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Research Article

Effect of High-Intensity Interval Training with Eryngium Campestre on Lipid Profile and Glycemic Indices in High-Fat Diet-Induced Obese Rats

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Abstract

Background: Obesity is a multi-factorial physical disorder that results in high serum lipid levels and glycemic disorders. On the other hand, regular exercise and administration of Eryngium Campestre (EC) have glucose and lipid-lowering effects.

Objectives: The present study aimed to review the effect of high-intensity interval training (HIIT) with EC on lipid profile and glycemic indices in high-fat diet (HFD)-induced obese rats.

Methods: Twenty-four obese rats were divided into four groups, including: (1) control, (2) HIIT, (3) EC, and (4) HIIT+EC. To investigate the effect of obesity on research variables, six rats were assigned to a healthy control group. During six weeks, groups 2 and 4 received HIIT three days per week, and groups 3 and 4 received 30 mg/kg EC by gavage. Data were analyzed using the Shapiro-Wilk test and one-way ANOVA with Tukey's *post hoc* test ($P \le 0.05$).

Results: Obesity significantly increased cholesterol (Cho), triglyceride (TG), insulin, and glucose levels ($P \le 0.05$). However, HIIT significantly decreased Cho, TG, insulin, and glucose levels ($P \le 0.05$), and EC significantly decreased Cho, TG, low-density lipoprotein (LDL), insulin, and glucose levels ($P \le 0.05$). Besides, HIIT+EC significantly decreased LDL and insulin ($P \le 0.05$). HIIT+EC could decrease LDL more than did HIIT ($P \le 0.05$).

Conclusions: Although HIIT and EC alone improved the lipid profile and glycemic indices in obese rats, HIIT combined with EC had greater effects on the decrease of LDL compared to HIIT.

Keywords: High-Intensity Interval Training, Eryngium, Lipids, Glycemic Index

1. Background

Nowadays, obesity is recognized as a major problem for global health and a multi-factorial physical disorder that results from high-calorie intake and low physical activity. Studies have shown that obesity is closely related to the development of diseases such as cardiovascular disease, cognitive impairment, cancer, motor disorders, and muscle mass loss (1). Metabolic syndrome is a collection of metabolic disorders such as high blood pressure, obesity, high blood triglycerides, and low levels of high-density lipoprotein (HDL), as well as insulin resistance. It is also a major cause of mortality (2). Various studies have shown that the prevalence of this syndrome is high not only in western countries but also in Asian ones. Control of risk factors in people with metabolic syndrome can reduce the risk of this syndrome and other chronic diseases such as cardiovascular disease and diabetes (3).

It seems that the first step to reducing risk factors of metabolic syndrome is lifestyle change (4). Despite significant improvements in medical science, factors such as patients' dissatisfaction after the administration of drugs and unpleasant side effects have led them to use alternative and traditional therapies. Herbal medicines have played an important role in reducing metabolic syndrome. Eryngium Campestre (EC), as one of the oldest medicinal plants, has attracted much attention recently. Early reports have shown anti-inflammatory and analgesic activities of EC (5). Besides, EC extracts have shown in vitro bioactivities such as anti-snake and scorpion venoms, as well as antibacterial, antifungal, antioxidant, and anti-hyperglycemic ef-

Copyright © 2020, Hormozgan Medical Journal. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited. fects (6). A study reported that EC improves glucose and insulin secretion (7). Moreover, EC extract has lipid-lowering effects in rats with high cholesterol (Cho) (8). Nowadays, experts believe that diet and medicine are not merely sufficient to treat metabolic syndrome disorders, but physical activity should be added to daily programs of the patients (9). Regular exercise can improve metabolic syndrome disorders such as hyperlipidemia, hyperglycemia, hypertension, quality of life, and depression (9). In this regard, it has been reported that resistance, aerobic, and endurance training with moderate intensity can improve HDL, lowdensity lipoprotein (LDL), triglyceride (TG), and insulin resistance in patients with metabolic syndrome (10). Paley and Johnson stated that although the optimal dose and type of exercise for metabolic syndrome disorders are unknown at present, the main challenge for health care professionals is how to motivate individuals to participate in training programs (11).

