Original Article

The Effect Of Endurance Exercise Training, Along With The Consumption Of Black Mulberry Leaf Aqueous Extract, On Heart Contractility In Overweight Rats

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Abstract

Aim: Endurance exercise is used as one of the clinical interventions in the prevention and treatment of cardiovascular diseases. Black mulberry leaves (Morus Nigra) containing phenolic compounds that have pharmacological properties are used to lower blood pressure and lower cholesterol. The aim of the present study was to evaluate the effect of black mulberry leaf aqueous extract alone and its combination with physical activity on heart contractility in overweight rats.

Method: 35 male Wistar rats were divided into 5 groups with free access to water and food. The control group was fed with normal food and 4 groups were fed with 60% high fat food for 12 weeks to cause hyperlipidemia. Then, endurance training and gavage of black mulberry leaf aqueous extract were performed for 6 weeks, 5 days a week. At the end, using the Power lap electro physiograph system, heart contractility indices, including heart rate (HR), arterial systolic pressure (SP), diastolic pressure (DP), left ventricular systolic pressure (LVSP), left ventricular end-diastolic pressure (LVEDP) The maximum rate of left ventricular pressure increase (+dp/dt max) and the maximum rate of left ventricular pressure decrease (dp/dt max -) were recorded.

Findings: The maximum rate of left ventricular pressure increase (dp/dt max +) and the maximum rate of left ventricular pressure decrease (dp/dt max-) in the exercise training group showed a significant increase compared to the normal diet control group and the high-fat diet control group ($P< 0.05$) and ($P<0.001$). These indicators showed a significant decrease in the extract consumption group compared to the control group and the exercise group ($P<0.001$) and ($P<0.01$). In the extract and exercise group, both indicators showed an increase compared to the extract group, but did not reach the level of the control and normal groups. Left ventricular systolic pressure (LVSP) and left ventricular end-diastolic pressure (LVEDP) showed a significant decrease in the extract group compared to the exercise group ($P<0.01$).

Conclusion: Consumption of black mulberry leaf extract caused heart muscle relaxation and decreased (dp/dt max +) and (dp/dt max -) compared to the control group. Adaptation to sports training and improving cardiac muscle contraction function partially compensated for this decrease and improved the decrease in cardiac function caused by the effect of black mulberry leaf extract.

Keywords: sport physiology, endurance exercise training, black mulberry leaf aqueous extract, heart contractility, overweight rats

Introduction

Exercise training as a useful non-pharmacological treatment for the prevention of cardiac events, improving cardiac function and protecting the heart from ischemic damage, by increasing the growth of the heart and improving the metabolism of cardiac cells, basically increases the function of the heart (1 and 2). Regular sports activity leads to a number of automatic and physiological adaptations, the result of which is an increase in cardiovascular performance

