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The comparison between effects of *Berberis vulgaris* Extract and aerobic exercise on none-alcoholic fatty liver in male rat

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ABSTRACT

The aim of this study was to evaluate the effects of Berberis vulgaris extract, aerobic exercise or their combination on the indicators of fatty liver, including serum C-reactive protein (CRP) and serum alanine aminotransferase (SGPT) in Wistar rats. Forty male Wistar rats were divided into 5 equal groups, including B. vulgaris extract, aerobic exercise, B. vulgaris extract combined with aerobic exercise, control and hyperlipidemic group. After blood sampling, CRP and SGPT levels were measured and the data were analyzed by ANOVA and least significance difference tests. SGPT enzyme activity in all experimental groups was reduced significantly compared with hyperlipidemic group (P<0.05). Also, the results of the CRP level in the group receiving the extract of B. vulgaris combined with aerobic exercise showed the lowest average and the largest difference with the hyperlipidemic group (P<0.05). Aerobic exercise combined with B. vulgaris extract could improve fatty liver and is beneficial in these patients.

Keywords: Fatty liver, Aerobic exercise, *Berberis vulgaris*, C-reactive protein

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INTRODUCTION

Recent studies have indicated that the prevalence of nonalcoholic fatty liver disease in communities is higher than previous estimates. The prevalence of nonalcoholic fatty liver disease in Iran in different studies has been obtained approximately 30% [1]. Increased levels of serum aminotransferases is a general symptom of advanced fatty liver or steatohepatitis. Studies have indicated that liver enzymes are an easy, available (probably the best) index for liver condition [2]. Increase in serum aspartate aminotransferase (SGOT), serum alanine aminotransferase (SGPT), or both is usual and/or their level rarely exceeds to less than 10 times the normal upper level. SGPT is more associated with the inflammation caused by fat accumulation in the liver than other liver enzymes, and its increased plasma level is associated with abdominal obesity, metabolic syndrome, dyslipidemia, hyperglycemia, hypertension, and type 2 diabete [3, 4, and 5]. C-reactive protein (CRP) is also examined to investigate infection progression or the pressure on liver [6].

Physical activity is thought to inversely correlate with CRP [6, 7]. Oxidative stress has been demonstrated to be involved in physiology of fatty liver [8]. Exercise increases second messengers in skeletal muscles [9] followed by improved intake of glucose and decreased insulin resistance. Therefore exercise is thought to contribute positively to treating, controlling, and preventing acquisition of nonalcoholic fatty liver. Studies of human and rodents indicate that exercise positively affects fatty liver and the ways of liver function in a relatively weight loss-independent manner. Exercise causes increase in the function of liver glucagone which is stimulant of glucose production pathways. Increased function of glucagone due to exercise causes some changes in expression of liver gene which agrees with increased lipid peroxidation [1, 9, 10].

Meanwhile aerobic exercise is a class of exercise through which the efficiency of energy production systems and cardiorespiratory resistance is enhanced, however, the level of free radicals increase, too (4). Free radicals, including reactive oxygen species (ROS), are referred to the molecules that are active and are easily transformed into active types [11].

Moreover the role of natural compounds, in addition to exercise, in treating diseases is being largely addressed. Chemical and herbal medicines, in addition to weight loss, are used to treat fatty liver [8, 11]. Medicinal plants are thought to exert better effects than chemical drugs because of fewer side effects [8, 11, 12]. One of these plants which cause weight loss, in addition to having antioxidant properties, is *Berberis vulgaris* L. because some studies have demonstrated that *B. vulgaris* could lower cholesterolemia through a mechanism different from that of stanin drugs [1, 3, 13].

As the exercise is associated with increased free radicals and *B. vulgaris* has antioxidant properties, exercise alongside the use of *B. vulgaris* extract could have a better effect on nonalcoholic fatty liver disease than exercise alone. Therefore, the present study was conducted to compare the effect of aerobic exercise alongside with *B. vulgaris* extract use with exercise alone on levels of SGPT, SGOT, and CRP in wistar rat with fatty liver.