2. Objectives

Considering the abovementioned statements about the effects of exercise activities and EC extracts on lipid profile and glycemic indices of people with metabolic syndrome, and because there is little information about the simultaneous effect of EC consumption and interval training on lipid profile and glycemic indices of obese people, the present study aimed to examine the effect of highintensity interval training (HIIT) with EC on the lipid profile and glycemic indices of high fat diet (HFD)-induced obese rats.

3. Methods

In a quasi-experimental study, 30 male Wistar rats were purchased and transferred to a laboratory. The rats were kept in clear polycarbonate cages with humidity of 45% to 55%, the dark/light cycle of 12/12 h, and a temperature of $23 \pm 2^{\circ}$ C. During the research period, standard food plates and water were provided freely. After a one-week adaptation to the laboratory environment, 24 rats were fed with standard HFD. To induce obesity, a fatty diet containing 45% of total energy from fat (20% soybean oil and 20% animal fat), 13% protein, and 47% carbohydrate (24 g fats, 24 g proteins, and 41 g carbohydrates per 100 g) was used for eight weeks (1). It should be noted that this study was performed according to the guidelines for the use and care of laboratory animals. The healthy control group was fed with normal food (a special diet of rats prepared by Behparvar Company, containing 58% carbohydrate, 13% fat, and 28% protein). In the present study, HFD was made by a laboratory expert according to previous research.

Obese rats were divided into four groups, including: (1) control, (2) HIIT, (3) EC, and (4) HIIT+EC. Also, to investigate the effect of obesity on research variables, the remaining six rats were assigned to a healthy control group. During six weeks, groups 2 and 4 performed HIIT three days per week. Training consisted of five interval sets, oneminute training, one-minute rest on a treadmill with 80 to 95% VO_{2max} , and a slow interval with 55% VO_{2max} . The sets increased to 10 sets in the last week. Before and after training, rats ran for five minutes, with 40% VO_{2max} to warm up and cool down (12). Groups 3 and 4 received 30 mg/kg EC extract daily by gavage for six weeks (13). Eryngium was collected from lands in the Alamut region of Qazvin province of Iran in the first week of May and identified by a botanist (M. Ahvazi). A voucher specimen of the plant has been deposited in the Central Herbarium of the Research Institute of Medicinal Plants affiliated to the Iranian Academic Center for Education, Culture, and Research (ACECR). Forty-eight hours after the last training session and EC gavage, all rats were surgically operated for evaluating the study parameters. They were anesthetized with xylazine 10% and ketamine 2%. After splitting the chest of rats, blood samples were collected directly by syringes from the heart of animals. Lipid profiles were assessed by the Biosystem Laboratories kit (Spain). Fasting glucose and insulin were assessed by the immunoassay with sandwich and competitive-type and Glucose Oxidase assay kit, respectively. The Shapiro-Wilk test was used to review the normality of data and one-way ANOVA with Tukey's post hoc tests to analyze the effects of HIIT and EC, as well as obesity, on research variables ($P \le 0.05$).

4. Results

Lipid profile and glycemic indices in the five study groups are presented in Figures 1 to 6. The results of the one-way ANOVA test showed significant differences in Cho (P = 0.001), TG (P = 0.001), LDL (P = 0.001), insulin (P = 0.001), and glucose (P = 0.001) levels between the five study groups. Nevertheless, there were no significant differences in HDL levels between the five study groups (P = 0.06).

The results of Tukey's *post hoc* test showed that the Cho level was significantly higher in the control group than in the healthy control group (P=0.01), but it was significantly lower in the HIIT and EC groups than in the control group (P = 0.001) and significantly lower in the HIIT (P = 0.004) and EC (P = 0.008) groups than in the HIIT+EC group (Figure 1). The TG level was significantly higher in the control group than in the healthy control group (P = 0.002), but it was significantly lower in the HIIT (P = 0.03) and EC (P = 0.002) groups than in the control group and significantly lower in the EC group than in the HIIT+EC group (P=0.007) (Figure 2). The LDL level was significantly lower in the EC (P = 0.02) and HIIT+EC (P = 0.001) groups than in the control group and significantly lower in the HIIT+EC group than in the HIIT group (P = 0.007) (Figure 4).