and an increase in cardiac performance capacity. A larger and stronger heart contributes to increased stroke volume and maximal cardiac output and exposes the heart to less stress in submaximal activities with lower heart rate (HR) at any intensity of exercise, overall. Cardiovascular adaptations lead to better functioning of the heart (3 and 4).
In fact, regular and frequent endurance exercises lead to the reconstruction and strengthening of the left ventricle and a significant improvement in the heart's function and increasing its tolerance against ischemia and blood flow, and as a result, myocardial diseases will progress more slowly and lead to a longer life and reduced periods. It will result in hospitalization for people (5 and 6) and for this reason, sports training has been suggested by experts as an efficient, low-cost and safe intervention as a strategy for the prevention and treatment of cardiovascular diseases. (7) And from this point of view, regular exercise can be considered as an effective factor in improving the quality of life and preventing cardiovascular diseases and reducing the complications of cardiovascular diseases. However, it has not been fully determined which type of exercise can improve cardiac function in a better and more beneficial way and prevent adverse remodeling (6 and 5) according to the intensity, type and duration of exercise.
Studies show that BP decreases after exercise and this decrease depends on the intensity, duration and number of training sessions per week (8, 9, 10, 11).
In a meta-analysis of 72 studies, it was shown that after adapting to regular aerobic exercise, an average decrease of 3 mmHg in resting blood pressure was observed, and these researchers concluded that regular endurance exercise has an effect on the nervous system and the renin-angiotensin system. It leads to the reduction of cardiovascular risk factors, blood pressure and vascular resistance. (12)
In endurance training, the longer the duration of exposure to sports training, the more effective it is in lowering blood pressure, but for patients and elderly people, a period of moderate endurance training is also known to be useful. In research that examined and showed three periods of training 61-90 minutes, 90-120 minutes and more than 120 minutes, a better reduction in systolic blood pressure was reported in the 61-90 minutes training group (13).
Black mulberry (Morus nigra) is a species of plant Morus and found in temperate and subtropical regions of Asia, Africa and North America (14) Black mulberry leaves contain chemicals such as coumarins, flavonoids, phenols that have pharmacological effects. to be (15)
The black mulberry leaf (Morus nigra) has medicinal value, which is used in traditional medicine for the treatment of diseases such as diabetes, hypercholesterolemia, menopause, obesity, and evidence of anti-inflammatory, pain-relieving and liver protection effects. Given (16) .. Recent studies, with the solubility of black mulberry leaf extract in organic solvents, have shown that black mulberry leaves are rich in phenolic compounds, which have a potential antioxidant activity in reducing oxidative stress and are effective in cardiovascular and neurodegenerative diseases. It is effective, and its phenolic source is effective in the treatment of blood fat reduction. (17-18) Considering the effect of exercise training on cardiac function and also the effect of different compounds of black mulberry leaf extract on blood vessels and muscles, the present study aims to evaluate the effect of aqueous extract of black mulberry leaf alone and its combination with endurance exercise on hemodynamic and contraction factors. Cardiac compliance was performed in overweight rats.

