JCHR (2025) 15(4), 767-781

Journal of Chemical Health Risks

sanad.iau.ir/journal/jchr

ORIGINAL ARTICLE

Effect of Aerobic Exercise and Cinnamon Extract on Leptin Gene Expression in Liver and Fat Tissues of Male Rats Fed by High Fat Diet

Maria Dehvari[1], AbdolAli Banaei Far[*1], Sajad Arshadi[1], Ardeshir Zafari[2]

[1]*Department of Exercise Physiology, Faculty of Physical Education and Sports Sciences, South Tehran Branch, Islamic Azad University, Tehran, Iran*

[2]*Department of Physical Education and Sports Sciences, Zanjan Branch, Islamic Azad University, Zanjan, Iran*

(Received: 22 October 2022 Accepted: 2 May 2023)

KEYWORDS

Exercise;
Leptin;
Obesity;
Cinnamon;
Liver;
High-fat food

ABSTRACT: Considering the desired effect of aerobic exercise, the effect of high-fat diets on obesity, and the beneficial effects of cinnamon; the present research seeks to answer the question of whether the implementation of aerobic exercise and cinnamon extract have different effects on the relative expression of leptin gene in the liver and fat tissues and also the mass of liver and fat tissues of male rats fed with a high-fat diet. The present experimental research was conducted using an animal model in the form of multi-group research (five groups: 1. control, 2. high-fat diet, 3. cinnamon extract and high-fat diet, 4. aerobic exercise and high-fat diet, 5. aerobic exercise and cinnamon extract and high-fat diet) Independent variables included aerobic exercise and cinnamon extract gavage of high-fat diet is also considered as a background variable. And Dependent variables are the level of leptin gene expression in the tissue of fat and liver, as well as body weight and the weight of liver and fat tissues. All groups received high_fat food in addition to normal food. The Training group participated in an aerobic exercise program. Cinnamon extract was given to cinnamon groups. All samples were anesthetized, killed, and operateon. The results show the effect of a high-fat diet on unfavorable changes in leptin gene expression, body weight, and the weight of fat tissue and liver. Performing aerobic exercise alone, consuming cinnamon extract alone, and the interaction of aerobic exercise and cinnamon extract cause desired changes in leptin gene expression in liver and fat tissue and the weight of liver and fat tissue compared to the high-fat diet group. Therefore; the Recommendation to take cinnamon extract along with exercise can cause desired and useful effects.

INTRODUCTION

The serum levels of leptin hormone in women and obese people are higher than in men and in people with normal weight, which is the reason is the increase in leptin gene expression in fat cells. Limited animal and human experience showed that treatment with leptin causes a decrease in food consumption, appetite, and body fat. The effect of leptin on the brain causes appetite regulation, weight control, and some other metabolic processes

*Corresponding author: alibanaeifar@yahoo.com (A.A. Banaei Far)
DOI: 10.22034/jchr.2023.1971267.1636

depended on it. Disturbance in leptin function causes weight gain and fat mass and obesity [1]. On the other hand, the reduction of energy consumption that results from the reduction of physical activities and sports training also plays a very important role in the occurrence of obesity [2, 3]. It seems that two factors of serum leptin level due to the effect on appetite and the ability to reduce energy intake and physical activities due to the ability to increase energy consumption, have a very important and decisive role in appetite regulation nutritional patterns, weight control, and body fat mass. Patterson et al showed that even three weeks of training can also prevent the adverse effects of a high-fat diet on the body weight of rats [4]. Kang et al showed that performing aerobic exercise in obese diabetics leads to a significant decrease in body fat percentage, body mass index, and body weight [5]. Bergouinan et al. also showed that during sports training and long-term physical activities, the regulation of energy balance occurs [6]. Ossanloo et al showed that the performance of endurance exercises reduces the lipid profile and body composition and homeostasis indicators of glucose in inactive young women [7]. Eftekhari et al showed that performing aerobic exercises causes improvement and reduction of body composition and lipid profile factors and leptin hormone [8]. Hagobian et al. studied the effect of eight weeks of endurance exercise and a high-fat diet on appetite-regulating hormones in rat's plasma. The results showed that exercise can eliminate the fattening effect of a high-fat diet [9].

Leptin is released into the blood after being produced in fat tissue. There are carriers in the blood-brain that cause leptin enters the central nervous system and reduce appetite by participating in suppressing the synthesis of appetite-increasing neuropeptide (neuropeptide Y). This hormone is free in the bloodstream and is also circulating in connection with protein-binding leptin. In hypothalamus neurons, leptin regulates food intake and body weight through its receptors. Blood flow leptin is increased in response to the increase in fat mass, and affects the appetite center located in the hypothalamus under normal conditions to reduce food intake. When there is an abnormal increase in body mass, the activity of this mechanism can reduce the absorption of food and prevent the excessive increase of fat mass to restore the body weight to the previous set point [1].Messier et al studied the effects of a diet enriched with fructose and a diet enriched with fat and the combination of two diets on body weight gain in rats for three months. A Significant increase in body weight in groups with a high-fat diets and a combination of two diets was observed [10]. Haldade et al and Sampey et al increased the body weight and body fat of mice by using a high-fat diet. Plasma level and expression level of the leptin gene are increased not only in people with high-fat diets but also in other people with related conditions such as type 2 diabetes and cardiovascular diseases [11-15]. Acute and chronic exercise training has been hypothesized as a regulatory factor that may be able to influence leptin metabolism. The effect of an exercise training session on leptin regulation is still debated, but serum leptin concentrations in response to long-term intense exercise training decreased in two studies (marathon running and ultra-marathon running). Also, no change was observed in leptin blood flow was not observed immediately after an acute training session at a low time and moderate intensity. This information shows that sufficient negative energy balance may cause acute and immediate changes in serum leptin levels. This information also states that the reduction of leptin levels after a long-term training session is possibly related to little energy availability due to the energy cost of exercise and not to the stimulation of exercise itself [1, 16]. Little change in circulating blood leptin concentration immediately after short-term exercise probably cannot be due to a delayed effect after training. For example, a decrease in serum leptin levels, 24 to 48 hours after a training session, has probably been related to changes in fat mass or fluctuations and changes in energy absorption. Therefore, increasing energy costs due to training has probably been a major reason for the observed decrease in leptin concentration during the recovery period. These changes likely to mediate the renewal of energy homeostasis during the return period after a period of increase energy consumption (such as acute exercise). Information about the effects of chronic exercise on leptin levels in the bloodstream is ambiguous and questionable. It has been stated that chronic training cannot change leptin levels without reducing body mass. Therefore, no independent effect of chronic exercise on bloodstream leptin levels in obese subjects can be observed. It is accepted that performing chronic exercise often reduces fat mass in obese individuals. Therefore, when changes in bloodstream leptin are observed; it is assumed that these changes represent a secondary effect of exercise on energy balance and not the stimulation of the exercise itself. In contrast, some studies have reported the independent effects of chronic exercise on leptin levels.In these studies; it is assumed that the effects of chronic exercise on bloodstream leptin levels are maybe independent of the negative energy balance caused by the training. In this regard, the expression of the duration and intensity of the training may only indicate the increase in the energy cost of training and is not necessary to express the independent effect of training. Some studies have reported that serum leptin concentration has been decreased only in women and not in men after the implementation of chronic exercise and this result indicates a gender-dependent effect. Absorption of energy (calories) in these studies is not well controlled and due to gender differences, maybe it is a secondary response to fluctuations and changes in energy balance and not the result of performing sports training and future studies should control the absorption and cost of energy, in which case it will be determined whether the obtained results are independent of changes in energy balance or not? On the other hand, chronic exercise studies should also be specifically designed to evaluate the impact and relevance of the dose-dependent relationship between the amount of exercise and leptin levels and how this effect and relationship in a special gender [17, 18]