The insulin level was significantly higher in the control group than in the healthy control group (P = 0.01). However, it was significantly lower in the HIIT (P = 0.001), EC (P= 0.001), and HIIT+EC (P = 0.04) groups than in the control group, significantly lower in the HIIT and EC groups than in the HIIT+EC group (P = 0.001), and significantly lower in the HIIT group than in the EC group (P = 0.002) (Figure 5). The glucose level was significantly higher in the control group than in the healthy control group (P = 0.01), but it was significantly lower in the HIIT (P = 0.002) and EC (P =0.001) groups than in the control group (Figure 6).

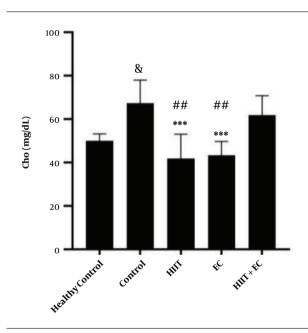


Figure 1. Cho levels in the five study groups; &, P < 0.05: significant increases compared to the healthy control group; ***, P < 0.001: significant decreases compared to the control group; ##, P < 0.01: significant decreases compared to the HIIT+EC group.

5. Discussion

The results of the present study showed that HIIT significantly decreased Cho, TG, insulin, and glucose levels; however, it had no significant effect on LDL and HDL levels. Nowadays, HIIT has a special place among the general public and researchers because of its very high efficiency. It improves body composition and affects health problems that are linked to obesity and insulin resistance. Studies have reported several mechanisms by which HIIT may affect the lipid profile (14). It has been shown that

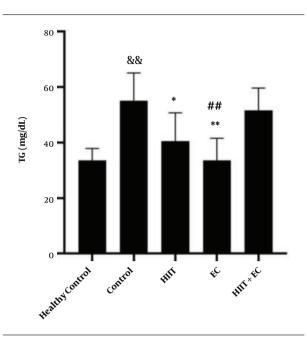


Figure 2. TG levels in the five study groups. &&, P < 0.01: significant increases compared to the healthy control group; *, P < 0.05, **, P < 0.01: significant decreases compared to the control group; ##, P < 0.01: significant decreases compared to the HIIT+EC group.

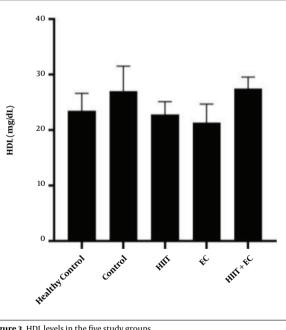


Figure 3. HDL levels in the five study groups

lipid oxidation increases during HIIT (14). Also, the levels of enzymes and hormones related to lipolysis may increase (14). The increases in hormones, such as catecholamine and growth hormones, have been observed during HIIT. Catecholamine stimulates lipolysis via the activation of

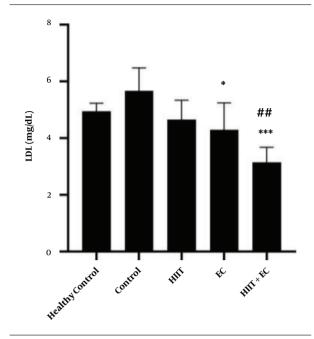


Figure 4. LDL levels in the five study groups. *, P < 0.05, ***, P < 0.001: significant decreases compared to the control group; ##, P < 0.01: significant decreases compared to the HIIT group.