Materials and Methods

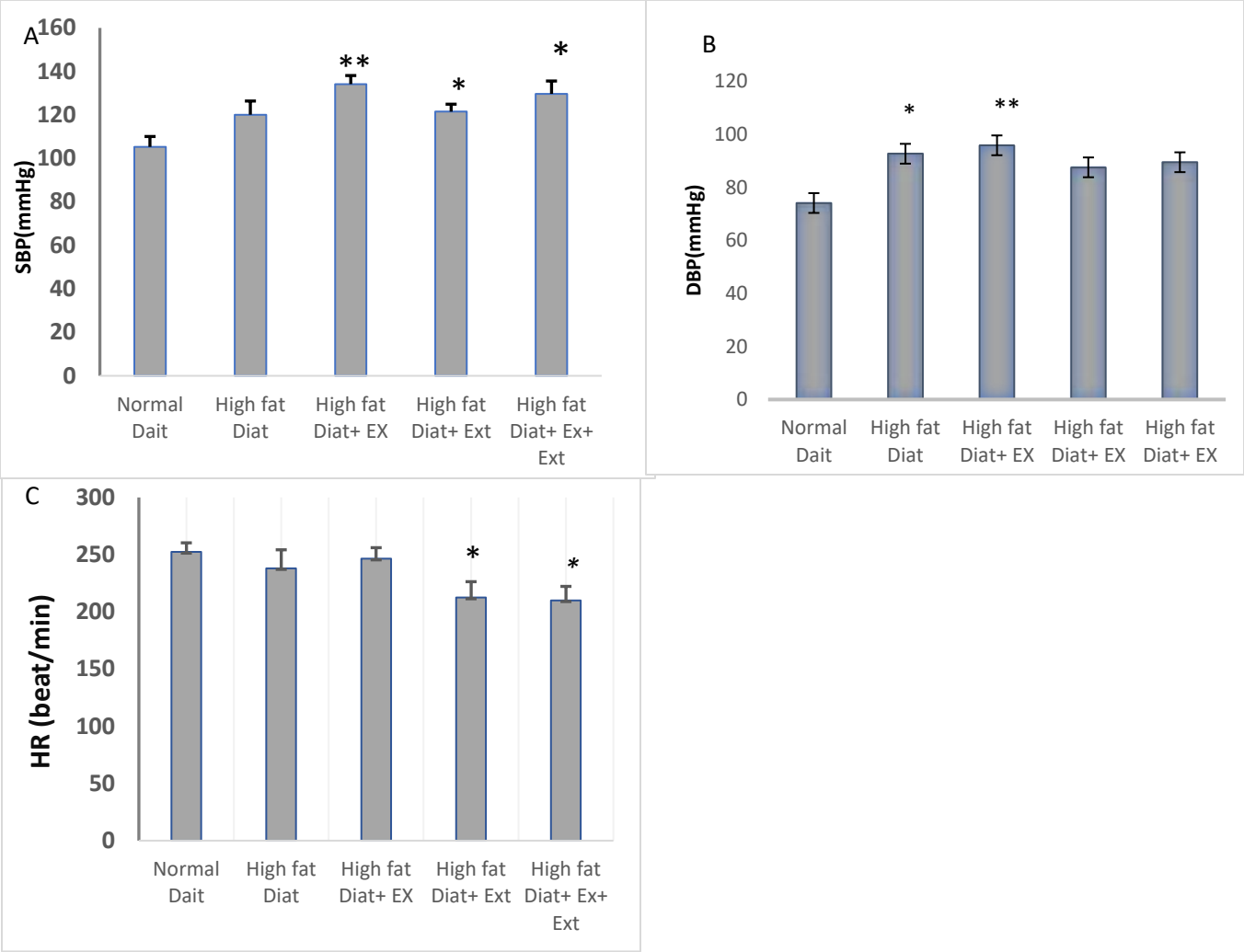
Method

35 male Wistar rats were divided into 5 groups with free access to water and food. The rats were kept in conditions of free access to water and food and 12 hours of darkness and 12 hours of light. For grouping, we divided the animals into 5 groups with 7 animals in each group, the control group, with normal feed and 4 groups, were fed with 60% high-fat feed for 12 weeks to cause hyperlipidemia. In case of death, one animal the groups were replaced by:
1- control group
2- High-fat diet control group
3- exercise training group
4- extract consumption group
5- Group of exercise training and extract consumption

The dose of black mulberry extract was 250 mg/kg/day orally and by gavage (18).
Sports training is done on a treadmill with a zero-degree incline, 5 days a week and each session lasts 60 minutes for 6 weeks. The speed of the treadmill was gradually increased to 75-80% of the maximum speed received during a test with maximum stress (19).
At the end, using the Physiograph Power lab system, heart contractility indices include: heart rate (BP), systolic pressure (SP), diastolic pressure (DP), maximum left ventricular systolic pressure (LVSP), left ventricular end-diastolic pressure (LVEDP), The speed of left ventricular pressure increase (+dp/dt max) was recorded as an index of contraction speed and the maximum speed of ventricular pressure decrease (-dp/dt max) was recorded as an indicator of left ventricular relaxation speed.
SPSS software was used for statistical calculations. First, the distribution of data was checked with the Kolmogorov-Smirnov test. If the distribution was normal, ANOVA statistical test was used. In the ANOVA test, if the difference between the groups was significant, Toke's post hoc test was used to determine the difference between the different groups. If the data distribution was not normal, equivalent non-parametric tests were used. The significance level of $p<0.05$ values was considered.

Results

The following results were obtained in the present study, which was conducted to determine the effect of endurance exercise combined with the consumption of black mulberry leaf extract on cardiac contractility indices and hemodynamic factors of male rats. Heart rate and systolic pressure showed a significant difference in the two extract consumption groups and the extract consumption group and combined exercise with the control group with normal feed consumption. ($p < 0.05$)
Diastolic blood pressure in two extract groups and exercise combined with extract group did not show any significant difference with the control group with normal diet ($p<0/05$).

