exercise and training can provide the effects of both types of exercise. However, endurance and resistance exercises have different and sometimes opposite adaptations (Kim & Bae, 2015). Endurance activity leads to an increase in capillary density, cardiovascular capacity, aerobic power and resistance to fatigue, as well as a decrease in the resting heart rate and body fat percentage. Moreover, aerobic exercise improves the oxidative capacity and insulin sensitivity of overweight youth and elderly people (Solomon et al., 2008). whereas strength training increases muscle strength, increases fat-free mass and decreases body fat

Many studies have investigated the effects of Concurrent training on strength and endurance adaptation (Leveritt et al., 2003). In this context, some research findings have revealed the detrimental effects of concurrent training on strength and endurance adaptation (Chtara et al., 2008). In many cases, endurance training opposes the adaptations produced by strength training (Inder et al., 1998). Most recent studies have shown that Concurrent strength and endurance training may interfere with improvements in physical fitness factors (Nieman et al., 2004). Moreover, training arrangements, that is, the order in which strength and endurance training is performed, may also affect the adaptation caused by training. To date, few studies have described the adaptation mechanisms in skeletal muscles with concurrent aerobic and resistance stimuli. Moreover, the results of the studies that investigated adaptation and performance changes in people who have performed concurrent exercises are not the same (Leveritt et al., 1999). Similarly, some researchers have observed interference in the acquisition of strength and aerobic endurance after the implementation of concurrent exercise programs (Hickson, 1980). For example, a study by Taipale (2013) showed that a Concurrent training session with the order of endurance/resistance and resistance/endurance had different hormonal and neuromuscular responses (Taipale et al., 2013). In addition, according to the reports of Huh et al. (2015), an increase in irisin density has been observed after a high-intensity interval training protocol and strength training. Owing to the beneficial effects of irisin and the effects of this hormone on white fat tissue as well as its thermogenic properties, this myokine is known as a therapeutic target for metabolic patients. Paying attention to the intensity and type of training is of particular importance regarding the effect of exercise on the release of irisin (Huh et al., 2015). In another study, 12 weeks of Concurrent training with caffeine consumption was considered an effective factor for favorable changes in the CTRP index. 12, CTRP-15 and insulin resistance in obese postmenopausal women (Khazaei et al., 2020).

Therefore, considering the prevalence of overweightness and obesity, related diseases and the detrimental effects resulting from them, the important role of regular sports activities as well as the effect of herbal supplements in this domain, the use of herbal medicines has increased in recent years. Other factors include the minimal side effects of herbal medicines compared with those of chemical drugs and the general tendency of societies to use traditional medicines. In this context, fenugreek can be considered a medicinal plant with long-term use and remarkable therapeutic properties (Alu'datt et al., 2024). Several studies have indicated the beneficial effects of fenugreek in reducing the levels of fats, especially blood cholesterol (Belguith et al., 2013). In this context, studies have shown that the soluble fibers in fenugreek seeds, particularly galactomannan, can be fermented by gut microbiota in the colon, resulting in the

propionate, and butyrate, which may contribute to the regulation of lipid metabolism and cholesterol homeostasis. (Afzal et al., 2026).

Moreover, many studies have shown the significant effects of diosgenin (bitter fenugreek saponin) on fat and glucose metabolism. The alkaloid found in fenugreek seeds, called trigonelline, which is a composition similar to nicotinic acid, can effectively reduce TG (Ghafari et al., 2023). For example, the results of a subgroup analysis revealed that fenugreek reduced TG and LDL levels and increased HDL levels more effectively in diabetic subjects and that fenugreek supplementation significantly improved the lipid profile (LDL, TG, TC and HDL). As a result, it can be considered an effective medicinal plant for reducing fat (Heshmat-Ghahdarijani et al., 2020). Finally, considering the lack of information about the changes in myokines after Concurrent training in different orders, as well as the importance of exercising in different orders and the lack of information about the effects of these exercises even on lipid profiles, the researchers were motivated to conduct this study. Therefore, to design the most effective training method, the present study was conducted with the aim of investigating the effects of concurrent training and fenugreek supplementation on the lipid profile and the levels of some myokines in overweight women.

Materials and methods

Participants and study design

The current study is a semi-experimental and applied study. The statistical population of this study consisted of overweight women (BMI above 25 and below 30) from Dashti city, which is located in Bushehr Province. Among them, 40 women were selected as samples, and after initial measurements, they were randomly divided into 4 groups: Concurrent training (10 women), fenugreek supplementation (10 women), Concurrent training/fenugreek supplementation (10 women) and the control group (10 women). The randomization process was performed via sealed opaque envelopes without identification. The researcher was responsible for blinding the participant groups. Moreover, the participants in the current study were not informed about the hypotheses of the study, but they were required to follow the nutritional recommendations.