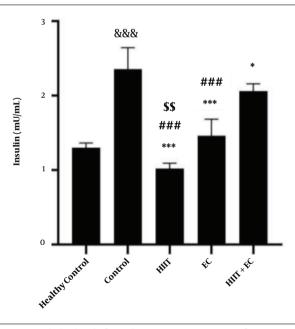


Figure 5. Insulin levels in the five study groups. &&&, P < 0.001: significant increases compared to the healthy control group; *, P < 0.05, *** P < 0.001: significant decreases compared to the control group; ###, P < 0.001: significant decreases compared to the HIIT+EC group; \$\$, P < 0.01: significant decreases compared to the EC group.

 β -adrenergic receptors in target tissues, mainly adipose tissue, and increases lipid oxidation. Beta-hydroxyacyl

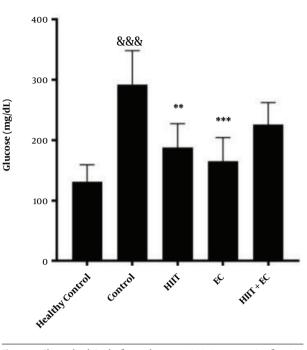


Figure 6. Glucose levels in the five study groups. &&&, P < 0.001: significant increases compared to the healthy control group; **, P < 0.01, ***, P < 0.001: significant decreases compared to the control group.

coenzyme-A dehydrogenase, which is an enzyme regulating lipid oxidation, increases after HIIT (15). Besides, appetite suppression and weight loss have been reported after HIIT (14). The proposed mechanism through which HIIT acutely reduces hypoglycemia risk is the stimulation of counter-regulatory hormones. Some studies have observed significant increases in growth hormone (GH) following HIIT (16). The findings of the present study are in line with research by He and Wang (17). They reviewed the effects of 12 weeks' HIIT on the serum lipid profile of patients with dyslipidemia and concluded that HIIT could be used as an intervention method to regulate the serum lipids of dyslipidemia patients (17). Also, the findings of the present study are in line with the findings by Boukabous et al. (18). They reported that two types of training, including HIIT and moderate-intensity continuous training (MICT) improved lipid profile and fasting blood glucose in older women (18).

In addition to exercise activities, nutritional therapy is an essential part of treatment for people with high blood lipids. The use of nutritional methods is an economic strategy to reduce all-cause early deaths for adults with obesity. In this regard, the results of the present study showed that EC consumption for six weeks significantly decreased Cho, TG, LDL, insulin, and glucose levels but had no significant effect on HDL levels. Many published studies have reported that EC consumption decreases lipid and glucose (19, 20). It seems that the possible mechanism is related to EC phenolic content that restores pancreatic tissue function (21). The anti-diabetic potential of phenolic compounds has been extensively investigated. These compounds control blood glucose through various mechanisms such as increasing tissue uptake of glucose via GLUT4, improving pancreatic β -Cell function through antioxidant activity, and liver glucose homeostasis. The probable mechanisms regarding dyslipidemia consist of stimulating cholesterol-7-alpha-hydroxylase (one of the main liver enzymes converting Cho into bile acids), decreasing inhibition of β -Hydroxy β -methylglutaryl-CoA(HMG-CoA), and finally reducing Cho absorption from the intestine (19). In line with the present study, the findings by Afshari et al. showed that the administration of EC in rats with type 2 diabetes mellitus improved insulin and lipid profile. Besides, the improvement of LDL and TG levels were observed at higher doses, conveying that the effects of EC are dosedependent so that higher doses had better effects (19). Also, the findings by Conea et al. showed that EC contains stigmasterol. Stigmasterol is a kind of bioactive substance inside plant compositions and a major component of sterol, which has LDL-lowering properties (reducing Cho absorption in the intestine) and consequently decreases Cho (20).

Regarding the interactive effects, the findings showed that six weeks of HIIT with EC administration significantly decreased LDL and insulin. Besides, HIIT with EC had more effects on the decrease of LDL than had HIIT. Although there was no study to determine the interactive effects of HIIT and EC consumption on lipid profile and glycemic indices of obese people to compare to the present study, it seems that HIIT combined with EC consumption can enhance the lipid and insulin lowering effects of EC. As the overload is one of the principles of training and different doses of herbal extracts can have different effects on lipid profile and glycemic indices, it is suggested that further studies review the effect of HIIT with different protocols of overload and EC consumption with different doses on lipid profile and glycemic indices of obese rats.