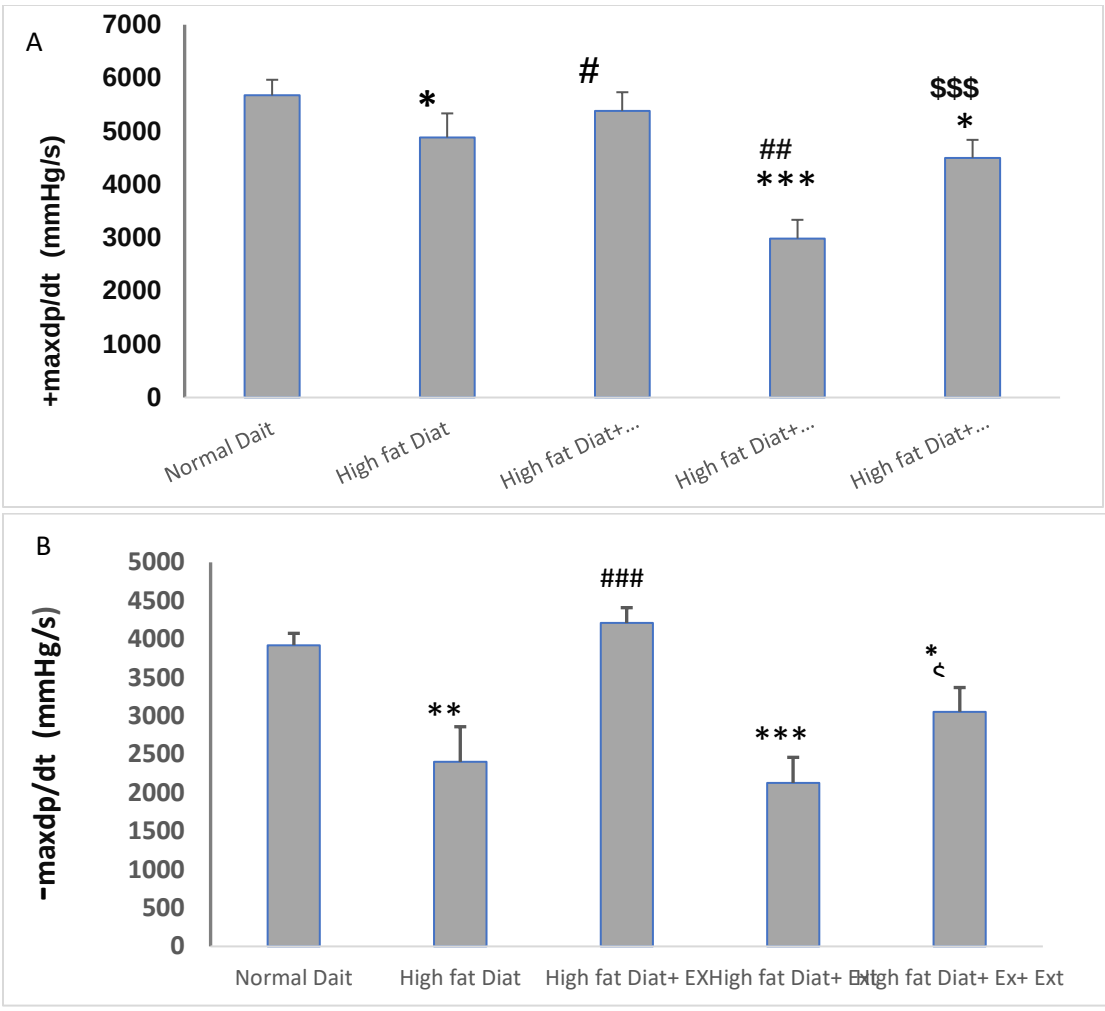


A: The effect of high-fat diet, exercise and blackberry extract on systolic blood pressure
B: Effect of high-fat diet, exercise and black mulberry extract on Diastolic blood pressure
C : Effect of high-fat diet, exercise and black mulberry extract on heart rate
***Significant difference at the %5 level with the normal diet group**

****Significant difference at the 1%level with the normal diet group**

*****Significant difference at the 0.1%level with the normal diet group**

Diastolic blood pressure in the high-fat diet group showed a significant difference at the 1% level with the normal diet group ($p<0.01$), and the high-fat diet and exercise group showed a significant difference at the 1.0% level with the normal diet group ($p<0.01$). 0.001).
The index (dp/dt max +) or the maximum rate of left ventricular pressure increase was investigated in 5 groups. In the high-fat diet group, this index showed a significant decrease compared to the normal diet control group ($P<0.05$).



A: The effect of high-fat diet, exercise and blackberry extract on maximum contraction speed
B: Effect of high-fat diet, exercise and black mulberry extract on maximal left ventricular relaxation rate
***Significant difference at the %5 level with the normal diet group**