Using medicinal plants or their effective substances is among complementary and alternative treatments for weight loss and control. Cinnamon can be mentioned among these plants. Pharmacology and toxicology research do not show a special risk to the private sector for using cinnamon in humans [19]. Khan et al showed that different doses of cinnamon reduce glucose, triglycerides, and cholesterol in people with type 2 diabetes. Also, cinnamon can improve the lipid profile of the blood serum [20]. Hasani Ranjbar et al stated that cinnamon causes a significant reduction in body weight without any specific side effects [21]. Russell et al showed that cinnamon reduces the risk factors for diabetes and cardiovascular diseases [22]. Dylan showed that cinnamon extract with inhibitory activities of cinnamic aldehyde and pro-anthocyanidin has antioxidant effects [23]. Chua et al stated that the ethanol extract of cinnamon has high antioxidant activity [24]. Mosley and et al studied the effects of cinnamon extract on oxidative stress and liver damage in rats. And showed that cinnamon extract can be used as a therapeutic diet in the treatment of some liver disorders without any side effects [25]. Balazade et al showed that cinnamon is useful in reducing blood pressure and serum levels of blood lipids [26]. During six weeks of cinnamon extract gavage in obese diabetic rats, Shalaby et al concluded that 100 and 400 mg doses of cinnamon extract reduce weight, blood fats, and blood sugar [27]. Sartorius et al stated that cinnamon improves insulin activity and reduces liver fat and improves glucose homeostasis [28]. Hamidpour et al showed the therapeutic effects of cinnamon in inhibiting the angiogenesis of cancer cells and preventing Alzheimer's disease, and antioxidant, anticholesterol, antidiabetic, and detoxification properties [29]. Rashid Lamir et al studied the effects of four weeks of aerobic exercise with cinnamon consumption on lipoprotein and blood sugar indices of women with type 2 diabetics and showed that exercise with cinnamon can improve blood sugar and fat levels of diabetic patients [30].

Therefore, according to the desired effect of aerobic exercise on leptin gene expression, the effect of high-fat diets on the occurrence of obesity and the development of metabolic diseases and the beneficial effects of cinnamon in weight loss and lipid factors and glucose homeostasis and also, the lack of study that has been able to measure the effect of these three variables on leptin gene expression at the same time; and also the contradictory results that have been obtained in the study on different human and animal groups, the necessity of implementation of research in this regard is clear and worthy of consideration. Therefore, the present research seeks to answer the question of whether the implementation of six weeks of aerobic exercise and gavage of cinnamon extract affects the relative expression of the leptin gene in fat tissue and liver and also the mass of fat tissues and liver of male mice fed with a high-fat diet.

MATERIALS AND METHODS

The present experimental research aims to determine and compare the effects of aerobic exercise and cinnamon extract gavage on leptin gene expression in the liver and fat tissues of male rats fed with a high-fat diet using an animal model (two-old months Wistar male rats) and was implemented in the form of a multi-group research project with a control group. The independent variables included the implementation of six weeks of aerobic exercise and cinnamon extract gavage. Six-week gavage of a high-fat diet is considered a background variable. Dependent variables are also the level of leptin gene expression in liver and fat tissues, as well as body weight, the weight of fat tissue, and the liver. 50 two-month-old male mice were prepared and after keeping in control conditions for two weeks, to get familiar with and adapt, to the living environment, nutritional, and training conditions; after weight matching, were randomly divided into five groups of ten. The groups of the current research include the control group (which did not participate in the program of aerobic exercise, cinnamon extract consumption, and consumption of high-fat food did not participate, and were sampled to determine the basic values of the research variables, high-fat diet group (which shows the number of changes in research variables after six weeks of consuming high-fat food). The group of cinnamon extract and high-fat diet (that show the number of changes in research variables after six weeks of consumption). The group of aerobic exercise group and high-fat diet (that shows the number of changes in research variables after six weeks of performing aerobic exercise) and the group of aerobic exercise and cinnamon extract and high-fat diet (which shows the number of changes in research variables after six weeks of aerobic exercise, and consumption of cinnamon extract). Maintenance conditions (temperature, environment humidity, and light-dark cycle), nutrition, cleaning and ventilation of the living environment, and other relevant items were observed according to existing standards. The First and second week, rats maintained under controlled conditions for compatibility with living environment, nutritional conditions(access to water and normal food for rodents from pars animal feed company`s products in the form of pellets in the amount of 10 grams per every 100 gram of body weight during the research period) and training (activity on the five-channel animal smart electric treadmill) with a constant electric shock at the rate of 0.1 MV , treadmill slope zero percent, speed 10-15 meter per minute, and duration of training 5-10 minutes a day

In the following days and weeks, weight measurement, consumption of high-fat food, consumption of cinnamon extract, aerobic exercise and finally measurement of research variables were performed(Table1).

All groups receiving high-fat food, received high-fat food emulsion (Table 2) daily, in the amount of 1.5 mg per kilogram of weight, as a gavage, for six weeks, in addition to normal food [31-33].

Table 1. Research protocol.

Group	Day 14	Third to eights week (six weeks)	Day +2
Control	Weigh measuring	----------	Measuring research variables
High-fat diet		High-fat diet gavage	
Cinnamon extract and high-fat diet		High-fat diet gavage and cinnamon extract (200mg)	
Aerobic exercise and a high-fat diet		High-fat diet gavage and performing aerobic exercise	
Aerobic exercise, Cinnamon extract, and a high-fat diet		High-fat diet gavage and cinnamon extract (200mg) and performing aerobic exercise	

Table 2. High-fat food composition.

material	Corn oil	sucrose	Whole milk powder	cholesterol	Multi-vitamin	Tween80	Propylene glycol	Salt	Distilled water
Amount(gram)	400	150	80	100	2.5	36.5	31	10	300

Exercise protocol

The training group participated in the aerobics training program on the treadmill for five days a week (Sunday, Monday, Tuesday, Thursday, and Friday) and for six weeks. The practice protocol of the present study was designed based on the studies of Sokhanvar Dastjerdi et al and Noura et al, On this basis, the strain, gender, age, and approximate weight of the subjects of the present study were also matched based on the mentioned study; Therefore, the relative intensity of work throughout the exercise program was equivalent to 70-75% of maximum oxygen consumption (Table 3). [34, 35]

Table 3. Six-week aerobic training program with intensity equal to 70-75% of maximum used oxygen.

