



The Effect of Aerobic Exercise and Eryngium Billardieri Extract Consumption on Women with Obesity and Type 2 Diabetes

Shiva Nazarieh¹, Mohsen Aminaei^{1*}, Rohullah Nikoei¹

1. Department of Sport Sciences, Shahid Bahonar University of Kerman, Kerman, Iran.

ARTICLE INFO	ABSTRACT
<p><i>Article type:</i> Research Paper</p>	<p>Introduction: This study aimed to evaluate the effect of aerobic exercise and eryngium billardieri extract consumption on insulin resistance and lipid profile in obese women with type 2 diabetes.</p>
<p><i>Article History:</i> Received: 25 Nov 2022 Accepted: 21 Jan 2023 Published: 07 Mar 2023</p>	<p>Methods: This quasi-experimental research used control group in pre- and post-tests. The subjects were 38 obese women with type 2 diabetes (Mean age 51.56 ± 5.21 years old and BMI 31.88 ± 2.57 kg/m²), who were randomly divided into four groups: control (C=9), Drug (Drug=10), Exercise (EX=9), and Exercise and drug (EX&Drug=10). The aerobic exercise protocol consisted of three exercise sessions per week for eight weeks. The Drug and Exercise and drug groups consumed 200ml of eryngium billardieri extract every day. Blood samples were collected 24h before and 48h after the last exercise to measure blood glucose, insulin, and lipid profile, including cholesterol, triglyceride, HDL, LDL, and VLDL. Statistical methods include the Kolmogorov-Smirnov, Levene, covariance (ANCOVA), and Bonferroni test.</p>
<p><i>Keywords:</i> Aerobic exercise Eryngium billardieri extract Insulin resistance Lipid profile</p>	<p>Results: A significant decrease was observed in plasma glucose, insulin, insulin resistance index, cholesterol, triglyceride, LDL, and VLDL. There was a significant increase in HDL after aerobic exercise and consumption of eryngium extract in type 2 diabetes in Drug groups compared to the control group.</p> <p>Conclusions: Based on the results, the effect of exercise and consumption of eryngium extract increased insulin sensitivity by improving insulin and GLUT4 function. In addition, lipid profile improvement was the positive effect of aerobic activity and consumption of eryngium extract by increasing the lipase enzyme activity and thus increasing the removal of adipose tissue.</p>
<p>► Please cite this paper as: Nazarieh Sh, Aminaei M, Nikoei R. The Effect of Aerobic Exercise and Eryngium Billardieri Extract Consumption on Women with Obesity and Type 2 Diabetes. J Nutr Fast Health. 2023; 11(1): 15-23. DOI: 10.22038/JNFH.2023. 69213.1413.</p>	

Introduction

Obesity and type 2 diabetes are essential and epidemic problems in most societies. Chronic diseases and mortality are associated with obesity. People with obesity have many more diseases, including type 2 diabetes, heart disease, osteoporosis, cancers, etcetera (1).

Diabetes is a metabolic disease with two leading causes: chronic hyperglycemia with disturbance in carbohydrate, fat, and protein metabolism and deficiency in insulin secretion or both. Type 1 diabetes is due to a disorder in insulin secretion, and type 2 diabetes is due to insulin inefficiency (2). The high prevalence of type 2 diabetes and its personal and economic costs make this a global issue. Correct treatment can reduce mortality and related complications. Pharmacological therapy is a new concept in

routine clinical practice, which has changed the algorithm of type 2 diabetes (3).

Diabetes is the most common cause of obesity. The overweight due to improper diet and lack of physical activity can significantly reduce the risk of type 2 diabetes by controlling harmful blood fats and increasing physical activity and proper diet. Cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) are risk factors for obesity, overweight, and body fat profile increase in blood level. The amount of these substances in people with obesity is much higher than in people with normal weight (Hadaeq et al., 2009). Diabetic patients have increased triglyceride and VLDL and decreased HDL levels (4).

The percentage of triglyceride distribution in VLDL of diabetic patients with ischemic heart

* Corresponding author: Mohsen Aminaei, Associate Professor, Department of Sport Sciences, Shahid Bahonar University of Kerman, Kerman, Iran. Tel: +983433257624, Email: maminai@uk.ac.ir.

© 2023 mums.ac.ir All rights reserved.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

disease is significantly high (5). Studies have shown that the drugs have a significant decrease in blood glucose-lowering in cholesterol, LDL, VLDL, and an increase in HDL (6). The leading indicator of diabetes type 2 is insulin resistance due to a decrease in insulin sensitivity observed in people with obesity (7).

The Eryngium is a plant of the Umbelliferon family with 274 species, of which nine are native to Iran. The Persian name of the dominant Eryngium Billardieri (E. Billardieri) species is the Boqanq. E. Billardieri has numerous pharmacological effects such as anti-inflammatory, antimicrobial, and antioxidant (8). In an animal study, E. Billardieri extracts oral consumption or intraperitoneal injection increased serum insulin and decreased serum malondialdehyde by protecting the pancreas from damage using streptozotocin and stimulating insulin secretion from healthy pancreatic beta cells (8).