5.1. Conclusions

Although HIIT and EC alone improved lipid profile and glycemic indices in obese rats, HIIT combined with EC had a greater effect on the decrease of LDL compared to HIIT.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

As the present study is part of the doctoral dissertation approved by the Science and Research Branch of Islamic Azad University, the authors of this article express their gratitude and appreciation for the spiritual support of the Research and Technology Department of this university branch.

Footnotes

Authors' Contribution: Laboratory studies and tests: Behnoush Ghadery; study and review: Farshad Ghazalian and Seyed Ali Hosseini; analysis and interpretation of data: Hossein Abed Natanzy and Alireza Shamsoddini.

Conflict of Interests: The authors declare that they have no conflict of interest.

Ethical Approval: Researchers received introduction letters from the Marvdasht Branch of Islamic Azad University with code IR.IAU.M.REC.1398.021.

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References

- Moradi A, Hosseini SA, Nikbakht M. Effect of Swimming Training and Crocin Consumption on Intrinsic Apoptosis Pathway in Muscle Tissue of High-Fat Diet-induced Obese Rats. *Middle East Journal of Rehabilitation and Health.* 2019; In Press (In Press). doi: 10.5812/mejrh.92612.
- AlSaraj F, McDermott JH, Cawood T, McAteer S, Ali M, Tormey W, et al. Prevalence of the metabolic syndrome in patients with diabetes mellitus. *Ir J Med Sci.* 2009;**178**(3):309–13. doi: 10.1007/s11845-009-0302-z. [PubMed: 19495843].
- Deedwania PC, Gupta R. Management issues in the metabolic syndrome. J Assoc Physicians India. 2006;54:797–810. [PubMed: 17214277].
- Tavassoli AA, Gharipour M, Khosravi A, Kelishadi R, Siadat ZD, Bahonar A, et al. Gender differences in obesogenic behaviour, socioeconomic and metabolic factors in a population-based sample of Iranians: the IHHP study. J Health Popul Nutr. 2010;28(6):602–9. doi: 10.3329/jhpn.v28i6.6609. [PubMed: 21261206]. [PubMed Central: PMC2995029].
- Wang P. Phytochemical Constituents and Pharmacological Activities of Eryngium L. (Apiaceae). *Pharmaceutical Crops*. 2012;3(1):99–120. doi: 10.2174/2210290601203010099.
- Kikowska M, Dworacka M, Kędziora I, Thiem B. Eryngium creticum

 ethnopharmacology, phytochemistry and pharmacological activity. A review. Revista Brasileira de Farmacognosia. 2016;26(3):392–9. doi: 10.1016/j.bjp.2016.01.008.
- Kasabri V, AbuDahab R, Afifi F, Naffa R, Majdalawi L. Modulation of pancreatic MIN6 insulin secretion and proliferation and extrapancreatic glucose absorption with Achillea santolina, Eryngium creticum and Pistacia atlantica; extracts: in vitro evaluation. *Journal of Experimental and Integrative Medicine*. 2012;2(3):245. doi: 10.5455/jeim.120612.or.036.
- Castro-Torres IG, de Jesus Cardenas-Vazquez R, Velazquez-Gonzalez C, Ventura-Martinez R, De la OM, Naranjo-Rodriguez EB, et al. Future therapeutic targets for the treatment and prevention of cholesterol gallstones. *Eur J Pharmacol.* 2015;**765**:366–74. doi: 10.1016/j.ejphar.2015.08.045. [PubMed: 26358204].