Aerobic training protocol	Training weeks					
	1	2	3	4	5	6
Training duration(minute in a day)	10	20	30	40	45	50
Treadmill speed(meter per minute)	25	26	27	28	29	30
Treadmill slope(percent)	15	15	15	15	15	15

Warm-up: five minutes of running with a speed of 10-15 meters per minute and zero percent slope; Increasing the speed and slope of the treadmill during 5-10 minutes in a stepwise manner until reaching the intensity of the desired exercise; Cool down: 5-10 minutes of running at a speed of 10-15 meters per minute and a zero-degree in slope

Cinnamon extract

Cinnamon extract is a colorless liquid with a strong, pleasant smell and burning taste, whose main ingredients include 80 to 85 %of cinnamaldehyde, 5% cinnamyl acetate, 4% eugenol, 3% caryophyllene, 2% linalool, 0.7% alphaterpineol, 0.7% of coumarin, 0.6% of 1-8-cineole and 0.4% of 4-L-terpinene. Cinnamon extract was given to mice as a gavge in the amount of 200 mg per kilogram of body weight [36].

Surgery and sample extraction

All samples were collected 48 hours after the last training session and after 12 hours of fasting, according to the predetermined schedule and by using the right method in the least possible time and with the least pain and discomfort were anesthetized (intrapleural injection of ketamine (90 mg per kg) and xylazine (10 mg per kg), killed and operated by a trained expert in the desiccator device. Liver and fat tissues were removed and placed inside 1.5 microliter microtubes, including RNA later in a 70-degree. To determine the amount of gene expression or leptin protein mRNA, the polymerase chain reaction method was used. The primers were collected in a lyophilized efflux vial and were diluted with TE buffer of Sina Gene Company in an amount that was mentioned on the vial. After that, inside the labeled pipes, 180 microliters of buffer TE and 10 microliters of forward primer (F), and 10 microliters of reverse primer (R) were poured. The sequence, length, and type of designed primer for the leptin gene were as follows.

- bp23_ (F)2_GTCAGTC5_CATTTCACACACGCA_
- bp33_ (R)2_CTTGGATA5_CAGTGTCTGGTCCAT_

The polymerase chain reaction was performed using the Green Mix Master 2X Plus Q Real kit of Viragen company. After the registration of the threshold cycles obtained from the samples of the groups, using the formulas ΔΔCt and $2^{-\Delta\Delta Ct}$ the expression of target and reference genes ratio were compared. The naturalness of the distribution of variables was evaluated by the Shapiro-Wilk test and the homogeneity variance of the variables by Levine's test. The average of the research variables among the groups was compared to determine the differences between groups, by using one-way variance analysis and Bonferroni's supplemental test and independent t-tests and two-way variance analysis. The significance level in all tests was $p \leq 0.05$.

RESULTS

The results of the one-way variance test showed that the difference between the variable of the weight of rat's body in the pre-test was non-significant among different research groups [P = 0.97 and F =(45 and 4)= 0.118); While in the post-test the results were significant between all groups.[F(4and45)=3322.78 and p<0.001)The results of the t-paired test showed that body weight changes within the control groups (P ≤ 0.001 and t(9)= 111.38) high-fat diet [t (9) = 250.46 and P ≤0.001] high-fat diet and exercise [t (9) = 124.48 and P ≤ 0.001] high-fat diet and cinnamon [P ≤ 0.001 and t (9) = 119.40] and high-fat diet and cinnamon and exercise [P ≤ 0.001 and t (t (9)= 133.99] were also significant; which shows an increase in body weight by 24.27% in the control group, 39.36% in the high-fat diet group, 20.05 % in the high-fat diet and exercise group, 30.10% in the high-fat diet and cinnamon group and 17.87 % in the high-fat diet and exercise and cinnamon group. The natural increase in body weight due to the increase in age which is calculated in the control group, shows that a high-fat diet causes weight increase.; While in the high-fat diet group and exercise and high-fat diet group and exercise and cinnamon calculated weight gain is less than the control group and the high-fat diet group and this significant difference is probably due to the effects of performing aerobic exercise in these two groups. In the high-fat diet and cinnamon also body weight gain has been between the control and high-fat diet group and In the high-fat and cinnamon diet group, which shows that using cinnamon prevents excessive body weight gain due to consuming a high-fat food. Finally, performing aerobic exercise and cinnamon consumption beside each other has had better effects and prevented excessive weight gain due to a high-fat diet. The difference between weight variables of fat [F (4 and 45) = 8695.211 and P ≤ 0.001] and liver [F (4 and 45) = 15048.35 and P ≤ 0.001] was also significant and similar to the pattern of body weight changes between all different research groups.

In Table 4, the mean and standard deviation of research variables is presented by different research groups. The results of the t-test in comparing the control and the high-fat diet groups to determine the extent and manner of the effect of using high-fat food showed that the level of leptin gene relative expression in liver and fat tissues, as well as the weight of the tissues of liver and fat differed from the control group. These results show the effect of a high-fat diet in increasing and unfavorable changes of leptin gene expression in fat tissue and the liver. In addition, both the body weight of rats and the weight of fat tissues and liver of rats in the high-fat group was more than the control group, which indicates the unfavorable effects of a high-fat diet on these variables (Table 5.)

Table 4. the leptin gene relative expression levels and the weight of rat's liver and fat tissues in different groups

Variables	Fat tissue		Liver tissue	
Groups	**Leptin**	**Weight tissue**	**Leptin**	**Weight tissue**
High-fat diet	1.54±0.28	2.80±0.02	1.7±0.04	9.75±0.03
Cinnamon and High-fat diet	0.95±0.02	2.57±0.02	1.3±0.03	8.67±0.13
Aerobic training and High-fat diet	0.64±0.03	1.55±0.02	0.89±0.03	8.88±0.01
Aerobic training, cinnamon, and Aerobic training	0.47±0.03	1.29±0.02	0.94±0.03	7.65±0.01
Control	1	2.20±0.03	1	9.05±0.01

Table 5. Dependent t-test results for comparing control and high-fat diet group.