The effective dose of E. Billardieri was 100mg/kg (9), which has anti-diabetic properties and positive effects on diminishing lipid profiles and liver enzymes in type 2 diabetic rats (10). The extract of E Billardieri can improve liver function in hypercholesterolaemic rats without leaving side effects on their renal functions (11). The drug could reduce triglycerides and glucose levels in diabetic rats by increasing antioxidant activity. In addition, Zarei et al. (2015) showed that the consumption of E. Billardieri extract improves the liver and kidney function of hypercholesterolemic and reduces harmful blood fats in rats (11). In addition, excessive consumption of medicinal plants may cause a drop in blood pressure (11). E. Billardieri extracts induced an anti-diabetic effect by reducing malondialdehyde and improving the antioxidant pathway of cells. Diabetes treatment was affected by this supplement, but glucose was not reduced. The reduction of malondialdehyde as an oxidative index significantly affected metformin (12). The consumption of E. Carlinae extract can prevent the development of heart problems due to diabetes (13). A few studies have shown the effect of Eryngium on humans. Rabiee et al. (2017) studied the effect of E. Billardieri supplements on some glycemic, ketoacidosis, and lipid indicators of diabetic men after exercise. Based on this study, consuming this supplement decreased blood glucose levels (14).

Rabiee et al. (2017) found a decrease in blood glucose levels after consuming E. Billardieri extract (14).

E. Billardieri consumption on HepG2 cells in vitro showed no toxicity effects at 0.5 and 1 mg/mL. This supplement has no cytotoxicity, increases insulin-resistance expression as a reduction in G6Pase and PEPCK levels, and has anti-hyperglycemic properties for diabetes treatments (15).

Physical activity, especially aerobic activity in patients with obesity and diabetes, weight loss, and blood sugar control are some of the most effective ways to treat and prevent obesity (16). Regular aerobic, continuous, or intense exercises may reduce body fat levels, insulin resistance index, and glucose levels. A study on aerobic exercise in diabetic patients reported a reduction in blood sugar and harmful fat levels, which reduced the effect of the factors causing metabolic diseases such as diabetes and cardiovascular diseases (17).

Obesity, a sedentary lifestyle, and a diet pattern with high saturated fat, refined carbohydrates, and low fiber content are the main risk factors for lifestyle in type 2 diabetes patients (18). Physical activity and exercise have several metabolic benefits, such as improving insulin sensitivity and resistance and increasing peak oxygen consumption, whose molecular basis remained incomplete (19, 20).

Fat oxidation is key in improving insulin action, and exercise increases fat storage in muscle and fat oxidation capacity (21).

Based on the studies, the purpose is simultaneous to investigate the effects of E. Billardieri and exercise on women with obesity and type 2 diabetes.

Materials and Methods

Participants

This quasi-experimental research used a pre- and post-test design with the control group. The population comprised 38 women with obesity and type 2 diabetes, a body mass index over 30, and fasting blood glucose of 126 to 180g/dl. The sampling method was purposive and convenient; the sample size was the entire volunteer list. The subjects volunteered to participate in the research and were nominated by the office of the Kerman Diabetes Association. The results of a general descriptive statistical analysis are shown in Table 1. The groups were randomly divided

into control (C=9), drug (DRG=10), exercise (EX=9), and drug and exercise (DRG&EX=10). The exclusion criteria included a history of diseases, including kidney, nerve, cardiovascular, depression, skin, joint, diabetic foot ulcer, and hypoglycemia through the last two months. Further, there was an inability to exercise, a lack of regular aerobic activity, as well as a loss of weight of over three kilograms in the past three months.

Ethical Statement

The study and experiments on human subjects were conducted by ethical standards, and procedures were carried out with the subjects' adequate understanding and written consent.

Exercise Protocol

The primary protocol includes 10min of warm-up and contains 2 to 3min of brisk walking, 5min stretching, and 2 to 3min of slow running. The heart rate monitor measured exercise intensity during the test. The primary protocol consisted of 8 weeks of 3s/w of low-intensity continuous aerobic exercise. The primary protocol consisted of 8w/3 sessions of low-intensity continuous aerobic exercise. Aerobic exercise was 35min with an intensity of 50% of the heart rate max and increased to 50min to 65% of the heart rate max (5% every week). The cooled-down program was performed at the end (22).