All participants signed an informed consent form (along with parental consent) to voluntarily participate in the current study according to the principles of the Helsinki Treaty. The participants were invited to this study by spreading announcements on the virtual networks of Dashti city. The inclusion criteria for this study included people with no history of taking supplements or anti-inflammatory drugs, people with minimal weight changes in the last year, and people aged 20–35 years. Furthermore, the criteria

for the withdrawal of the participants from this study were the absence of more than one session in the exercise program; accidents; injury; disruptive diseases; and the occurrence of any intervening factor that affects the effective participation of the subjects in the training sessions. The demographic information of the participants was also measured via valid tools and questionnaires. Before the start of the intervention, the participants' height, weight, body mass index (BMI) and age were recorded. To measure weight, a Seka scale made in Germany with an accuracy of 0.1 kg was used, and a Seka caliper with an accuracy of 0.1 cm was used to measure the height of the participants. In addition, body mass index was calculated by dividing weight (kg) by height (cm) to a power of 2.

Sport training was conducted for 8 weeks, with 3 sessions per week. After 5 minutes of warm-up, the training group participants performed circular resistance activity (3 times with 14 repetitions at 50% of a maximum repetition and 30 seconds of rest between each station and 2 minutes of rest between each of the 6 stations) (1–3). The stations included a squat, a chest press, a seated leg curl (machine), a shoulder press, a leg press and a seated cable row. After 10 minutes of rest, they subsequently performed aerobic activity with an intensity of 70% of the maximum heart rate for 30 minutes. Notably, to determine the maximum of one repetition maximum (1RM), the 1RM was measured from the participants of the resistance training group via the Brzycki method. In this way, a barbell was chosen for each participant so that the participant could perform a maximum of 6–8 repetitions via that barbell. The performed barbell, along with the repetitions, was subsequently placed in the appropriate formula. Measurements were made at all 6 stations (Table 1). In addition, the standard formula of age 220 years was used according to the intensity required in each session (Ghaderi et al., 2022).

In the present study, a Glucorex B fenugreek capsule with the health code 0544805717522703 manufactured by Iran's Barij Essence Company was used. Each capsule contained 335 mg of dry fenugreek seed extract. The supplement group and training/supplement group consumed two capsules of 335 mg of fenugreek twice a day after breakfast and dinner. The placebo group also received two placebo capsules daily (containing wheat flour) similar to the supplement.

To check the biochemical variables, before the start of the 8-week program, 5 cc of blood was taken from the cubital vein of the left elbow from each participant in the fasting state (between 7 and 8 a.m.) by a nurse. Forty-eight hours after initial blood collection, the intervention groups were subjected to the selected protocol for 8 weeks. Then, 48 hours after the last training session and after the participants took the supplement in a similar way as that conducted in the pretest period, blood collection was conducted for the second time. The blood samples were incubated at room temperature for 20 minutes to allow them to clot; then, the

Table 1. Concurrent training protocol.

Resistance training							Aerobic training		
	number of stations	repetitions	rest between stations (seconds)	number of turns (Round)	Rest between each turn (seconds)	1RM (intensity %)	Week	Running time (min)	Maximum beat (intensity %)
First	6	14	30	2	90	%50	First	20	55%
Second	6	14	30	2	90	%50	Second	20	55%
Third	6	14	30	2	90	%50	Third	24	60%
Fourth	6	14	30	3	120	%50	Fourth	24	60%
Fifth	6	14	30	3	120	%50	Fifth	26	65%
Sixth	6	14	30	3	120	%50	Sixth	26	65%
Seventh	6	12	30	4	150	%50	Seventh	28	70%
Eighth	6	12	30	4	150	%50	Eighth	30	70%

samples were centrifuged for 10 minutes at a speed of 3,000–35,00 rpm, and the serum was separated. They were kept in four separate microtubes at a temperature of -80°C. The amount of irisin was measured via an ELISA kit with a measurement range of 0.05–15 pg/ml and a sensitivity of 0.023 pg/ml, and Myonectin was measured via an ELISA kit with a catalog number of CK-E91376, a measurement range of 0.05–10 pg/ml and a sensitivity of 0.03 pg/ml. Both of these kits were manufactured by East Biofarm Company of America. All of the ethical principles of the current study were reviewed by the ethics committee of Bushehr University of Medical Sciences and approved with the special code of IR.BPUMS.REC.1403.045.

Statistical analysis

For analysis of the data, a paired t test was used to compare pretest and posttest values, and one-way ANCOVA was used to compare the effectiveness of the three exercise interventions on the variables. The independent variable was the training method, and the dependent variable consisted of the values of the variables after the training and exercise were applied. The pretest values were used as covariates in this analysis. Preliminary checks were conducted to ensure that the assumptions of normality, linearity, homogeneity of variances and homogeneity of the regression slope were not violated. For analyzing the data, SPSS version 22 software was used, and a significance level of $p < 0.05$ was considered in this study.

Results

According to the results obtained from the dependent t test in Table 2, in the training, supplement and supplement/training intervention groups, a significant decrease was observed in the TG and LDL values in comparison with the baseline values ($p < 0.05$). Moreover, considering the HDL, irisin and Myonectin levels,

in the training group and the supplement/training group, an increase in HDL-C was observed compared with the pretest values, and in the supplement group, a significant increase in HDL-C ($P < 0.05$) was detected. However, in the supplement group, no significant difference was observed in the irisin and Myonectin levels, and in the control group, no significant difference was observed in any of the investigated variables.