Variables	Groups	Mean & standard deviation	Statistical indicators		
			Amount t	**df**	**p**
Rat's weight before training	**Control**	208 ±1.49	0.318	18	0.754
	High-fat diet	207.8 ±1.31			
Rat's weight after training	**Control**	258.5 ±1.26	-61.65	18	0.001
	High-fat diet	289.6 ±.096			
Fat tissue leptin	**Control**	1	-10.38	18	0.001
	High-fat diet	1.54±0.28			
Fat tissue weight	**Control**	2.20±0.03	-49.23	18	0.001
	High-fat diet	2.80±0.02			
Liver tissue leptin	**Control**	1	-60.85	18	0.001
	High-fat diet	1.7±0.04			
Liver tissue weight	**Control**	9.05±0.01	-25.38	18	0.001
	High-fat diet	9.75±**0.01**			

The results of the two-way variance test showed that both performing aerobic exercise alone (P=0.001) and using cinnamon alone (P=000.1) have significant effects on the relative expression of the leptin gene in fat tissue of male rats fed with a high-fat diet and cause a decrease and a desired change in the expression of this gene compared to the high-fat diet group (Figure 1). The interaction of aerobic training with cinnamon extract was not significant on changes in leptin gene relative expression in fat tissues of male rats fed with high-fat diet.(P=0.14), although it decreased and makes a desired change in the expression of this gene compared to the high-fat diet group (Table 6).

The results of the two-way analysis of variance showed that performing aerobic exercise had a significant effect on the relative expression of the leptin gene in the liver tissue of male rats fed with a high-fat diet (P=0.001) and cause a decrease in the expression of this gene, compared to the high-fat diet group (Figure 2) Cinnamon extract consumption has not had a significant effect on the relative expression of the leptin gene of liver tissue of male rats fed a high-fat diet. (P = 0.957), although it has decreased the expression of this gene compared to the high-fat diet group. The interactive effect of performing the aerobic exercise with cinnamon extract consumption was not significant on the changes of leptin gene relative expression in the liver tissue of male rats fed with a high-fat diet.(p=0.434) although it caused a decrease in the expression of this gene compared to the high-fat diet group (Table 6).

Table 6. Two-way variance analysis results of the research variables.

Variables	Change source	Squares total	Df	F	p	Effect Amount
Leptin gene relative expression in fat tissue	**Training**	3.56	1	107.93	0.001	0.701
	Cinnamon	0.68	1	20.64	0.001	0.31
	Interaction of Training & Cinnamon	0.071	1	2.16	0.14	0.045
Leptin gene relative expression in liver tissue	**Training**	1.89	1	34.73	0.001	0.43
	Cinnamon	0.001	1	0.003	0.957	0.001
	Interaction of Training & Cinnamon	0.03	1	0.055	0.434	0.012
Fat tissue weight(gram)	**Training**	14.18	1	354.21	0.001	0.885
	Cinnamon	0.105	1	2.63	0.112	0.054
	Interaction of Training & Cinnamon	0.285	1	7.12	0.01	0.134
Liver tissue weight(gram)	**Training**	6.64	1	113.05	0.001	0.711
	Cinnamon	11.23	1	191.18	0.001	0.806
	Interaction of Training & Cinnamon	0.623	1	11.65	0.001	0.202

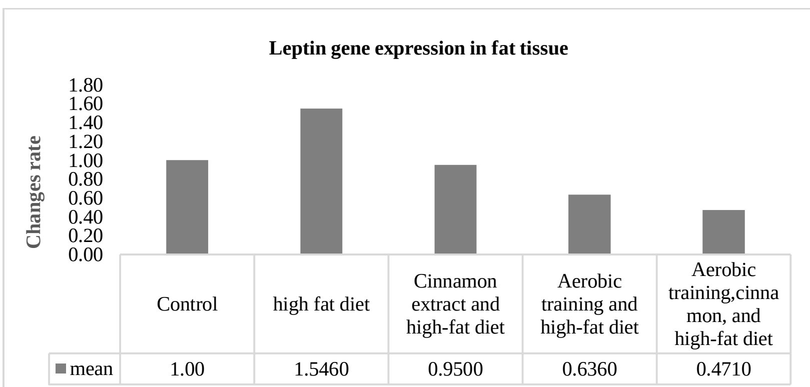

Figure 1. Changes in the relative expression of the leptin gene in fat tissue

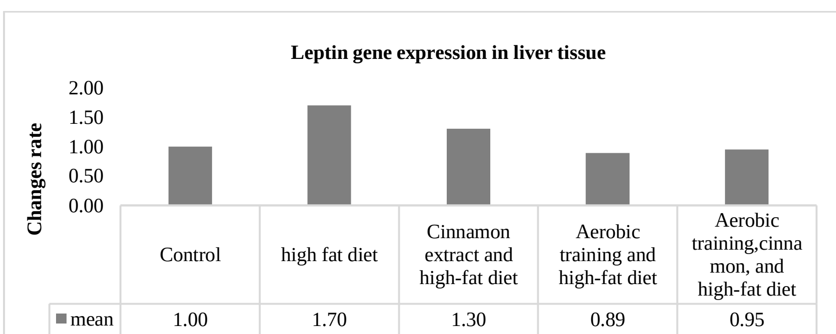

Figure 2. Changes in the relative expression of the leptin gene in liver tissue.

Aerobic exercise has had a significant effect on the weight of fat tissue in male rats fed with a high-fat diet (P=0.001) and caused a decrease in fat tissue weight of male rats fed with a high-fat diet compared to the high-fat diet group. Consumption of cinnamon extract has not had a significant effect on the fat tissue weight of male rats fed with a high-fat diet compared to the high-fat diet group (p=0.112). The interactive effect of performing aerobic exercise along with consumption of cinnamon extract was significant on weight changes of fat tissue in male rats fed with a high-fat diet (P=0.001) and caused a decrease in fat tissue weight compared to the high-fat diet group (Figure 3).

Both performing aerobic exercise alone (P=0.001) and the consumption of cinnamon extract alone (P=0.001) have a significant effect on changes in liver tissue weight in male rats fed with a high-fat diet and caused a decrease in liver tissue weight compared to the high-fat diet group. The interactive effect of performing aerobic exercise along with the consumption of cinnamon extract was significant on changes in liver tissue weight in male rats fed with high-fat diet (P=0.001) and caused a decrease in the weight of the liver tissue compared to the high-fat diet group (Figure 4).