Table 1. General descriptive statistical analysis among groups in pre and post-test

Groups	C	DRG	EX	DRG&EX
Age (yrs)	51.30±5.16	50.80±5.45	53.40±5.27	50.77±5.15
Height (cm)	162.0±6.75	161.19±7.31	159.0±4.32	160.06±7.35
Body mass (kg)	85.37±9.04	84.19±6.77	78.13±3.12	82.97±6.13
BMI (kg/m ²)	32.31±3.21	32.13±1.88	30.92±1.14	32.17±2.28

Control group (C=9), Drug group (DRG=10), Drug and Exercise group (DRG&EX=9), and Exercise group (EX=10), Body Mass Index (BMI)

Measurements

The subjects filled out the health questionnaire and consent form. Anthropometrical measurements, including the subjects' height and weight, were measured using a digital scale (Sahand, Iran, with an accuracy of 1g) and a Stature Meter. Data were collected in two stages, 24h before the first exercise and 48h after the last exercise session. The data included blood glucose (Glucometer Emperor Model BGM-601, China), insulin (ELISA kit, China), lipid profiles (triglycerides and cholesterol Pars Azmoun kit,

IRAN), HDL, LDL, and VLDL (Randox kit, England with a sensitivity of 1mg/dl). The dose of E. Billardieri extract (Boqanq) was determined via a pilot study. The groups, including DRG and DRG&EX, received 200ml of E. Billardieri extract (100ml in the morning and 100ml in the evening). The same amount of placebo was determined for the control and EX groups. The insulin resistance was calculated by the following formula (13):

$$\text{Insulin resistance} = [\text{fasting insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mmol/L)/18}] / 22.5$$

Table 2. Mean and Standard deviation of variables among groups in pre and post-test

Groups	C	DRG	EX	DRG&EX	
Pre-test	Glucose (mg. dl)	148.55±16.40	141.60±12.13	161.88±16.99	150.20±17.89
	Insulin levels (μU/ml)	12.78±1.95	10.99±2.51	13.84±2.07	11.93±2.37
	Insulin Resistance (min)	4.75±1.18	3.90±1.23	5.59±1.21	4.50±1.34
	Total Cholesterol (mg/dl)	197.33±39.90	196.00±64.14	210.00±70.35	198.50±51.53
	Triglyceride (mg/dl)	123.66±42.07	153.40±56.06	156.88±23.97	110.50±48.11
	HDL (mg/dl)	45.33±105.85	42.60±9.43	41.77±10.65	42.20±7.87
	LDL (mg/dl)	127.22±32.25	123.50±55.95	123.33±61.36	132.10±45.18
	VLDL (mg/dl)	41.44±12.89	43.40±11.85	46.00±14.38	43.50±7.97
Post-test	Glucose (mg. dl)	149.33±17.24	138.50±13.34	157.77±19.14	141.10±16.48
	Insulin levels (μU/ml)	12.91±2.14	10.92±2.53	13.45±2.12	10.92±2.30
	Insulin Resistance (min)	4.83±1.38	3.80±1.24	5.30±1.25	3.87±1.21
	Total Cholesterol (mg/dl)	200.33±37.51	195.50±63.31	189.44±55.49	183.30±40.573
	Triglyceride (mg/dl)	124.66±38.37	151.40±56.43	145.55±27.69	100.13±45.26
	HDL (mg/dl)	44.66±9.82	42.20±7.91	44.66±10.13	45.30±6.78
	LDL (mg/dl)	131.55±33.28	122.90±53.47	115.77±44.81	122.50±39.92
	VLDL (mg/dl)	42.00±12.05	42.80±10.27	38.11±10.50	39.57±10.15

Control group (C=9), Drug group (DRG=10), Drug and Exercise group (DRG&EX=9), Exercise group (EX=10), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), and Very Low-Density Lipoprotein (VLDL)

Statistical Analysis

The normal distribution of data was analyzed by the Shapiro-Wilk test. Homogeneity of variance as a prerequisite for the covariance was determined by Levene's test. ANCOVA was

determined for data analysis and differences groups by the Bonferroni post hoc test ($P \leq 0.05$). The SPSS statistical software Version 22 was used for data analysis.

Table 3. Analysis of covariance (ANCOVA) to compare groups in the post-test

	F	P
Glucose (mg. dl)	4 4.37	0.027*
Insulin levels (μ U/ml)	7.27	0.001*
Insulin Resistance	5.10	0.005*
Total Cholesterol	6.07	0.002*
Triglyceride (mg/dl)	6.07	0.002*
HDL (mg/dl)	4.56	0.009*
LDL (mg/dl)	6.77	0.001*
VLDL (mg/dl)	13.83	0.001*

High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), and Very Low-Density Lipoprotein (VLDL), * Significant at level $p \leq 0.05$.

Table 4. Bonferroni posthoc test of means difference comparing groups in post-test