An examination of the intergroup changes and analysis of covariance results in Table 3 revealed significant differences in HDL ($E_s = 0.88$, $P < 0.0001$), LDL ($E_s = 0.89$, $P > 0.0001$), TG ($E_s = 0.94$, $P > 0.0001$), irisin ($E_s = 0.88$, $P > 0.0001$) and Myonectin ($E_s = 0.85$, $P < 0.0001$) levels between the training groups. Moreover, for all the variables, the supplement/training group had a greater effect than did the initial values. To find the place of intergroup differences, the LSD post hoc test was used, which is summarized in the table 4.

Discussion

As mentioned earlier, obesity is considered a chronic metabolic disease and an important challenge in people's daily lives. The results of the present study revealed that 8 weeks of concurrent training caused a significant increase in the secretion of the hormones irisin and Myonectin, as well as a significant decrease in lipid profile indices (LDL and TG) and a significant increase in HDL in the training group and in the supplement group. Therefore, the results of the Myonectin variable found in this study are in line with the results of studies conducted by Shahidi et al. (2019) and Safarzadeh et al. (2017). In this context, both studies concluded that circular resistance training can be an effective intervention method for increasing the plasma levels of Myonectin in obese and overweight people. More specifically, Shahidi et al. reported that 6 weeks of resistance training for 3 sessions per week significantly increased Myonectin levels (SHAHIDI et al., 2019). In addition, Safarzadeh et al. reported a

Table 2. Results related to age, height, weight, and body mass index in the four groups

Variable		Training	Supplement	Supplement/training	Control
Age (year)		30.86 ± 1.16	30.75 ± 0.89	32.87 ± 0.83	31.23 ± 1.53
Weight (kg)	Pretest	76.31 ± 2.75	76.97 ± 3.98	75.93 ± 2.21	75.55 ± 3.23
	Posttest	71.50 ± 2.77	74.02 ± 3.72	70.50 ± 2.07	75.75 ± 3.83
Height (cm)		165.59 ± 1.74	164.45 ± 2.07	164.38 ± 1.98	164.49 ± 2.12
BMI (kg/m ²)	Pretest	27.42 ± 1.08	27.68 ± 0.91	27.76 ± 1.15	27.57 ± 1.99
	Posttest	26.39 ± 1.09	27.16 ± 0.87	26.44 ± 1.08	27.57 ± 1.23

significant increase in Myonectin levels in the experimental group after 8 weeks of circular resistance training in 33 obese men (Safarzade et al., 2016).

In another study, it seems that changes in the plasma levels of Myonectin are independent of changes in the absolute or relative amount of body fat or changes in the lipid profile such that the increase in muscle intracellular calcium concentration caused by ionomycin leads to a significant increase in Myonectin. On the other hand, it has also been reported that the increase in the intracellular levels of cAMP due to forskolin and epinephrine also leads to an increase in the expression of Myonectin (Seldin et al., 2012). Another study suggested that the potential of skeletal muscle endocrine glands to secrete Myonectin is not unrelated to fat metabolism, and these effects may be due to the increase in the density of fatty acid-binding protein 4 (FABP4), fatty acid transport protein 1 (FATP1), and fatty acid translocase (FATCD36) proteins, which are proteins that bind and transport fatty acids in adipocytes (Sun et al., 2023).

On the other hand, according to Huh et al.'s (2015) reports, an increase in irisin concentration has been observed after intense interval training protocols and strength training. These researchers believe that paying attention to the intensity and type of training and exercise is of particular importance in the effectiveness of training in the expression of irisin (Huh et al., 2016). The results of the current study are in line with the findings of Huh et al. (2015) regarding the expression of irisin in three types of aerobic exercise programs. Huh et al. (2015) studied intense, resistance and low-intensity aerobic exercise and reported that the increase in irisin occurs immediately after all 3 types of training, but the highest amount is after strength training compared with aerobic training. This result is likely due to muscle damage followed by an increase in creatine kinase (Zhang et al., 2014).

Furthermore, regarding the effects of concurrent training on the lipid profile, the findings of the following studies are in line with the findings of the current study. For example, in a study on the effects of 8 weeks of concurrent training on leptin levels in the

serum, lipid profile and body composition of inactive overweight men, performing periodic aerobic, continuous and strength training simultaneously with sauna improved the lipid profile, body composition and serum concentration of leptin. Although these changes were relatively greater in the aerobic training group (39), a finding that is in agreement with findings of studies such as Amini et al. (2016) and Wooten et al. (2008), it is also consistent with other related studies on sport training that investigated aerobic training in nonathlete subjects and reported improvements in lipid profile indices (Amini et al., 2016, (Wooten et al., 2008, Tofighi et al., 2017). Confirming these findings, it has been reported in a review article in this field that at least 8 weeks of aerobic or anaerobic interval training is necessary to improve high-density lipoprotein-cholesterol levels, and in studies lasting less than eight weeks, no change in the lipid profile has been reported (Kessler et al., 2012). Weight loss is also associated with significant changes in the lipid profile in obese individuals, particularly reductions in triglycerides, cholesterol, and low-density lipoprotein cholesterol.