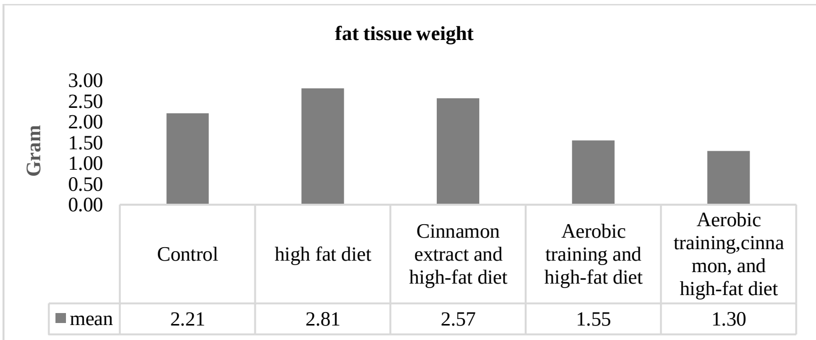

Figure 3. Changes in fat tissue weight

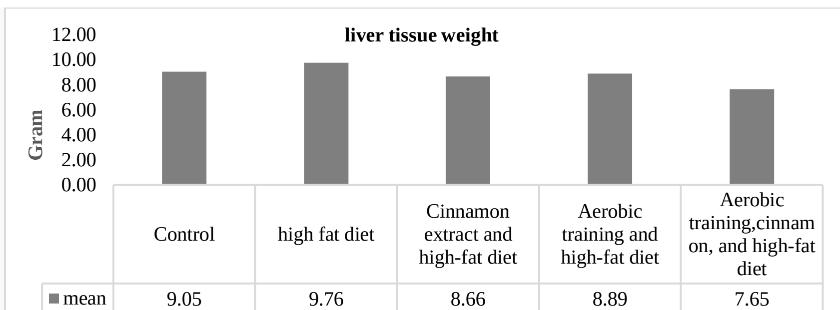

Figure 4. Changes in liver tissue weigh.t

DISCUSSION

The pattern of changes in leptin gene expression in fat tissue showed that consuming high-fat food causes an increase of 54% and unfavorable changes in the expression of this gene compared to the control group. Performing six weeks of aerobic exercise along with a high-fat diet moderates the unfavorable effects of a high-fat diet, and reduced the expression of this gene by 58.44 % compared to the high-fat diet group. Consumption of cinnamon extract for six weeks along with a high-fat diet also moderates the unfavorable effects of a high-fat diet and reduced the expression of this gene by 38.31% in the diet group. The interaction of performing aerobic exercise and consumption of cinnamon extract for six weeks along with the high-fat diet also moderates the unfavorable effects of the high-fat diet and decreased the expression of this gene by 69.48 % compared to the high-fat diet group (Figure 1.) How leptin gene expression changes in fat tissue is relevant to the pattern of changes in fat mass. Consumption of high-fat food, because of an increase and an unfavorable change in fat tissue mass by 27.27 % compared to the control group. Performing aerobic exercise for six weeks along with a high-fat diet moderates the unfavorable effects of a high-fat diet and reduces the mass of fat tissue by 44.64 % in comparison to the high-fat diet group. Consumption of cinnamon extract for six weeks along with a high-fat diet also moderates the unfavorable effects of a high-fat diet and reduces fat tissue mass by 8.21 % compared to the high-fat diet group. Interaction of performing aerobic exercise and consumption of cinnamon extract for six weeks along with the high-fat diet also moderates the unfavorable effects of a high-fat diet and increases fat tissue mass by 53.92 % compared to the high-fat diet group. (Figure 3). With this description, it can be seen that the interactive effects of performing aerobic exercise for six weeks and consumption of cinnamon extract along with a high-fat diet moderates the unfavorable effect of a high-fat diet better and more effectively on leptin gene expression and fat tissue mass and these two with better and more effective and these two variables (exercise and cinnamon) could strengthen each other's effects. The pattern of leptin gene expression changes in the liver tissue showed that consumption of high-fat food caused an increase by 70% and unfavorable changes expression of this gene were compared to the control group. Performing aerobic exercise for six weeks along with a high-fat diet moderates the unfavorable effects of a high-fat diet and decreased the expression of this gene by 47.65% in comparison to the high-fat diet group. Consumption of cinnamon extract for six weeks along with a high-fat diet also moderates the unfavorable effects of a high-fat diet and decreased the expression of this gene by 23.53% compared to the high-fat diet group. The interaction of performing aerobic exercise for six weeks and consumption of cinnamon extract along with a high-fat diet also moderates the unfavorable effects of a high-fat diet and decreased the expression of this gene by 44.70% compared to the high-fat diet group. (Figure 2) how leptin gene expression changes in liver tissue is relevant to the pattern of liver tissue mass changes. Eating high-fat food causes an increase and unfavorable change in liver tissue mass by 7.73 %compared to the control group. Performing aerobic exercise for six weeks along with a high-fat diet moderates the unfavorable effects of a high-fat diet and reduces liver tissue mass by 8.92% in the high-fat diet group. Consumption of cinnamon extract along with a high-fat diet also moderates the unfavorable effects of the high-fat diet and reduced the liver tissue mass by 11.07 % compared to the high-fat diet group. Interaction of performing aerobic exercise for six weeks and consumption of cinnamon extract along with the high-fat diet also moderates the unfavorable effects of a high-fat diet and reduces the liver tissue mass by 21.53% compared to the high-fat diet group (Figure 4). With this description, it can be seen that the interactive effects of six weeks of aerobic exercise and cinnamon extract along with a high-fat diet moderate the unfavorable effects of a high-fat diet better and more effectively on leptin gene expression and liver fat mass and these two variables (exercise and cinnamon) could strengthen each other's effects.

Rostami et al in a research titled the relationship between dietary fat intake from different sources with leptin gene expression in Visceral and subcutaneous fat tissue in Tehrani Adults stated that there is a significant difference between leptin gene expression in visceral and subcutaneous fat tissues. Also, no significant difference was observed between leptin gene expression levels in obese and non-obese people. In addition, a significant correlation was observed between fat intake in a diet with the percentage of fat and leptin gene expression in visceral and subcutaneous fat tissues. So changing and increasing fat intake especially from animal sources can increase the mass of fat tissue and increase leptin gene expression. It seems that the serum level of leptin in obese people is more influenced by diet than in non-obese people [37]. Many studies have been done on the relationship between fatty acid intake in diets and serum concentration and leptin gene expression [38-42]. The results of some of them showed that the type of fat received, did not affect on serum concentration and leptin gene expression level [39, 40, and 43]. However, the results of other research show that the type of fat received affected serum concentration and leptin gene expression level. This difference can be controlled by different human and animal research populations, by using different nutritional evaluations and control by considering all kinds of confounding variables, which shows the importance of conducting more studies in this field [44-49]