Groups	C	DRG	EX	DRG&EX
Glucose (mg. dl)	C	---	---	---
	DRG	4.196	---	---
	EX	4.28	0.802	---
	Drug&EX	9.80*	5.61	5.52
Insulin levels (μ U/ml)	C	---	---	---
	DRG	0.22	---	---
	EX	0.43	0.28	---
	Drug&EX	1.15*	0.93*	0.65
Insulin Resistance	C	---	---	---
	DRG	0.22	---	---
	EX	0.34	0.12	---
	Drug&EX	0.72*	0.50	0.38
Total Cholesterol	C	---	---	---
	DRG	3.70	---	---
	EX	21.61*	17.90*	---
	Drug&EX	18.21*	14.31*	3.59
Triglyceride (mg/dl)	C	---	---	---
	DRG	1.003	---	---
	EX	7.95	8.98	---
	Drug&EX	11.40*	12.65*	3.98
HDL (mg/dl)	C	---	---	---
	DRG	0.14	---	---
	EX	3.03	-3.17	---
	Drug&EX	3.30*	3.44	0.27
LDL (mg/dl)	C	---	---	---
	DRG	5.83	---	---
	EX	20.95*	15.45*	---
	Drug&EX	15.69*	10.18	5.27
VLDL (mg/dl)	C	---	---	---
	DRG	-0.76	---	---
	EX	7.51*	6.76*	---
	Drug&EX	8.13*	7.38*	0.62

Control group (C=9), Drug group (DRG=10), Drug and Exercise group (DRG&EX=9), Exercise group (EX=10), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), and Very Low-Density Lipoprotein (VLDL), * Significant at level $p \leq 0.01$.

Results

Table 2 shows the statistical analysis of dependent variables such as glucose, insulin levels, insulin resistance, total cholesterol,

triglycerides, HDL, LDL, and VLDL according to study groups.

The statistical results of the covariance test were ($F(3, 33) = 44.37, P = 0.027$) by removing the possible effect related to glucose. Table 3 shows a significant difference in glucose levels. The

results of the Bonferroni post-hoc test showed a significant difference in the post-test of glucose in the C groups with the EX&DRG group ($P \leq 0.05$), but there was an insignificant difference between EX with Drug, EX with C, and DRG with EX&DRG groups ($P > 0.05$) (Table 4).

The statistical results of the covariance test were ($F(3, 33) = 7.27, P = 0.001$) after removing the possible effect related to insulin levels. Table 3 presents a significant difference in insulin levels. The results of the Bonferroni post-hoc test showed a significant difference in the C groups with the EX&DRG group and the Drug group with the DRG&EX group ($P \leq 0.05$), but there was an insignificant difference in EX with DRG; EX with C groups ($P > 0.05$) (Table 4).

Table 3 reports the significant difference in insulin resistance ($F(3, 33) = 5.10, P = 0.005$). The results of the post-hoc test showed a significant difference in the C groups with the EX&DRG group ($P \leq 0.05$), but an insignificant difference was in EX with DRG, EX with C, and DRG with EX&DRG groups ($P > 0.05$) (Table 4).

Table 3 shows a significant difference in the statistical covariance test related to total cholesterol ($F(3, 33) = 6.06, P = 0.002$). Interesting results from the post-hoc test showed a significant difference in total cholesterol in the C with the EX&Drug, the Drug with DRG&EX, C with EX, and DRG with EX groups ($P \leq 0.05$). However, there was an insignificant difference in EX with DRG&EX and C with DRG groups ($P > 0.05$) (Table 4).

The triglyceride was analyzed by the statistical covariance test. A significant difference was found ($F(3, 33) = 6.07, P = 0.002$) after removing the possible effect reported in Table 3. The post-hoc results test showed a significant difference in the C groups with the EX&DRG group and the Drug group with the DRG&EX group ($P \leq 0.05$). However, there was an insignificant difference in EX with DRG, EX with C, and C with DRG groups ($P > 0.05$) (Table 4).

Table 3 shows a significant difference ($F(3, 33) = 4.56, P = 0.009$) in the statistical covariance test HDL. The results of the Bonferroni test showed a significant difference in the C with the EX&DRG ($P \leq 0.05$). However, there was an insignificant difference in EX with DRG&EX, C with DRG, the DRG with DRG&EX, C with EX, and DRG with EX groups ($P > 0.05$) (Table 4).

A significant difference in the statistical covariance test of LDL ($F(3, 33) = 6.77, P = 0.001$)

is reported in Table 3. The results of LDL in the post-hoc test showed a significant difference were in C with the EX&DRG, C with EX, and DRG with EX groups ($P \leq 0.05$). Nevertheless, there was an insignificant difference in EX with DRG&EX, the DRG with DRG&EX, and C with DRG groups ($P > 0.05$) (Table 4).

According to Table 3, the statistical covariance test of VLDL found a significant difference ($F(3, 33) = 6.77, P = 0.001$). The post-hoc test results showed a significant difference in the C with the EX&DRG, the DRG with DRG&EX, C with EX, and DRG with EX groups ($P \leq 0.05$). However, there was an insignificant difference in EX with DRG&EX and C with DRG groups ($P > 0.05$) (Table 4).