On the other hand, no heterogeneous and completely similar studies were found in terms of the choice of training protocol and the sex of the human subjects. The lack of related studies on overweight women makes it difficult to explain the mechanisms of the effect of resistance training on Myonectin reduction. In this regard, and inconsistent with the current study, Shahidi et al. (2019) reported that 4 weeks of resistance training did not significantly increase the Myonectin levels of inactive young men in the experimental group. It seems that the selection type of resistance training program and the duration of 4 weeks of resistance training by the researchers did not affect the serum levels of Myonectin (Kazemi et al., 2020).

To date, no studies on irisin in combination with fenugreek supplementation or concurrent training have reported inconsistent results; however, according to some reports (Huh et al., 2015), an increase in the irisin concentration was observed after the resistance training protocol, which is consistent with the results of the present study (Huh et al., 2015). However, some studies have shown that the amount of irisin available in the blood

Table 3. Comparison of changes in variables across the four groups.

Variable	Group	Pretest	Posttest	Intragroup changes		Intergroup changes		
				T	P	F	P	effect size
LDL (mg/dl)	Training	135.06 ± 71.3	129.52 ± 97.3	4.16	* 0.004	16.17	€ 0.0001	0.85
	Supplement	133.72 ± 38.2	130.12 ± 30.3	2.68	* 0.01			
	Training/ Supplement	134.35 ± 14.3	125.07 ± 08.3	7.92	* 0.0001			
	Control	129.51 ± 03.2	129.06 ± 01.3	0.73	0.51			
HDL (mg/dl)	Training	30.96 ± 75.2	34.42 ± 71.2	2.29	* 0.04	45.36	€ 0.0001	0.86
	Supplement	29.53 ± 05.3	33.51 ± 00.2	2.34	* 0.04			
	Training/ Supplement	32.04 ± 42.3	38.88 ± 73.2	5.10	* 0.001			
	Control	30.11 ± 22.3	29.40 ± 47.1	0.73	0.49			
TG (mg/dl)	Training	189.03 ± 49.9	182.26 ± 16.9	2.97	* 0.03	20.18	€ 0.0001	0.89
	Supplement	190.32 ± 04.5	186.76 ± 65.6	2.53	* 0.04			
	Training/ Supplement	187.29 ± 97.6	169.10 ± 52.9	6.75	* 0.0001			
	Control	187.86 ± 25.8	188.68 ± 63.9	0.03	0.95			
irisin (ng/ml)	Training	6.51 ± 45.0	7.15 ± 35.0	10.87	* 0.0001	44.54	€ 0.0001	0.88
	Supplement	6.67 ± 27.0	7.03 ± 13.0	1.98	0.08			
	Training/ Supplement	6.10 ± 47.0	8.09 ± 50.0	13.47	* 0.0001			
	Control	6.95 ± 20.0	6.94 ± 21.0	0.19	0.85			
Myonectin (ng/ml)	Training	4.26 ± 23.0	6.06 ± 13.0	11.09	* 0.0001	21.73	€ 0.0001	0.85
	Supplement	4.66 ± 18.0	5.03 ± 15.0	1.29	0.11			
	Training/ Supplement	3.67 ± 36.0	6.02 ± 21.0	12.44	* 0.0001			
	Control	3.67 ± 36.0	3.69 ± 19.0	0.87	0.77			

€ Intergroup differences * Intragroup differences

Table 4. Tukey's post hoc test results to find the place of differences in intergroup changes.

Group	Group	LDL	HDL	TG	Irisin	Myonectin
Training	Supplement	0.67	0.45	0.47	0.005	0.0001
	Supplement/ Trainin	0.001	0.0001	0.002	0.0001	0.0001
	Control	0.008	0.0001	0.04	0.0001	0.0001
Supplement	Supplement/ Training	0.0001	0.0001	0.0001	0.0001	0.0001
	Control	0.008	0.07	0.03	0.001	0.001
Training/Supplement	Control	0.0001	0.0001	0.0001	0.0001	0.0001

circulation is positively correlated with the bicep circumference, body mass index, glucose, intestinal endogenous peptide (insulin secretion inhibitors) and insulin-like growth factor-1. On the other hand, the level of irisin is negatively correlated with age and the levels of insulin, glyceride and adiponectin, which indicates that irisin may play a role in compensatory mechanisms of metabolic regulation. Irisin is a myokine that increases as a result of sports activities and exercise. After exercise and physical activity, the release of PGC-1 α , a transcription-activating molecule, increases, stimulating the release of the membrane protein FNDC5 in the muscle cells (Martinus et al., 2006).

Many studies have been conducted on various properties of the fenugreek plant, and its therapeutic effects on various subjects have been reported (Murlidhar et al., 2012), but its effects on hu-

-man myokine levels have not been investigated. In addition, the effects of fenugreek supplementation and concurrent training on the properties of irisin and Myonectin have not been investigated. Fenugreek is one of the oldest medicinal plants and belongs to the pea family, whose seeds contain 6–10% lipids, 44–59% carbohydrates and 20–30% protein (Mohammadzadeh et al., 2015). Diosgenin increases the amount of PPAR γ (peroxisome proliferator-activated receptor gamma (MCP-1)) in white fat tissue, causing the differentiation of fat cells and reducing the size of fat cells. Moreover, the secretion of monocyte chemoattractant protein (monocyte chemotactic protein 1) is decreased in fat cells, whereas the level of adiponectin acid is increased, which inhibits inflammation in fat cells. Next, large micelles of bile acids and saponin molecules are formed in the small intestine, and these micelles prevent the absorption of cholesterol and cause it to be

excreted in feces (Reddy et al., 2011). Diosgenin also causes a decrease in the amount of TG and a decrease in the release of the mRNAs of fat-forming genes. Fenugreek seeds slow the absorption of fats and sugars and therefore regulate the production of cholesterol in the liver (Kim et al., 2023).