****Significant difference at the 1%level with the normal diet group**

*****Significant difference at the 0.1%level with the normal diet group**

#Significant difference at the 5%level with the high-fat diet group

##Significant difference at the 1%level with the high-fat diet group

###Significant difference at the level of 0.1%with the high-fat diet group

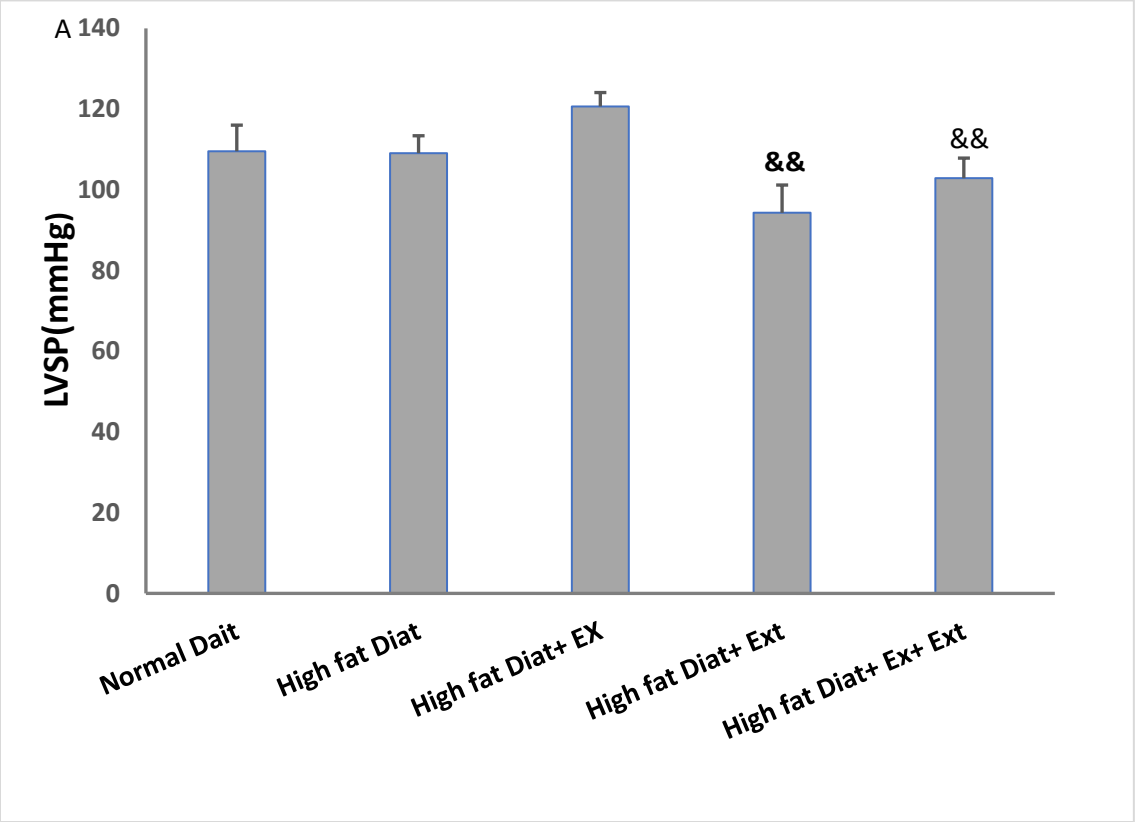
$Significant difference at the 5%level with the high-fat diet and exercise group

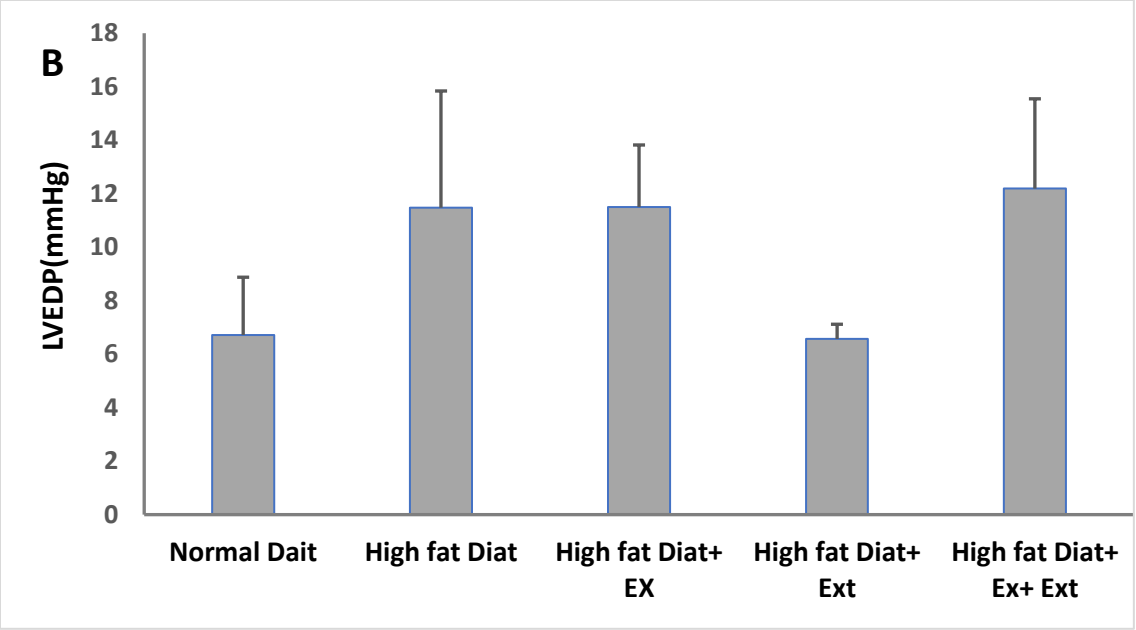
$$Significant difference at the 1%level with the high-fat diet and exercise group