Discussion

The effect of exercise and E. billardieri extract consumption on plasma glucose

The glucose in the DRG&EX group is significantly lower compared to the C group. The difference was in DRG and EX with C groups. An increase in time protocol over eight weeks may reveal differences between the two groups. Aerobic exercise and drug consumption significantly affected reduced glucose compared to the C group, but Drugs or exercise alone did not have a significant effect. Rabiee et al. (2017) showed that E. Billardieri extract consumption decreased blood glucose levels, but there was insignificant compared to the group placebo, which is consistent with the results of the present study (14). However, the effect of long-term use of this drug may lead to a decrease in fasting glucose. In addition, García-Cerrillo et al. (2017) investigated the impact of E. Billardieri extract consumption on heart problems caused by diabetes and confirmed that E. Billardieri extract consumption alone might cause unaffected plasma glucose (13). E. Billardieri extract possibly affects glycohemoglobin and can modulate excess glucose through a non-enzymatic mechanism (23). The present study differed from the study of (13) primarily because of the duration of the training and the lack of ability to control diet in humans as opposed to animal samples.

Many studies have confirmed the effect of aerobic exercise on glucose levels. The present study showed that the DRG&EX group had a significant difference from the control group, and the EX group had an insignificant difference from

the control group. Exercise and consumption of *E. Billardieri* extract may significantly affect fasting glucose levels. Fatty acids in adipose tissue accumulate and disrupt the transfer of GLUT4 to the muscle cells, and exercise prevents their accumulation and increases the oxidation of fatty acids. Weight loss and increasing physical activity are essential strategies related to diabetes and cardiovascular disease (24).

The Effect of Exercise and Consumption of E. Billardieri Extract on Insulin Levels

There were significant differences in insulin levels between the C group and the EX&DRG; group and between the DRG group and the DRG&EX group. However, there was an insignificant difference in EX with the DRG and EX with the C groups. Rabiee et al. (2017) observed a significant difference in insulin levels in the exercise and drug group with the exercise group, which was consistent with the present study. Based on this study, aerobic exercises increase insulin action, GLUT4 gene expression, glycogen synthetase, and hexokinase activity (14). In addition, a decrease was reported in the release of glucose and an increase in the transfer of glucose from the blood into the muscles due to the rise in the muscle capillaries (25-27). The increased activity of sports increases gene expression of GLUT4 through the activation of AMPK, which is then transferred to plasma. This process improves the entry of glucose into the muscle cell (24). Aerobic exercises make biochemical changes in muscles, increasing capillary density and oxidative enzymes, improving glucose transport and metabolism, increasing insulin to bind to muscle cell receptors, and reducing the need for insulin.

The Effect of Exercise and Consumption of E. Billardieri Extract on Insulin Resistance Index

This study showed that the insulin resistance index in the DRG&EX was significantly lower than in the control group, but it was insignificant compared to the Drug group and the exercise group. A significant difference was observed in exercise groups with and without *E. Billardieri* extract in the insulin resistance (14). Azimidokht et al. (2015) indicated that intermittent exercise positively affects the insulin resistance index (28). Caro et al. (2013) showed that the insulin resistance index is significantly lower in the active group compared to the inactive group. Therefore, regular exercise results in higher

insulin sensitivity (29). Stuart et al. (2013) found that 8 weeks of cycle training decreased insulin resistance, but exercise without weight bearing does not decrease insulin resistance but an increase in muscle insulin receptors and GLUT4 expression (30). Malin et al. 2013 concluded that exercise with weight loss increases the function of beta cells in people with prediabetic symptoms (31). Exercise helps improve insulin sensitivity by increasing muscle mass and improving insulin signaling (32). The present study showed that fats such as triglycerides, cholesterol, LDL, and VLDL have decreased significantly due to exercise. Effect of aerobic exercises on recovery improving insulin resistance attributed to the activation of AMPK and increased activity of phosphoinositide-3 kinase (PI3-Kinase) and Akt/PKB (33). It seems the exercise and consumption of *E. Billardieri* extract together can affect on insulin resistance index.

The Effect of Exercise and E. Billardieri Extract Consumption on Cholesterol Levels

Obesity and diabetes are associated, and *E. Billardieri* extract consumption may affect the lipid profile of women with obesity and type 2 diabetes. Blood variables, including cholesterol, triglyceride, HDL, LDL, and VLDL, may change in the obesity process. The present study showed that plasma cholesterol levels were significantly lower in EX and DRG&EX groups with and without drugs compared to the C group, but this difference was insignificant in the EX with DRG&EX groups. The presence of tannin (a substance with antioxidant properties) in the *E. Billardieri* extract reduces fat absorption and facilitates fat transfer into the cell. In the present study, cholesterol levels were not affected by the consumption of this drug. Nutrition, individual differences, and environmental factors are the possible reason. Following aerobic training, cholesterol levels decreased in the training group compared to the C group. The adaptations following aerobic activity are increased mitochondria volume and lipolysis enzyme activities, which increase the ability to catabolize fats during activity. Exercise can be a possible reason for reducing blood cholesterol levels in the EX and DRG&EX groups. Although the HDL mechanism is still unclear, lecithin-cholesterol acetyltransferase (L-CAT) and hepatic lipase (HL) may facilitate the role of HDL in the reverse transport of cholesterol from the arterial wall (34). In the present study, the cholesterol levels

of the two exercise groups were lower than the control group, which may be due to exercise. The consumption of E. Billardieri extract played a lesser role in reducing cholesterol levels.