- Schmitt A, Maurus I, Rossner MJ, Roh A, Lembeck M, von Wilmsdorff M, et al. Effects of Aerobic Exercise on Metabolic Syndrome, Cardiorespiratory Fitness, and Symptoms in Schizophrenia Include Decreased Mortality. *Front Psychiatry*. 2018;9:690. doi: 10.3389/fpsyt.2018.00690. [PubMed: 30622486]. [PubMed Central: PMC6308154].
- Myers J, Kokkinos P, Nyelin E. Physical Activity, Cardiorespiratory Fitness, and the Metabolic Syndrome. *Nutrients*. 2019;11(7). doi: 10.3390/nu11071652. [PubMed: 31331009]. [PubMed Central: PMC6683051].
- Paley CA, Johnson MI. Abdominal obesity and metabolic syndrome: exercise as medicine? *BMC Sports Sci Med Rehabil.* 2018;10:7. doi: 10.1186/s13102-018-0097-1. [PubMed: 29755739]. [PubMed Central: PMC5935926].
- Machado MV, Vieira AB, da Conceicao FG, Nascimento AR, da Nobrega ACL, Tibirica E. Exercise training dose differentially alters muscle and heart capillary density and metabolic functions in an obese rat with metabolic syndrome. *Exp Physiol.* 2017;**102**(12):1716–28. doi: 10.1113/EP086416. [PubMed: 28921743].
- Safari HR, Esmaeili S, Naghizadeh MS, Falahpour M, Malekaneh M, Anani Sarab GR. The Effects of Aqueous Extract of Eryngium Campestre on Ethylene Glycol-Induced Calcium Oxalate Kidney Stone in Rats. Urol J. 2019;16(6):519–24. doi: 10.22037/uj.v0i0.4287. [PubMed: 31473993].
- Cassidy S, Thoma C, Houghton D, Trenell MI. High-intensity interval training: a review of its impact on glucose control and cardiometabolic health. *Diabetologia*. 2017;60(1):7-23. doi: 10.1007/s00125-016-4106-1. [PubMed: 27681241]. [PubMed Central: PMC6518096].
- 15. Zaer Ghodsi N, Zolfaghari MR, Fattah A. The Impact of High Intensity

Interval Training On Lipid Profile, Inflammatory Markers and Anthropometric Parameters in Inactive Women. *Medical Laboratory Journal*. 2016;**10**(1):56–60. doi: 10.18869/acadpub.mlj.10.1.56.

- Rempel M, Yardley JE, MacIntosh A, Hay JL, Bouchard D, Cornish S, et al. Vigorous Intervals and Hypoglycemia in Type 1 Diabetes: A Randomized Cross Over Trial. *Sci Rep.* 2018;8(1):15879. doi: 10.1038/s41598-018-34342-6. [PubMed: 30367116]. [PubMed Central: PMC6203731].
- He YY, Wang WR. [Effects of a 12-week high intensity interval training on blood lipid of dyslipidemia patients with different apolipoprotein E genotypes]. *Zhongguo Ying Yong Sheng Li Xue Za Zhi*. 2019;**35**(1):28–33. Chinese. doi: 10.12047/j.cjap.5749.2019.007. [PubMed: 31245949].
- Boukabous I, Marcotte-Chenard A, Amamou T, Boulay P, Brochu M, Tessier D, et al. Low-Volume High-Intensity Interval Training (HIIT) versus Moderate-Intensity Continuous Training on Body Composition, Cardiometabolic Profile and Physical Capacity in Older Women. J Aging Phys Act. 2019;27(4):879–89. doi: 10.1123/japa.2018-0309. [PubMed: 31034304].
- Afshari M, Mohammadshahi M, Malayeri AR, Zaheri L. Antidiabetic, hepato-protective and hypolipidemic effects of Eryngium caucasicum extract in streptozotocin-nicotinamide induced type 2 diabetes in male rats. *Iraq Medical Journal*. 2019;3(1).
- Conea S, Parvu AE, Taulescu MA, Vlase L. Effects of Eryngium planum and Eryngium campestre extracts on ligatureinduced rat periodontitis. *Digest Journal of Nanomaterials and Biostructures*. 2015;10(2):693– 704.
- 21. Kim Y, Keogh JB, Clifton PM. Polyphenols and Glycemic Control. *Nutrients*. 2016;**8**(1). doi: 10.3390/nu8010017. [PubMed: 26742071]. [PubMed Central: PMC4728631].