$$$Significant difference at the 0.1%level with the high-fat diet and exercise group

In the high-fat diet and exercise group, this index showed a significant increase compared to the high-fat diet group. (0.01) P showed a significant decrease in the high-fat diet group and consumption of index extract (dp/dt max +) compared to the normal and high-fat diet groups. The high-fat diet group with the extract and exercise showed a significant difference (dp/dt max +) compared to the high-fat diet and exercise group at the level of 0.1% ($p<0.001$) and a significant difference at the level of 5% compared to the control group showed normal nutrition ($p<0.05$).

The index (dp/dt max -) or the maximum rate of reduction of left ventricular pressure in the high-fat diet group showed a significant decrease of 1% compared to the normal diet control group ($P<0.01$). In the high-fat diet and exercise group, this index showed a significant increase compared to the high-fat diet group ($P<0.001$). In the group of high-fat diet and extract consumption, this index showed a significant decrease compared to the normal diet control group ($P<0.001$). Also, in the group of extract consumption and exercise, the index (dp/dt max -) was significantly different from the control group with normal diet. It showed a significant difference compared to the high-fat diet and exercise group ($P<0.05$).





A: The effect of high-fat diet, exercise and blackberry extract on left ventricular systolic pressure
B: Effect of high-fat diet, exercise and blackberry extract on left ventricular end-Diastolic pressure
&& Significant difference at the 1% level with the exercise and high fat diet group

The left ventricular systolic pressure index or LVSP showed a significant difference in the extract and high-fat diet group as well as the exercise and extract group compared to the exercise and high-fat diet group ($P<0.01$).
The index of left ventricular end-diastolic pressure (LVEDP) or isovolumic pressure increased in the high-fat diet group compared to the normal diet group. This index showed a 50% decrease in the high-fat diet and extract consumption group compared to the exercise group. But in the high-fat diet group, exercise and extract increased.
The LVSP index did not show any significant difference in the three groups of normal diet, high-fat diet and exercise. However, a significant decrease was seen in the groups that consumed black mulberry leaf extract, i.e. the extract group and the extract and exercise group. A 50% decrease in the LVEDP index or left ventricular pressure at the end of diastole was observed in the extract group compared to the exercise training group.

Discussion

In the present study, which was carried out to determine the effect of endurance exercise along with the consumption of black mulberry leaf aqueous extract on heart contractility indices and hemodynamic factors of male rats along with the consumption of high-fat food, there was a significant decrease in the extract consumption group in the index heart rate, systolic pressure, the maximum rate of left ventricular pressure increase (dp/dt max +) and the maximum rate of ventricular pressure decrease (dp/dt max -) were observed compared to the control group, which indicates a weaker heart function in the consumption group. The extract is compared to the control group. Also, in the exercise training group, the systolic pressure index showed a slight increase compared to the control group and the high-fat diet group. Therefore, there is a possibility that the intensity and pressure of intense endurance training is the cause of this increase. In a study, it was shown that light to moderate endurance sports training after heart attack, index
LVSP improved the sham group. Also, interestingly, exercise produced a similar improvement in MI-induced LVSP reduction, as well as similar results in LVEDP. /dt) and (-dp/dt) improved significantly after 4 weeks of exercise training in both sham and MI rats, and the heart rate decreased, which results are not consistent with the present study, so we compared the type and intensity of exercise in the present study. With other studies, we concluded that there is