The Effect of Exercise and Consumption of E. Billardieri Extract on Triglyceride Levels

This study showed significant differences in triglyceride levels after aerobic exercise and consumption of E. Billardieri extract in the four groups of C, DRG, EX, and DRG&EX. The DRG&EX group had significantly lower plasma levels of triglycerides than the C group. However, an insignificant difference was observed between the two training groups with and without E. Billardieri extract. A significant difference did not find in the triglyceride levels of the two exercise groups with and without E. Billardieri extract consumption (14). The triglyceride levels were significantly lower in the E. Billardieri extract group than in the control group (11). The probable reason is the presence of tannin in the E. Billardieri extract and its effect on reducing fat absorption and facilitating fat transfer in the cell. However, in the present study, the consumption of E. Billardieri extract did not affect triglyceride levels. Complete control of nutrition and environmental factors may help to find better results.

The Effect of Exercise and Consumption of E. Billardieri Extract on HDL Levels.

This study found a significant increase in HDL in the DRG&EX group compared to the C group. Zarei et al. (2015) observed a significant difference between the levels of HDL following the consumption of E. billardieri extracts in rats, which is not consistent with the results of the present study (11). An animal sample under more significant environmental and nutrition control might explain this difference. Some researchers have concluded that the intensity of exercise could affect the increase of HDL levels so that HDL levels can increase significantly after high-intensity exercises compared to low-intensity exercises (35). Several factors seem to affect HDL with various exercises, including weight, sex, protocol, and duration of training. Apolipoprotein (Apo A-1) increases the HDL levels enhancing the activity of the enzymes lipoprotein lipase and lysine cholelysineacyltransferase and decreasing the activity of the hepatic lipase enzyme (36). There was no effect of exercise alone on HDL levels, but

the intensity or duration of exercise may not be sufficient to affect HDL levels.

The Effect of Exercise and E. Billardieri Extract Consumption on LDL and VLDL Levels

LDL levels significantly decreased in the C with the EX&DRG and EX groups and DRG with EX groups. VLDL levels significantly decrease the C with the EX&DRG, the DRG with DRG&EX, and EX, and DRG with EX groups. LDL levels in the E. Billardieri extract group in rats were significantly lower than in the control group (11). As a result of tannin in this supplement, fat absorption is reduced, and fat transfer is facilitated. Animal studies may significantly control the diet and activity, which may explain the differences in studies. A few studies have shown that aerobic exercise reduces VLDL and LDL levels (36, 37). Burning fat as an energy source in aerobic exercise reduces the levels of LDL and VLDL in exercise groups. Exercise activity increases the activity of the lipoprotein lipase enzyme and decreases hepatic triglyceride lipase (HTGL). Increased lipoprotein lipase activity increases the catabolism of lipoproteins rich in triglycerides. Therefore, LDL and VLDL levels decrease with physical activity (36).

Research Limitations

Research limitations for inclusion in the study include the following:

Gender: The subjects of this study were females.

Type 2 diabetes: The subjects of this research had type 2 diabetes.

Fasting blood sugar: 126-180 mg/dl

BMI: 30 and upper 30 kg/m²

Exercise protocol: The training protocol was the same for all subjects.

The uncontrollable limitation of the research included:

Nutrition: The subjects were recommended to follow a similar diet during the study.

Physical activities lifestyle: The subjects were advised not to do physical activity outside the exercise program.

Motivation and mental state: Subjects were encouraged during the exercises.

According to the limitations and results, topics such as exercise intensities, inflammatory factors such as adipokine, dose-dependent consumption of Bogan extract, the long-term effect of Bogan consumption, and Bogan consumption and exercise in preventing obesity and diabetes need to be researched.

Conclusion

Based on the results, aerobic exercises with the consumption of *E. Billardieri* extract (Boqanq) extract significantly improved the insulin resistance index and lipid profile in people with type 2 diabetes. The possible reason for increasing insulin sensitivity and improving insulin function and GLUT4 may be the exercise and consumption of *E. Billardieri* (Boqanq) extract, which are the main factors in transferring glucose into muscle cells. Aerobic activities may be responsible for improved lipid profiles. An increase in the activities of lipase enzymes reduces harmful fats such as triglycerides, cholesterol, LDL, and VLDL and increases the production of good fats such as HDL.

Conflict of Interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest. There was no financial interest in this manuscript's subject matter or materials. The financial cost of this research was paid through the professors' grant and the student's expenses.

Acknowledgments

The authors thank all the loved ones who helped the researcher conduct this research. In addition, the authors thank the subjects and those who assisted with data collection. Authors' contributions include:

Mohsen Aminaei: had a substantial contribution to the concept or design or the acquisition, analysis, or interpretation of data for the article and final approval of the publication. Shiva Nazarieh: had data collection, analysis, and drafting of the article contribution. Rohullah Nikoei: revised the research for important intellectual content.