The existing compounds in cinnamon may control and reduce obesity by affecting the expression of various genes expressions. Due to its polyphenols, cinnamon has useful insulin-like effects in controlling blood sugar and fats and can regulate appetite. In addition, by increasing the body's metabolism, it can cause the breakdown of fats and excess tissue energy consumption. Cinnamon, due to its flavonoids, has high antioxidant activity, anti-cancer effects, and anti-microbial and anti-bacterial effect due to having 65 to 80 percent cinnamaldehyde and 5 to 10 percent eugenol and its inhibitory effects on nitric oxide production have anti-inflammatory effects and protection against myocardial ischemia and cardiovascular diseases [19]. Anderson et al showed that cinnamon decreased the negative effects of high-fructose and high-fat diets on insulin signaling and improves overall improvement of insulin sensitivity [50]. Kim et al showed the effects of cinnamon polyphenols on the up-regulation of vital cell proteins and the activation of adenosine monophosphate kinase pathways, which reduces pro-inflammatory cytokines and cell protection [51]. Haidari et al stated that daily consumption of cinnamon in the amount of 250 and 500 mg per kg of body weight for 28 days can moderate and reduce inflammation and oxidative stress of toxic compounds in the diet. The existing toxic compound found in diets such as acrylamide increases malondialdehyde factors, alpha tumor necrosis factor, C-reactive protein, leptin, and alanine transaminase and finally reduce the capacity of anti-oxidation. The consumption of cinnamon was able to adjust and reduce the mentioned variables; Although it did not affect liver enzymes and adiponectin [52]. Ahmadi et al stated that injection of cinnamon plant extract with a dose of 25 mg kg^{-1} of body weight twice a day, can increase leptin levels and body weight can compensate for the lipid profile in rats and cause a moderation and a significant reduction in the level of these variables [53]. Ashrafy et al stated that cinnamon is a plant that by reduction of the level of oxidative stress probably, causes the correction of oxidative indices. High-fat diets probably, cause tissue damage in the liver, through the creation of oxidative stress. By having strong anti-oxidant properties, cinnamon extract also prevents harmful effects of high-fat diet damage on the tissue structure of the liver. A high-fat diet causes microscopic lesions in the tissue structure of the liver. Cinnamon extract has strong antioxidant properties and through increasing the power of anti-oxidant, leads to the improvement of liver damage caused by consumption of a high-fat diet [33].

Adaptation in the energy system not only enables the body to be more efficient in energy production; rather, the use of the type of fuel (such as fat) causes more efficiency in energy production during endurance training in comparison to other training. Energy stored in the form of fat is used more, which causes visible changes in the physical composition. for this transfer from the fat tissue to its consumption in the muscles, there are changes in the secretory glands which are primarily responsible for the release of hormones to allow the body to be more efficient in energy production. Increasing available substrates for use, increase endurance activity time. Depending on the intensity of endurance training, training substrates change. People who trained for endurance for a longer period, time consume more fat as fuel than people who did not train. As a result of endurance training, the key enzymes involved in the Krebs cycle and the electron transport device contribute significantly to increasing the capacity of muscle tissues for fat oxidation compared to carbohydrate oxidation increase. The number, size, and surface area of the mitochondrial membrane in filaments muscles increase. Glucose release is facilitated with the help of glucose transporters, and people can use available fatty acids more, all of which lead to increased efficiency and better oxidation of fat sources to produce energy. several reasons can be used to explain the behavior of leptin towards muscle training physical activity and sports training; reduces fat mass, plays a decisive role in energy consumption,[54] is effective on the concentrations of different hormones effective on regulating metabolism and appetite such as ghrelin, resistin, adiponectin, [31,55] and metabolites such as fatty acids, lactic acid, and triglycerides. Rohner, and Alavizadeh et al stated that performing eight weeks of aerobic exercise decreased plasma levels of leptin [56, 57]. Aerobic training three sessions a week, including 10 minutes of warm-up, 30 minutes of aerobic exercises (a two-minute increase in aerobic exercise time up to 44 minutes per week), and 10 minutes of cooling, which started with 55% of the maximum heart rate in the first week and to comply with the principle of load adds up to 75% of the maximum heart rate continued in the last week. Reduction of weight variables, body mass index, and fat percentage resulting from aerobic exercise was also significant [56].

Gokbel et al showed that in long-term aerobic training, immediately after training, 24 hours after training, and during the recovery period, the concentration of leptin decreases significantly [58]. Okazaki et al also investigated the effect of moderate-intensity aerobic exercise and diet for one week on reducing fat and leptin concentration in inactive obese and non-obese middle-aged women. Based on these findings, leptin concentration and fat mass decreased, but the decrease in leptin concentration was not related to weight loss [59]. Based on these reasons it seems that the change in leptin behavior in response to exercise is dependent on several factors. These factors include intensity and duration of exercise, nutritional status of subjects, day and night rhythm of leptin, time of blood sampling and, degree of caloric imbalance due to training. It comes from practice. Finally, it is observed that the interactive effects of performing six weeks of aerobic exercise and consuming cinnamon extract along with the high-fat food cause better and more effective adjustment of the unfavorable effects of a high-fat diet on leptin gene expression and fat tissue mass and these two variables (exercise and cinnamon) have been able to strengthen each other's effects, while they could not strengthen each other’s effect in the liver tissue and consuming cinnamon extract for six weeks along with high-fat diet has had better and more favorable effects on leptin gene expression and liver tissue mass. Therefore, apart from the desired and accepted effects of physical activities and sports exercises on fat tissue and the liver; recommended taking cinnamon extract can also have desirable and useful effects.

Research limitation

Failure to control the activity level of rats in the cage. Failure to control the amount of water and food consumed by rats in the cage.

ACKNOWLEDGEMENTS

The authors would like to thank who involved in the process of preparing these data including laboratory personnel.

Conflict of interests

There is no conflict of interest.

REFERENCES

1. Bouassida A., Zalleg D., Bouassida S., 2006. Leptin, Its Implication in Physical Exercise and Training. Jssm. 5, 172-181.

2. Dishman R.K., Washburn R.A., 2004. Physical Activity Epidemiology. Champaign: Human Kinetics.

3. Le Mura L.M., Van Duvillard P., 2004. Clinical Exercise physiology. Philadelphia, LWW.

4. Patterson C.M., Dunn-Meynell A.A., Levin B.E., 2008. Three weeks of early-onset exercise prolongs obesity resistance in DIO rats after exercise cessation. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 294(2), 290-301.

5. Kang S., Woo J.H., Shin K.O., Kim D., Lee H.J., 2009. Circuit resistance exercise improves glycemic control and Adipokines in females with type II diabetes mellitus. Journal of Sports Sciences and Medicine. 8, 682-688.

6. Bergouignan A., Momken I., Schoeller D.A., Normand S., Zahariev A., Lescure B., Simon C., Blanc S., 2010. Regulation of energy balance during long-term physical inactivity induced by bed rest with and without exercise training. J Clin Endocrinol Metab. 95, 1045-1053.

7. Ossanloo P., Najar L., Zafari A., 2012. The Effects of Combined Training (Aerobic Dance, Step Exercise and Resistance Training) on Body Fat Percent and Lipid Profiles in Sedentary Females of AL_ZAHRA University. European Journal of Experimental Biology. 2(5), 1598-1602.

8. Eftekhari E., Zafari A., Gholami M., 2016. Physical activity, lipid profiles and leptin. The Journal of Sports Medicine and Physical Fitness. 56(4), 465-469.

9. Hagobian T.A., Sharoff C.G., Stephens B.R., Wade G.N., Silva J.E., Chipkin S.R., 2009. Effects of exercise on energy-regulating hormones and appetite in men and women. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 296(2), 233-42.