MATERIALS AND METHODS

In this experimental study 40 male wistar rats, six weeks old, acquiring fatty liver by high-fat diet were kept in Animal Laboratory of Shahrekord University of Medical Sciences at 22-27°C for six weeks. Food and water were freely available throughout the study. The assignment of the rats to the groups was done in a manner so that the five groups were homogeneous for age and weight. Wistar rats were randomly assigned to five equal groups (three experimental groups and two control groups) of eight each. Group 1 underwent aerobic exercise three 45-min sessions a week for six months. Group 2 was daily gavaged by *B. vulgaris* extract at 400 mg/kg. Group 3 underwent aerobic exercise alongside taking *B. vulgaris* extract. Group 4 (hyperlipidemic group) received only high-fat meals and group 5 (control group) was left untreated with no exercise, drug, or high-fat meals.

- **Diet formulation**

To make the rat's livers fatty, Persintra-M lotion (to prepare 100 g of Persintra-M lotion, 1 g cholesterol, palm oil of 80% purity, and intralipid liquid per 100 g egg yolk were used). To induce hypercholesterolemia 25 mg cholesterol was concentrated to 2 mL and daily gavaged to the rats (5). In addition, the rat's meal was brought to 1% cholesterol and 20% sugar by palm oil, sugar, and cow fat.

- **Exercise plan**

All the exercise period was divided into three phases. In the first (adaptation) phase, the rats walked on treadmill at 5-10 m/min and 0° steep for 10 min for one week. After the rats adaptation to treadmill, in overload phase the speed and duration of exercise at different sessions were increased gradually within three weeks to reach to the specified rate, 20 m/min for 40 min. Finally in fixation phase, the exercise continued at 20 m/min for 40 min for two weeks. Of 40 min exercise in the final phase, 5 min (at 10 m/min) was specified to warm-up and at the end of any sessions for cool-down the treadmill speed was declined within 5 min.

It is noteworthy that the exercise intensity for diabetic rats in the previous studies was determined as equal to lactate threshold. To stimulate the rats to run, audio stimulant (knocking on the treadmill wall) was used. For this purpose, electrical stimulant at low voltage alongside audio stimulant was initially used and after the rats were conditioned to concurrent two stimulants, only audio stimulant was used in later sessions for observance of ethics of animal studies. For adaptation the rats of the control group walked on treadmill at 10 m/min and 0 degree steep 5 min a week.

- **Extraction and the extract use**

In this study, *B. vulgaris* samples were obtained from reliable sources and used after the samples were confirmed by Medical Plants Research Center. The plant was purchased as dried and pulverized by a mechanical mill (Moulinex, Japan). To prepare hydroalcoholic extract, the powder of *B. vulgaris* root was dissolved in 2 L water and alcohol 70% and the solution was left at laboratory temperature for 72 hours. Then the solution was filtered, concentrated by rotary, and incubated at 37°C for three days. To prepare the extract at 400 mg/kg, 80 mg of the extract, with reference to 200 g weight of the rats, was dissolved in 1 mL distilled water and was daily gavaged to the rats.

- **Data analysis**

The data were analyzed by descriptive and analytical statistics. Descriptive statistics were mean and standard deviation and illustrations were graphs. Analytical statistics was ANOVA used to compare means and least

significance difference (LSD) used to investigate inter-group differences. All data analysis was done by SPSS 20 and P<0.05 was considered as the level of significance.

RESULTS

There was a significant difference in activity of SGPT in all experimental groups compared to the hyperlipidemic group (P<0.05) (Fig 1).