References

1. Ren Z, Sun W, Wang S, Ying J, Liu W, Fan L, et al. Status and transition of normal-weight central obesity and the risk of cardiovascular diseases: A population-based cohort study in China. *Nutrition, Metabolism and Cardiovascular Diseases*. 2022;32(12):2794-802.
2. Organization WH. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. World Health Organization; 1999.
3. Arrieta F, Iglesias P, Pedro-Botet J, Becerra A, Ortega E, Obaya JC, et al. Diabetes mellitus and cardiovascular

risk: Update of the recommendations of the Diabetes and Cardiovascular Disease working group of the Spanish Diabetes Society (SED, 2018). *Clínica e Investigación en Arteriosclerosis (English Edition)*. 2018;30(3):137-53.

4. Dullaart RP, de Vries R, Lefrandt JD. Increased large VLDL and small LDL particles are related to lower bilirubin in Type 2 diabetes mellitus. *Clinical Biochemistry*. 2014;47(16-17):170-5.

5. Murakami T, Urata T, Yamada N, Kawakubo K, Yoshida T, Kawamura H, et al. Lipoprotein abnormalities in type 2 diabetic patients. Increased distribution of triglycerides (TG) in very low density lipoprotein (VLDL) and decreased apolipoprotein E/VLDL-TG ratio are risk for ischemic heart disease. *Artery*. 1997;22(6):309-27.

6. Reaven GM, Johnston P, Hollenbeck CB, Skowronski R, Zhang J, Goldfine I, et al. Combined metformin-sulfonylurea treatment of patients with noninsulin-dependent diabetes in fair to poor glycemic control. *The Journal of Clinical Endocrinology & Metabolism*. 1992;74(5):1020-6.

7. Misra A, Alappan NK, Vikram NK, Goel K, Gupta N, Mittal K, et al. Effect of supervised progressive resistance-exercise training protocol on insulin sensitivity, glycemia, lipids, and body composition in Asian Indians with type 2 diabetes. *Diabetes Care*. 2008;31(7):1282-7.

8. Hosseini K, Touri E, Vaez H, Garjani A, Asgharian P, Tarhriz V. Evaluation of Anti-diabetic Effects of *Eryngium Billardieri* on Streptozotocin-induced Diabetes in Male Mice. 2021.

9. Rezaei Saber AP, Taghilou H, Aftabi S, Karimi Johani R. *Pejouhesh dar Pezeshki (Research in Medicine)*. 2022;46(2):57-67.

10. Promkum C, Butryee C, Tuntipopipat S, Kupradinun P. Anticlastogenic effect of *Eryngium foetidum* L. Assessed by erythrocyte micronucleus assay. *Asian Pacific Journal of Cancer Prevention*. 2012;13(7):3343-7.

11. Zarei A, Ashtiyani SC, Hamidzadeh S, Rezaei A, Ramezani M, Aalizadeh A. The study of the effects hydro-alcoholic extract of *Eryngium billardieri* on lipid profiles levels and liver and renal functions tests in hypercholesterolemic rats. *J Chem Pharm Res*. 2015;7(2):200-6.

12. Shirazi M, Monajemi R, Shahanipoor K. Comparison of aqueous and alcoholic extracts of *Eryngium billardieri* fruit with metformin in the treatment of type 2 diabetes in male Wistar rats. *New Cellular and Molecular Biotechnology Journal*. 2020;10(40):51-64.

13. García-Cerrillo D, Noriega-Cisneros R, Salgado-Garciglia R, Manzo-Avalos S, Clemente-Guerrero M, Montoya-Pérez R, et al. Improvement of diabetic cardiomyopathy by *Eryngium carlinae*. *The FASEB Journal*. 2017;31:944.15-15.

14. Rabiee G, Abedi B, Fatollahi H. The Effect of "*Eryngium billardieri*" Supplementation on Acute Glycemic Response, Ketoacidosis and Lipid Profile in