10. Messier C., Whately K., Liang J., Du L., Puissant D., 2007. The effects of a high-fat, high-fructose, and combination diet on learning, weight, and glucose regulation in C57BL/6 mice. Behavioral Brain Research. 178(1),139-145.

11. Halade G.V., Rahman M.M., 2010. High fat diet-induced animal model of age-association obesity and osteoporosis. The Journal of Nutritional Biochemistry. 21(12), 1162-1169.

12. Sampey B.P., Vanhoose A.M., Winfield H.M., Freeman A.J., Muehlbauer M.J., Fueger P.T., Newgard C.B., Makowski L., 2011. Cafeteria diet is a robust model of human metabolic syndrome with liver and adipose inflammation, Comparison to high fat diet. Obesity. 19(6), 1109-1117.

13. Bacci S., Menzaghi C., Ercolino T., Ma X., Rauseo A., Salvemini L., 2004. The +276 G/T single nucleotide polymorphism of the adiponectin gene is associated with coronary artery disease in type II diabetic patients. Diabetes Care. 27(8), 2015-2020.

14. Ouchi N., Parker J.L., Lugus J.J., Walsh K., 2011. Adipokines in inflammation and metabolic disease. Nature Reviews Immunology. 11(2), 85-97.

15. Nigro E., Scudiero O., Ludovica Monaco M., Palmieri A., Mazzarella G., Costagliola C., Bianco A., Daniele A.,2014. New Insight into Adiponectin Role in Obesity and Obesity-Related Diseases. 10, 1155.

16. Kyriazis G.A., 2005. The Effects of a Single Exercise Bout on Plasma Leptin Concentration in Obese Males. A thesis proposal submitted for the degree of Master of Arts in the College of Education at the University of Central Florida, Orlando.

17. Fernandes M.S., Silva L.d., Kubrusly M.S., Lima T., Muller C.R., Amé rico A., Fernandes .M.P, Cogliati B., Stefano J.T., Lagranha C.J., Evangelista F.S., Oliveira C.P., 2020. Aerobic Exercise Training Exerts Beneficial Effects Upon Oxidative Metabolism and Non-Enzymatic Antioxidant Defense in the Liver of Leptin Deficiency Mice. Front Endocrinol. 11, 502-588.

18. Takahashi H., Kotani K., Tanaka K., Egucih Y., Anzai K., 2018. Therapeutic Approaches to Nonalcoholic Fatty Liver Disease: Exercise Intervention and Related Mechanisms. Front Endocrinol. 9, 588. doi: 10.3389/fendo.2018.00588.

19. Mollazadeh H., Hosseinzadeh H., 2016. Cinnamon effects on metabolic syndrome: a review based on its mechanisms. Iran J Basic Med Sci. 19,1258-1270. http://dx.doi.org/10.22038/ijbms.2016.7906.

20. Khan A., Safdar M., Ali Khan M.M., Khattak K.N., Anderson R.A., 2003. Cinnamon improves glucose and lipids of people with type II diabetes. Diabetes Care. 26(12), 3215-3218.

21. Hasani-Ranjbar S., Nayebi N., Larijani B., Abdollahi M., 2009. A systematic review of the efficacy and safety herbal medicine used in the treatment of obesity. World Journal of Gastroenterology. 15(25), 3073.

22. Roussel A.M., Hininger I., Benaraba R., Ziegenfuss T.N., Anderson R.A., 2009. Antioxidant effects of a cinnamon extract in people with impaired fasting glucose that are overweight or obese. Journal of the American College of Nutrition. 28(1), 16-21.

23. Dylan W.P., Roshni C.G., Francesca S., Nichole E.L., 2009. Cinnamon Extract Inhibits Tau Aggregation Associated with Alzheimer’s disease. Journal of Alzheimer’s disease. 17, 585-597.

24. Chua M.T., Tung Y.T., Chang S.T., 2009. Antioxidant activities of extracts from the twigs Cinnamomum osmophloeum. Bioresource Technology. 99, 1918-1925.

25. Moslehy S.S., Husein K., 2009. Hepatoprotective effect of cinnamon extracts against carbon tetrachloride induced oxidative stress and liver injury in rats. Biol Res. 42, 93-98.

26. Badalzadeh R., Shaghaghi M., Mohammadi M., Dehghan G., Mohammadi Z., 2014. The effect of cinnamon extract and long-term aerobic training on heart function, biochemical alterations and lipid profile following exhaustive exercise in male rats. Coronary Artery Disease. 2, 8.

27. Shalaby M.A., Saifan H.A., 2014. some pharmacological effects of cinnamon and ginger herbs in

obese diabetic rate. Journal of Intercultural Ethno pharmacology. 3(4), 144.

28. Sartorius T., Peter A., Schulz N., Drescher A., Bergheim I., Machann J., 2014. Cinnamon extract improves insulin sensitivity in the brain and lowers liver fat in mouse models of obesity. PloS One. 9(3),e92358.

29. Hamidpour R., Hamidpour M., Hamidpour S., Shahlari M., 2015. Cinnamon from the selection of traditional applications to its novel effects on the inhibition of angiogenesis in cancer cells and prevention of Alzheimer's disease, and a series of function such as antioxidant, anti-cholesterol, antidiabetic, antibacterial, antifungal, nematicidal, acaracidal, and repellent activity. Journal of Traditional and Complementary Medicine. 5(2), 66-70.

30. Rashid Lamir A., Alizadeh A., Ebrahimi A.A., Dastani M., 2011. Effects of 4 Weeks of aerobic exercise with the consumption of cinnamon on lipoprotein parameters and blood glucose in type II diabetic women. Shahid Sadoughi University of Medical Sciences and Health Service. 20(5), 605-614.

31. Zou Y., Li J., Lu C., Wang J., Ge J., Huang Y., 2006 High-fat emulsion-induced rat model of nonalcoholic steatohepatitis. Life Sci. 79(11), 1100-7.

32. Machado M.V., Michelotti G.A., Xie G., Almeida P.T., Boursier J., Bohnic B., 2015. Mouse models of diet-induced nonalcoholic steatohepatitis reproduce the heterogeneity of the human disease. PloS One. 10(5), e0127991.

33. Ashrafy E., Hosseini S.E., 2018. Protective effects of Cinnamon hydro-alcoholic extract on liver lesions induced non-alcoholic fatty liver disease and sodium nitrite poisoning in adult male rats. J Shahrekord Univ Med Sci. 19(6), 13-23.

34. Sokhanvardastjerdi S., Banaeifar A., Arshadi S., Zafari A.,2020. The Effect of 12 Weeks Aerobic Training on PDX-1 and GLUT2 Gene Expression in the Pancreatic Tissue of Type 2 Diabetic Rats. Iranian Journal of Diabetes and Obesity. 12(2), 98-103.