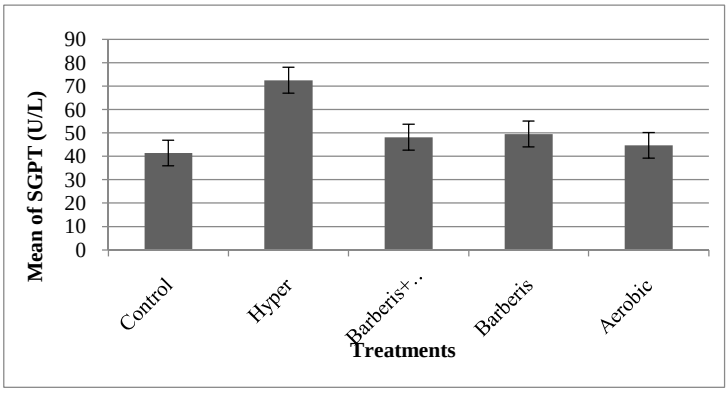

Figure1. The comparison of serum levels of SGPT activity in experimental groups and hyperlipidemic group

Also there was a significant difference in CRP serum level of all three experimental groups, *B. vulgaris* extract, aerobic exercise, and aerobic exercise alongside *B. vulgaris* extract, and hyperlipidemic group (P<0.05) (Fig 2).

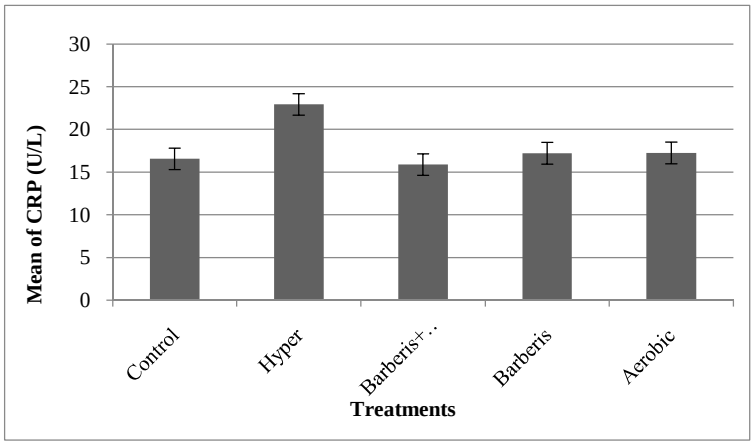

Figure2. The comparison of C-reactive protein between the experimental groups and hyperlipidemic group

DISCUSION

By the findings of the present study, investigation of activity of SGPT in comparison with hyperlipidemic group by ANOVA and LSD demonstrated that all experimental groups exhibited a significant decrease as compared with the group fed with a high-fat diet. So that the highest difference in SGPT activity was obtained in *B. vulgaris* group followed by aerobic exercise group, and *B. vulgaris* combined with aerobic exercise group (Fig1). Therefore it is inferred that use of *B. vulgaris* extract could be effective on treatment of nonalcoholic fatty liver, while aerobic exercise alone could be effective, as well (40-41). Although simultaneous use of these two treatments for this disease has led to a significant difference, the effect was less considerable than that observed in the other two experimental groups.

Therefore the present study findings are consistent with Iloon Kashkouli et al study on the effect of *B. vulgaris* on nonalcoholic fatty liver [1] and Marques et al study of treadmill exercise effect on nonalcoholic fatty liver in rats fed with high-fat diet, indicating a significant difference in SGPT and SGOT activity, hepatic steatosis and visceral fat [9]. In a study conducted by Ahmad Mir et al, to investigate the effect of aerobic exercises on liver enzymes in men

with nonalcoholic fatty liver, a remarkable decrease in liver enzymes (SGOT and SGPT) and liver tissue fat were seen [10].