The results of the present study revealed a significant decrease in TG and LDL and a significant increase in HDL in the training/supplement group compared with the training group, and it can be concluded from the values that the fenugreek supplement had a significant effect on reducing the lipid profile and weight loss. These results are in line with those of studies by Sharma et al. (2023) and Kamali Sarvestani and Hosseini et al. (2014), who compared the therapeutic effects of fenugreek and atorvastatin on hyperlipidemia (Sharma et al., 2015). The results of their study revealed that, compared with fenugreek, atorvastatin has stronger antihyperlipidemic effects and can significantly reduce the serum levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) and low-density lipoprotein (VLDL), but a significant increase in high-density lipoprotein (HDL) in the fenugreek-consuming group compared with the group that took atorvastatin (Hosseini et al., 2023). Similarly, in Kamali Sarvestani et al.'s study, the simultaneous effects of aerobic training and fenugreek supplementation at a dose of 20 mg on the lipid profile of inactive obese women were investigated, which revealed a significant decrease in LDL and a significant increase in HDL, similar to the findings of Hosseini et al.'s study (Ghafari et al., 2023).

On the other hand, studies that have shown inconsistent results include the study of Kassaian et al., where the consumption of fenugreek seed powder caused a significant decrease in the amount of sugar, TG and VLDL and no significant change in HDL in diabetic patients (Srichamroen et al., 2009). Moreover, a study conducted by Ghafari et al. revealed a significant decrease in TG, TC and LDL and no significant change in HDL after 6 weeks of HIIT training along with the consumption of fenugreek supplements (Ghafari et al., 2023).

On the basis of the findings of the present study, the implementation of concurrent training with respect to the intensity and duration of the period can ultimately lead to an increase in the secretion of irisin and Myonectin according to the mechanism of muscle contraction. Notably, if the consumption of fenugreek supplements is also accompanied, the amounts of these myokines would increase more. Furthermore, understanding the mechanism and effects of this exercise and training type and the fenugreek plant may have favorable effects on reducing blood fat levels and may play an important role in weight loss.

Conclusion

In conclusion, six weeks of concurrent training improved circulat-

-ing irisin and Myonectin levels and favorably modified lipid profile indices in overweight women. The combination of concurrent training and fenugreek supplementation was associated with greater improvements in lipid profile variables compared with training alone. However, the specific contribution of fenugreek supplementation to myokine responses remains unclear and requires further investigation. These findings suggest that concurrent training may be an effective strategy for improving metabolic health in overweight individuals.

What is already known on this subject?

Obesity or overweight, a chronic metabolic disease, is considered one of the main challenges of public health worldwide.

What this study adds?

The combination of concurrent training and fenugreek supplementation was associated with greater improvements in lipid profile variables compared with training alone.

Organ Cross-Talk Tips:

- Concurrent training may be an effective strategy for improving metabolic health in overweight individuals with improving muscle and lipid metabolism.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest in the present research.

Ethical approval All of the ethical principles of the current study were reviewed by the ethics committee of Bushehr University of Medical Sciences and approved with the special code of IR.BPUMS.REC.1403.045.

Informed consent Performed.

Author contributions

Conceptualization: S.A.; Methodology: E.D.; Software: M.B.; Validation: S.M.; Formal analysis: S.A.; Investigation: E.D., M.B;

Resources: S.A.; Data curation: E.D.; Writing -original draft: S.M.; Writing-review & editing: E.D.; Visualization: M.B.; Supervision: S.A.; Project administration: E.D.; Funding acquisition: M.B..