35. Noura M., Arshadi S., Zafari A., Banaeifar A., 2020. The effect of running on positive and negative slopes on TNF-α and INF- γ gene expression in the muscle tissue of rats with Alzheimer's disease. Journal of Basic Research in Medical Science. 7(1), 35-42.

36. Shang C., Lin H., Fang X., Wang Y., Jiang Z., Qu Y., Xiang M., Shen Z., Xin L., Lu Y., Gao J., Cui X., 2021. Beneficial effects of cinnamon and its extracts in the management of cardiovascular diseases and diabetes. Food Funct. 12, 12194–12220. DOI: 10.1039/d1fo01935j.

37. Rostami H., Tavakoli H.R., Yuzbashian E., Zarkesh M., Aghayan M., Hedayati M., Forouzanfar R., Mirmiran P., Khalaj A., 2018. The Association of Dietary Fat Sources with Leptin Gene Expression from Visceral and Subcutaneous Adipose Tissues among Tehranian Adults. Iranian Journal of Endocrinology and Metabolism. 20(4), 160-168.

38. Teng K.T., Nagapan G., Cheng H.M., Nesaretnam K., 2011. Palm olein and olive oil cause a higher increase in postprandial lipemia compared with lard but had no effect on plasma glucose, insulin and adipocytokines. Lipids. 46, 381-8.

39. Murakami K., Sasaki S., Takahashi Y., Uenishi K., Yamasaki M., Hayabuchi H., 2007. Nutrient and food intake in relation to serum leptin concentration among young Japanese women. Nutrition. 23, 461-468.

40. Yannakoulia M., Yiannakouris N., Blu-her S., Matalas A.L., Klimis Z.D., Mantzoros C.S., 2003. Body fat mass and macronutrient intake in relation to circulating soluble leptin receptor, free leptin index, adiponectin, and resistin concentrations in healthy humans. J Clin Endocrinol Metab. 88, 1730-1736.

41. Shen W., Wang C., Xia L., Fan C., Dong H., Deckelbaum R.J., 2014. Epigenetic modification of the leptin promoter in diet-induced obese mice and the effects of N-3 polyunsaturated fatty acids. Sci Rep. 4, 5282.

42. Romacho T., Glosse P., Richter I., Elsen M., Schoemaker M.H., Van T.E.A., 2015. Nutritional ingredients modulate adipokine secretion and inflammation in human primary adipocytes. Nutrients. 7, 865-886.

43. Miller G.D., Frost R., Olive J., 2001. Relation of plasma leptin concentrations to sex, body fat, dietary intake, and peak oxygen uptake in young adult women and men. Nutrition. 17, 105-11.

44. Kratz M., von Eckardstein A., Fobker M., Buyken A., Posny N., Schulte H., 2002. The impact of dietary fat composition on serum leptin concentrations in healthy

nonobese men and women. J Clin Endocrinol Metab. 87, 5008-5014.

45. El Midaoui A., Haddad Y., Filali-Zegzouti Y., Couture R., 2017. Argan Oil as an Effective Nutri-Therapeutic Agent in Metabolic Syndrome:A Preclinical Study. Int J Mol Sci. 18, pii: E2492.

46. Jurado-Ruiz E., Varela L.M., Luque A., Berna G., Cahuana G., Martinez-Force E., 2017. An extra virgin olive oil rich diet intervention ameliorates the nonalcoholic steatohepatitis induced by a high-fat "Western-type" diet in mice. Mol Nutr Food Res. 61.

47. Chu N., Stampfer M., Spiegelman D., Rifai N., Hotamisligil G., Rimm E., 2001. Dietary and lifestyle factors in relation to plasma leptin concentrations among normal weight and overweight men. Int J Obes Relat Metab Disord. 25, 106-14.

48. Duque-Guimarães D.E., de Castro J., Martinez-Botas J., Sardinha F.L., Ramos M.P., Herrera E., 2009. Early and prolonged intake of partially hydrogenated fat alters the expression of genes in rat adipose tissue. Nutrition. 25, 782-789.

49. Pisani L.P., Oyama L.M., Bueno A.A., Biz C., Albuquerque K.T., Ribeiro E.B., 2008. Hydrogenated fat intake during pregnancy and lactation modifies serum lipid profile and adipokine mRNA in 21-day-old rats. Nutrition. 24, 255-261.

50. Anderson R.A., Qin B., Canini F., Poulet L., Rousse, A.M., 2013. Cinnamon Counteracts the Negative Effects of a High Fat/ High Fructose Diet on Behavior, Brain Insulin Signaling and Alzheimer-Associated Changes. PLoS One. 8(12), e 83243.

51. Kim S. M., Cho G.J., Yannakoulia M., Hwang T. G., Kim I. H., Park E.K., 2011. Lifestyle modification increases circulating adiponectin concentrations but does not change vaspin concentrations. Metabolism. 60(9). DOI: 10.1016/j.metabol.2011.01.013

52. Haidari F., Mohammadshahi M., Abiri B., Zarei M., Fathi M., 2020. Cinnamon extract supplementation improves inflammation and oxidative stress induced by acrylamide: An experimental animal study. Avicenna J Phytomed (AJP). 10(3), 243-252.

53. Ahmadi R., Omidali F., Pishghadam S., 2017. Investigating the effect of hydroalcoholic extract of cinnamon bark on blood leptin hormone levels in Wistar rats under air pollution. Animal Research Journal Iranian Biology Journal. 30(1), 13-21

54. Dyck D.J., 2005. Leptin Sensitivity in Skeletal muscle is modulated by Diet and Exercise. Exercise and Sport. DOI: 10.1097/00003677-200510000-00007.

55. Meier U., Gressner A.M., 2004. Endocrine Regulation of Energy Metabolism: Review of pathobiochemical and clinical chemical aspects of Leptin, Ghrelin, Adiponectin, and Resistin. Clinical Chemistry. 50, 1511-1525.

56. Alavizade N.S., Naghibzade A., Drodi S., Hoseni M., Sakhi A., Rashid Lamir A., 2018. Effect of Eight-week aerobic training combined with Green Coffee consumption on ABCG8 gene expression, serum Leptin and HDL levels of overweight women. J Neyshabur Univ Med Sci. 6(2), 72-81.

57. Rohner-Jeanrenaud F., 2002. Aspects of the Neuroendocrine Regulation of Body weight Homeostasis. American Endocrinology. 63, 125-128.

58. Gökbel H., Baltaci A.K., Üçok K., Okudan N., Moĝulkoç R., 2005. Changes in serum leptin levels in strenuous exercise and its relation to zinc deficiency in rats. Biological Trace Element Research. 106(3), 247-252.

59. Okazaki T., Himeno H., Nanri H., Ogata M., Ikeda M., 1999. Effects of mild aerobic exercise and a mild hypocaloric diet on plasma leptin in sedentary women. Clin Exp Pharmacol Physiol. 26(5-6), 415-20 .