- Diabetic Men after one bout Incremental Exercise. *Research on Biosciences and Physical Actiuity*. 2017;4(6):53-61.
15. Kheirollahzadeh F, Eftekhari E, Ghollasi M, Behzadi P. Anti-hyperglycemic effects of *Eryngium billardierei* F. Delaroche extract on insulin-resistance HepG2 cells in vitro. *Molecular Biology Reports*. 2022;1-11.
16. Limongelli G, Monda E, D'Aponte A, Caiazza M, Rubino M, Esposito A, et al. Combined effect of Mediterranean diet and aerobic exercise on weight loss and clinical status in obese symptomatic patients with hypertrophic cardiomyopathy. *Heart Failure Clinics*. 2021;17(2):303-13.
17. Khademosharie M, Amiri Parsa T, Hamedinia MR, Hosseini-Kakhk SAR. Effects of two aerobic training protocols on Vaspin, Chemerin and lipid profile in women with type 2 diabetes. *Iranian South Medical Journal*. 2014;17(4):571-81.
18. Lindström J, Absetz P, Hemiö K, Peltomäki P, Peltonen M. Reducing the risk of type 2 diabetes with nutrition and physical activity—efficacy and implementation of lifestyle interventions in Finland. *Public Health Nutrition*. 2010;13(6A):993-9.
19. Golbidi S, Badran M, Laher I. Antioxidant and anti-inflammatory effects of exercise in diabetic patients. *Experimental Diabetes Research*. 2011;2012.
20. Kumar AS, Maiya AG, Shastry B, Vaishali K, Ravishankar N, Hazari A, et al. Exercise and insulin resistance in type 2 diabetes mellitus: A systematic review and meta-analysis. *Annals of Physical and Rehabilitation Medicine*. 2019;62(2):98-103.
21. Yavari A, Najafipoor F, Aliasgarzadeh A, Niafar M, Mobasser M. Effect of aerobic exercise, resistance training or combined training on glycaemic control and cardio-vascular risk factors in patients with type 2 diabetes. *Biology of Sport*. 2012;29(2):135-43.
22. Terada T, Friesen A, Chahal BS, Bell GJ, McCargar LJ, Boulé NG. Feasibility and preliminary efficacy of high intensity interval training in type 2 diabetes. *Diabetes Research and Clinical Practice*. 2013;99(2):120-9.
23. Noriega-Cisneros R, Ortiz-Avila O, Esquivel-Gutiérrez E, Clemente-Guerrero M, Manzo-Avalos S, Salgado-Garciglia R, et al. Hypolipidemic activity of *Eryngium carlinae* on streptozotocin-induced diabetic rats. *Biochemistry Research International*. 2012;2012.
24. Kadoglou NP, Vrabas IS, Kapelouzou A, Lampropoulos S, Sailer N, Kostakis A, et al. The impact of aerobic exercise training on novel adipokines, apelin and ghrelin, in patients with type 2 diabetes. *Medical Science Monitor*. 2012;18(5):CR290.
25. Oki K, Yamane K, Kamei N, Nojima H, Kohno N. Circulating visfatin level is correlated with inflammation, but not with insulin resistance. *Clinical Endocrinology*. 2007;67(5):796-800.
26. Smith JK, Dykes R, Douglas JE, Krishnaswamy G, Berk S. Long-term exercise and atherogenic activity of blood mononuclear cells in persons at risk of developing ischemic heart disease. *Jama*. 1999;281(18):1722-7.
27. Church TS, Barlow CE, Earnest CP, Kampert JB, Priest EL, Blair SN. Associations between cardiorespiratory fitness and C-reactive protein in men. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2002;22(11):1869-76.
28. Azimidokht SMA, Mogharnasi M, Kargar shouroki MK, Zarezade mehrizi AA. The effect of 8 weeks interval training on insulin resistance and lipid profiles in type 2 diabetic men treated with metformin. *Journal of Sport Biosciences*. 2015;7(3):461-76.
29. Caro J, Navarro I, Romero P, Lorente RI, Priego MA, Martínez-Hervás S, et al. Metabolic effects of regular physical exercise in healthy population. *Endocrinología y Nutrición (English Edition)*. 2013;60(4):167-72.
30. Stuart CA, South MA, Lee ML, McCurry MP, Howell ME, Ramsey MW, et al. Insulin responsiveness in metabolic syndrome after eight weeks of cycle training. *Medicine and Science in Sports and Exercise*. 2013;45(11):2021.
31. Malin SK, Solomon TP, Blaszczak A, Finnegan S, Filion J, Kirwan JP. Pancreatic β -cell function increases in a linear dose-response manner following exercise training in adults with prediabetes. *American Journal of Physiology-Endocrinology and Metabolism*. 2013;305(10):E1248-E54.
32. Kim YJ, Kim HJ, Lee SG, Jang SI, Go HS, Lee WJ, et al. Aerobic exercise for eight weeks provides protective effects towards liver and cardiometabolic health and adipose tissue remodeling under metabolic stress for one week: A study in mice. *Metabolism*. 2022;130:155178.
33. Kodama S, Miao S, Yamada N, Sone H. Exercise training for ameliorating cardiovascular risk factors—focusing on exercise intensity and amount. *International Journal of Sport and Health Science*. 2006;4(Special_Issue_2_2006):325-38.
34. Plowman SA, Smith DL. *Exercise physiology for health fitness and performance: Lippincott Williams & Wilkins*; 2013.
35. Banz WJ, Maher MA, Thompson WG, Bassett DR, Moore W, Ashraf M, et al. Effects of resistance versus aerobic training on coronary artery disease risk factors. *Experimental Biology and Medicine*. 2003;228(4):434-40.
36. Lennon SL, Quindry J, Hamilton KL, French J, Staib J, Mehta JL, et al. Loss of exercise-induced cardioprotection after cessation of exercise. *Journal of Applied Physiology*. 2004;96(4):1299-305.
37. Sulague RM, Suan NNM, Mendoza MF, Lavie CJ. The associations between exercise and lipid biomarkers. *Progress in Cardiovascular Diseases*. 2022.