References

- Bhupathiraju, S. N., & Hu, F. B. (2016). Epidemiology of obesity and diabetes and their cardiovascular complications. *Circulation research*, 118(11), 1723-1735. <https://doi.org/10.1161/CIRCRESAHA.115.306825>.
- Bastien, M., Poirier, P., Lemieux, I., & Després, J. P. (2014). Overview of epidemiology and contribution of obesity to cardiovascular disease. *Progress in cardiovascular diseases*, 56(4), 369-381. <https://doi.org/10.1016/j.pcad.2013.10.016>
- Bray, G. A., Frühbeck, G., Ryan, D. H., & Wilding, J. P. (2016). Management of obesity. *The Lancet*, 387(10031), 1947-1956. [https://doi.org/10.1016/S0140-6736\(16\)00271-3](https://doi.org/10.1016/S0140-6736(16)00271-3).
- Albrecht, E., Norheim, F., Thiede, B., Holen, T., Ohashi, T., Schering, L., Lee, S., Brenmoehl, J., Thomas, S., Drevon, C. A., Erickson, H. P., & Maak, S. (2015). Irisin - a myth rather than an exercise-inducible myokine. *Scientific reports*, 5, 8889. <https://doi.org/10.1038/srep08889>
- Athanasίου, N., Bogdanis, G. C., & Mastorakos, G. (2023). Endocrine responses of the stress system to different types of exercise. *Reviews in Endocrine and Metabolic Disorders*, 24(2), 251-266. <https://doi.org/10.1007/s11154-022-09758-1>
- Pedersen, B. K. (2019). Physical activity and muscle-brain crosstalk. *Nature Reviews Endocrinology*, 15(7), 383-392. <https://doi.org/10.1038/s41574-019-0174-x>.
- Tari, A. R., Norevik, C. S., Scrimgeour, N. R., Kibro-Flatmoen, A., Storm-Mathisen, J., Bergersen, L. H., ... & Wisløff, U. (2019). Are the neuroprotective effects of exercise training systemically mediated? *Progress in cardiovascular diseases*, 62(2), 94-101. <https://doi.org/10.1016/j.pcad.2019.02.003>.
- Boström, P., Wu, J., Jedrychowski, M. P., Korde, A., Ye, L., Lo, J. C., ... & Spiegelman, B. M. (2012). A PGC1- α -dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature*, 481(7382), 463-468. <https://doi.org/10.1038/nature10777>
- Polyzos, S. A., Kountouras, J., Shields, K., & Mantzoros, C. S. (2013). Irisin: a renaissance in metabolism?. *Metabolism*, 62(8), 1037-1044. <https://doi.org/10.1016/j.metabol.2013.04.008>.
- Ellingsgaard, H., Hauselmann, I., Schuler, B., Habib, A. M., Baggio, L. L., Meier, D. T., ... & Donath, M. Y. (2011). Interleukin-6 enhances insulin secretion by increasing glucagon-like peptide-1 secretion from L cells and alpha cells. *Nature medicine*, 17(11), 1481-1489. <https://doi.org/10.1038/nm.2513>
- Peterson, J. M., Mart, R., & Bond, C. E. (2014). Effect of obesity and exercise on the expression of the novel myokines, Myonectin and Fibronectin type III domain containing 5. *PeerJ*, 2, e605. <https://doi.org/10.7717/peerj.605>
- Seldin, M. M., & Wong, G. W. (2012). Regulation of tissue crosstalk by skeletal muscle-derived myonectin and other myokines. *Adipocyte*, 1(4), 200-202. <https://doi.org/10.7717/peerj.605>
- Norheim, F., Raastad, T., Thiede, B., Rustan, A. C., Drevon, C. A., & Haugen, F. (2011). Proteomic identification of secreted proteins from human skeletal muscle cells and expression in response to strength training. *American Journal of Physiology-Endocrinology and Metabolism*. <https://doi.org/10.1152/ajpendo.00326.2011>
- Gorzi, A., Mehrabi, O., Agha Alinejad, H., Rahmani, A. and Ghasemnian, A. A. (2017). The Effect of Endurance, Strength and Concurrent Training on Plasma Level of IL-6 and Cortisol in Untrained Men. *Strategic Studies on Youth and Sports*, 16(35), 225-234. https://faslname.msy.gov.ir/article_199.html?lang=en
- Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *British Journal of Sports Medicine*. 2020;54(24):1451–1462. <https://doi.org/10.1136/bjsports-2020-102955>.
- RIGI, A., BANITALEBI, E., KAZEMI, A., & AZIMIAN, E. (2017). Comparison of order of concurrent training on anthropometric characteristics, serum IL-15 levels and insulin resistance index in postmenopausal women. <https://www.sid.ir/paper/30810/en>
- Solomon, T. P., Sistrun, S. N., Krishnan, R. K., Del Aguila, L. F., Marchetti, C. M., O'Carroll, S. M., ... & Kirwan, J. P. (2008). Exercise and diet enhance fat oxidation and reduce insulin resistance in older obese adults. *Journal of applied physiology*, 104(5), 1313-1319. <https://doi.org/10.1152/jappphysiol.00890.2007>
- Leveritt, M., Abernethy, P. J., Barry, B., & Logan, P. A. (2003). Concurrent strength and endurance training: the influence of dependent variable selection. *Journal of Strength and Conditioning Research*, 17(3), 503-508. [https://doi.org/10.1519/1533-4287\(2003\)017<0503:CSAETT>2.0.CO;2](https://doi.org/10.1519/1533-4287(2003)017<0503:CSAETT>2.0.CO;2)
- Chtara, M., Chaouachi, A., Levin, G. T., Chaouachi, M., Chamari, K., Amri, M., & Laursen, P. B. (2008). Effect of concurrent endurance and circuit resistance training sequence on muscular strength and power development. *The Journal of Strength & Conditioning Research*, 22(4), 1037-1045. <https://doi.org/10.1519/JSC.0b013e31816a4419>
- Inder, W. J., Hellemans, J., Swanney, M. P., Prickett, T. C. R., & Donald, R. A. (1998). Prolonged exercise increases peripheral plasma ACTH, CRH, and AVP in male athletes. *Journal of Applied Physiology*, 85(3), 835-841. <https://doi.org/10.1152/jappl.1998.85.3.835>
- Nieman, D. C., Davis, J. M., Brown, V. A., Henson, D. A., Dumke, C. L., Utter, A. C., ... & McAnulty, L. S. (2004). Influence of carbohydrate ingestion on immune changes after 2 h of intensive resistance training. *Journal of applied physiology*, 96(4), 1292-1298. <https://doi.org/10.1152/jappphysiol.01064.2003>
- Leveritt, M., Abernethy, P. J., Barry, B. K., & Logan, P. A. (1999). Concurrent strength and endurance training: a review. *Sports medicine*, 28(6), 413-427. <https://doi.org/10.2165/00007256-199928060-00004>
- Hickson RC. Interference of strength development by simultaneous training for strength and endurance. *European Journal of Applied Physiology and Occupational Physiology* 1980; 45(2-3): 255-63. <https://doi.org/10.1007/BF00421333>
- S. Taipale, R., & Häkkinen, K. (2013). Acute hormonal and force responses to combined strength and endurance loadings in men and women: the "order effect". *PloS one*, 8(2), e55051. <https://doi.org/10.1371/journal.pone.0055051>
- Huh, J. Y., Siopi, A., Mougios, V., Park, K. H., & Mantzoros, C. S. (2015). Irisin in response to exercise in humans with and without metabolic syndrome. *The Journal of Clinical Endocrinology & Metabolism*, 100(3), E453-E457. <https://doi.org/10.1210/jc.2014-2416>