a possibility that the intensity of endurance training is the cause of these differences in results. In general, low- to moderate-intensity exercise reduces heart dysfunction caused by MI. Therefore, these researchers concluded that exercise training in the aged rat model after MI through suppression of apoptosis, oxidative stress, inflammatory responses and activation of AMPK/SIRT1/PGC-1α signaling pathway. It improves heart function (20) It should be mentioned that in the present study, exercise caused a slight increase in systolic blood pressure in the exercise group, which is probably due to the high intensity of the exercise, although in the extract consumption group, we saw a decrease in blood pressure. systolic blood, which is consistent with other studies (15-21).

Another mechanism of lowering blood pressure is increasing the serum level of NO, in a research conducted in 2014 in Indonesia, it showed that the levels of NO after 7 days of treatment in the mulberry leaf extract group at 30, 60 and 90 minutes after From the prescription, it increased. It was also shown that mulberry extract can maintain the concentration of NO in the body for a long time. (Indonesia) Other active components of mulberry leaves include substances such as flavones, steroids, triterpenes, amino acids, vitamins and minerals, including L-arginine, which is an antihypertensive amino acid and plays a role in NO synthesis. (21-22).

In a study, the diameter of large and small blood vessels in rabbit ears before and after 7 days, consumption of black mulberry leaf extract did not have a significant difference, but it showed a significant difference immediately after administration of the extract at 60 and 90 minutes, black mulberry has prokinetic effects. It is a laxative that is mediated through cholinomimetic, antimuscarinic and Ca2+ antagonist mechanisms. These researchers concluded that the ethanolic extract of mulberry leaves can dilate the blood vessel of rabbit ear. Also, the presence of compounds such as saponins, alkaloids, phenolic compounds and flavonoids, black mulberry fruit inhibited the contractions caused by carbachol and potassium ion in rabbits in a dose-dependent manner (15).

Also, in another research, the ability of phenolic compounds from Morus Nigra to modulate the activity of ATPase and sarco-endoplasmic Ca2+ enzyme (SERCA1) was investigated. While the results of the theoretical and experimental approaches were consistent regarding the identification of enzyme binding sites to SERCA1, it was shown that Albaol A, by being immersed in the luminal gate of the SERCA1 release site, inhibited Ca2+. Kuwanonu exerted an inhibitory effect on the cytosolic region of SERCA1 by preventing ATP binding, and these were accompanied by conformational changes. (23)

In another study that linked the prokinetic, laxative and antidiarrheal effects of Morus nigra to muscarinic and Ca2+ blocking agents and described its mechanism, it was shown that the presence of anticholinergic compounds and Ca2+ antagonists can make black mulberry a suitable source. To create and dilate the bronchi, in asthma, it has also been found that black mulberry leaf extract can limit tachycardia caused by obstruction and create muscle relaxation in cardiovascular patients. (24)

Vasodilator effects of black mulberry leaf extract and its possible mechanisms on pig basilar artery revealed that these mechanisms may be mediated through functional antagonism of thromboxane angiotensin II receptors or through suppression of angiotensin Ca2+-induced contraction, inhibition of influx I and stimulation of H2 receptors. Mulberry leaf extract also contains significant amounts of nitrites, nitrates, and several phenolic compounds that are probably associated with relaxation and relaxation of muscle fibers.

.By administration of black mulberry leaf extract, pig basilar artery was greatly relaxed, while it was already constricted by 46619-u. Black mulberry leaf extract suppressed angiotensin I-induced contraction in healthy pig artery basilar endothelium rings. (21)

Conclusion

Consumption of aqueous extract of mulberry leaves probably by increasing the serum level of NO and also by suppressing the contraction caused by angiotensin Ca2+, inhibiting the influx of I and stimulating H2 receptors caused a decrease in the hemodynamic factors of the heart and relaxation of the heart muscle. Endurance training has the opposite effect and increases strength. The contraction of the heart muscle partially compensated the relaxation of the heart muscle.

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