Khazaei, B., Daneshjoo, A., & Izadi, A. (2020). Effect of 12 Weeks of Concurrent Training with Caffeine Supplementation on Selected Adipokines and Insulin Resistance in Obese Postmenopausal Women. *Journal of Applied Exercise Physiology*, 16(32), 31-42. <https://doi.org/10.22080/jaep.2020.19022.1952>

Alu'datt MH, Rababah T, Al-Ali S, et al. Current perspectives on fenugreek bioactive compounds and their potential impact on human health: A review of recent insights into functional foods and other high value applications. *Journal of Food Science*. 2024;89(4):1835–1864. <https://doi.org/10.1111/1750-3841.16970>.

Belguith-Hadriche, O., Bouaziz, M., Jamoussi, K., Simmonds, M. S., El Feki, A., & Makni-Ayedi, F. (2013). Comparative study on hypocholesterolemic and antioxidant activities of various extracts of fenugreek seeds. *Food chemistry*, 138(2-3), 1448-1453. <https://doi.org/10.1016/j.foodchem.2012.11.003>

Afzal, B., Farooq, F., Khalid, L., Abdi, G., & Muhammad Aadil, R. (2026). Fenugreek and gut microbiota: effects, mechanisms, and health implications. *International Journal of Food Properties*, 29(1). <https://doi.org/10.1080/10942912.2026.2672776>

Ghafari, Z., Mogharnasi, M., & Ghahremani, R. (2023). The Effect of 6 Weeks of High Intensity Interval Training with Fenugreek Supplementation on Lipid Profile and Body Composition Indices in Overweight and Obese Women. *Armaghane Danesh*, 28(2), 171-188. <https://doi.org/10.52547/armaghanj.28.2.1>

Heshmat-Ghahdarijani, K., Mashayekhiasl, N., Amerizadeh, A., Teimouri Jervejani, Z., & Sadeghi, M. (2020). Effect of fenugreek consumption on serum lipid profile: A systematic review and meta-analysis. *Phytotherapy research*, 34(9), 2230-2245. <https://doi.org/10.1002/ptr.6690>

Ghaderi, G. S., ABBASSI, D. A., Abdi, A., & Saeidi, A. (2022). The Effect of Combined Training and Caffeine Supplementation on Toll-like Receptor 2 (TLR2), TLR4, and Dectin-1 in Obese Men. <https://www.sid.ir/paper/951352/en>

SHAHIDI, F., & KASHEF, M. (2019). The effect of 4 and 6 weeks of resistance training on serum levels of myonectin and IGF-1 in sedentary young men. <https://www.sid.ir/paper/10483/en>

Safarzade, A., & Moazam-Vahid, L. (2016). Effect of eight weeks resistance training on plasma myonectin concentration in obese men. *Journal of Applied Exercise Physiology*, 12(24), 119-128. <https://doi.org/10.22080/jaep.2017.1466>

Seldin, M. M., Peterson, J. M., Byerly, M. S., Wei, Z., & Wong, G. W. (2012). Myonectin (CTRP15), a novel myokine that links skeletal muscle to systemic lipid homeostasis. *Journal of Biological Chemistry*, 287(15), 11968-11980. <https://doi.org/10.1074/jbc.M111.336834>

Sun Z, Liu Z, Xi J, et al. Effects of myonectin on porcine intramuscular adipocyte differentiation and exogenous free fatty acid utilization. *Cell Biology International*. 2023;47 / 34(8):3757–3764. <https://doi.org/10.1080/10495398.2023.2224838>

Huh, J. H., Ahn, S. V., Choi, J. H., Koh, S. B., & Chung, C. H. (2016). High serum irisin level as an independent predictor of diabetes mellitus: a longitudinal population-based study. *Medicine*, 95(23), e3742. <https://doi.org/10.1097/MD.0000000000003742>

Zhang, Y., Li, R., Meng, Y., Li, S., Donelan, W., Zhao, Y., ... & Tang, D. (2014). Irisin stimulates browning of white adipocytes through mitogen-activated protein kinase p38 MAP kinase and ERK MAP kinase signaling. *Diabetes*,

63(2), 514-525. <https://doi.org/10.2337/db13-1106>

Foroutan, Y., BEHPOOR, N., & Tadibi, V. (2019). The effect of 8 weeks of concurrent training on serum leptin levels, lipid profiles and body composition of overweight inactive men. <https://www.sid.ir/paper/68561/en>

Amini, R., Rajabi, H., Amir Seifadini, M. R., & Divsalar, K. (2016). Study of changes in adiponectin, leptin, and plasma lipid profile of Inactive men the result 24 session, playing futsal. *Research in Sports Medicine and Technology*, 14(12), 11-22. <https://doi.org/10.18869/acadpub.jsmt.14.12.11>

Wooten, J. S., Biggerstaff, K. D., & Anderson, C. (2008). Response of lipid, lipoprotein-cholesterol, and electrophoretic characteristics of lipoproteins following a single bout of aerobic exercise in women. *European journal of applied physiology*, 104(1), 19-27. <https://doi.org/10.1007/s00421-008-0770-2>

Tofighi, A., Jamali, B., Babaei, S., & Amaghani, A. (2017). Effect of regular exercise on serum levels of homocysteine and lipid profile in obese female. *Medical Journal of Tabriz University of Medical Sciences*, 39(5), 20-27. <https://mj.tbzmed.ac.ir/Article/19510>

Kessler, H. S., Sisson, S. B., & Short, K. R. (2012). The potential for high-intensity interval training to reduce cardiometabolic disease risk. *Sports medicine*, 42(6), 489-509. <https://doi.org/10.2165/11630910-000000000-00000>

Kazemi, A., Kerendi, H., & Shoaee, V. (2020). Comparison of the effect of resistance training with and without blood flow restriction on serum levels of IGF-1, testosterone and myonectin in young men. *Journal of Sport Biosciences*, 12(1), 93–107. <https://doi.org/10.22059/jsb.2020.283358.1347>

Huh, J. Y., Mougios, V., Kabasakalis, A., Fatouros, I., Siopi, A., Douroudos, I. I., ... & Mantzoros, C. S. (2014). Exercise-induced irisin secretion is independent of age or fitness level and increased irisin may directly modulate muscle metabolism through AMPK activation. *The Journal of Clinical Endocrinology & Metabolism*, 99(11), E2154-E2161. <https://doi.org/10.1210/jc.2014-1437>

Martinus, R., Corban, R., Wackerhage, H., Atkins, S., & Singh, J. (2006). Effect of psychological intervention on exercise adherence in type 2 diabetic subjects. *Annals of the New York Academy of Sciences*, 1084(1), 350-360. <https://doi.org/10.1196/annals.1372.024>

Murlidhar Meghwal, M. M., & Goswami, T. K. (2012). A review on the functional properties, nutritional content, medicinal utilization and potential application of fenugreek. doi/full/10.5555/20133129457

Mohammadzadeh, A., Gol, A., & Oloumi, H. (2015). The Effects of Fenugreek Seed Powder on Oxidant and Antioxidant Factors in Male Rats with Acetaminophen-induced Liver Toxicity. *Journal of Babol University of Medical Sciences*, 17(9), 44-51. <https://doi.org/10.22088/jbums.17.9.44>

Reddy, R. R., & Srinivasan, K. (2011). Effect of dietary fenugreek seeds on biliary proteins that influence nucleation of cholesterol crystals in bile. *Steroids*, 76(5), 455-463. <https://doi.org/10.1016/j.steroids.2010.12.015>

Kim, J., Noh, W., Kim, A., et al. (2023). The effect of fenugreek in type 2 diabetes and prediabetes: A systematic review and meta-analysis of randomized controlled trials. *International Journal of Molecular Sciences*, 24(18), 13999. <https://doi.org/10.3390/ijms241813999>

Sharma, S., Mishra, V., Jayant, S. K., & Srivastava, N. (2015). Effect of *Trigonella foenum graecum* L on the activities of antioxidant enzyme and their expression in tissues of alloxan-induced diabetic rats. *Journal of evidence-based complementary & alternative medicine*, 20(3), 203-211. <https://doi.org/10.1177/2156587215573664>

Hosseini, S. A., Hamzavi, K., Safarzadeh, H., & Salehi, O. (2023). Interactive effect of swimming training and fenugreek (*Trigonella foenum graecum* L.) extract on glycemic indices and lipid profile in diabetic rats. *Archives of Physiology and Biochemistry*, 129(2), 349-353.

<https://doi.org/10.1080/13813455.2020.1826529>

Srichamroen, A., Thomson, A. B., Field, C. J., & Basu, T. K. (2009). In vitro intestinal glucose uptake is inhibited by galactomannan from Canadian fenugreek seed (*Trigonella foenum graecum* L) in genetically lean and obese rats. *Nutrition Research*, 29(1), 49-54.

<https://doi.org/10.1016/j.nutres.2008.11.002>