B. vulgaris has a great antioxidant activity as many other medicinal plants due to containing anthocyanins and other flavonoids [11-15], therefore use of its extract could lead to decreased inflammatory factors such as CRP. Zeilaee and et al in their study demonstrated that use of *B. vulgaris* extract caused decrease in CRP, but the decrease was not significant [13]. In this study the lowest mean CRP variation was belong to *B. vulgaris* extract combine with aerobic exercise group and therefore indicate the greatest difference from hypolipidemia group and then *B. vulgaris* group and aerobic exercise group showed a small difference in decrease in CRP compared to hyperlipidemic group respectively (Fig 2). No study has yet investigated the simultaneous effect of *B. vulgaris* extract and aerobic exercise. However Golzarand et al showed that *B. vulgaris* extract effects on inflammatory factors such as interleukin 6 and CRP in type 2 diabetes has no change in CRP [3], which is not consistent with the present study.
Since this study investigated on the nonalcoholic fatty liver rats on one hand and could cause predisposition to type 2 diabetes in adulthood on the other hand [3, 4,15], so for prevention of dangerous complications of fatty liver and diabetes, use of *B. vulgaris* extract, as an important medicinal plant, will be effective alongside practicing aerobic exercises also it can be recommended as a preventive and therapeutic strategy to decrease the consequences of the disease, such as increased inflammatory factors and psychological complications due to the disease as well as to save the healthcare costs.

CONCLUSION

Finally, since the present study was conducted throughout six weeks of aerobic exercise, longer studies (for example 8-12 weeks) could yield different findings. On the other hand, because the present study investigated nonhuman subjects, studies of aerobic exercises alongside use of *B. vulgaris* extract with human subjects, both male and female, are recommended. Moreover, in addition to SGPT and CRP, other effective factors such as insulin resistance, lipid profile and liver tissue should be studied.

REFERENCES

[1]Iloon Kashkooli R, Najafi SS, Sharif F, Hamedi A, Hoseini Asl MK, Najafi Kalyani M, et al. *Hepat Mon*, **2015**, 15(2):e25067.
[2]Hovanlo-F. *Journal of the Medical School*, **2012**, (1):14-19.
[3]Golzarand M, Ebrahimi-Mamaghani M, Arefhosseini SR, Ali Asgarzadeh A. *Journal of Diabetes and Metabolic Disorders*, **2008**, 7, 3-7
[4]Beladi-Mousavi SS, Bashardoust B, Nasri H, Ahmadi A, Tolou-Ghamari Z. *J Parathyr Dis*, **2014**, 2(1): 51-52.
[5]Lala MA, Nazar CMJ, Lala HA, Singh JK. *J Renal Endocrinol*, **2015**, 1:e05.
[6]Eric P, Plaisance, Peter W, Grand Jean, Department of Health and Human Performance. **2006**; Auburn University, Audurn, Alabama, USA.
[7]Borodulin K, Laatikainen T, Jousilahti P. *Atherosclerosis*, **2006**, 185(2): 381-7.
[8]Khodadadi S. *Immunopathol Persa*, **2015**; 1:e01.
[9]Marques C, Motta V, Torres T, Aguila M, *Brazilian Journal of Medical and Biological Research*, **2010**, 43(5):467-75.
[10]Ahmad Mir, Mohsen Aminai, Hamid Marefati. *International Research Journal of Applied and Basic Sciences*, **2012**, 3, (9).
[11]Nasri H, Rafieian-Kopaei M. *J Nephropharmacol*, **2013**; 2(1): 1–2
[12]Mardani S, Nasri H, Hajian S, Ahmadi A, Rafieian-Kopaei M. , **2014**, 3(1):35-40
[13]Zilaee M, Kermany T, Tavalaee S, Salehi M, Ghayour-Mobarhan M and et al. *Phytotherapy Research*, **2014**, 28(8):1211-15
[14]Tamadon MR, Baradaran A, Rafieian-Kopaei M. *J Renal Inj Prev*, **2013**; 3(2):41-42
[15]Rahimi-Madiseh M, Heidarian E, Rafieian-kopaei M. *J HerbMed Pharmacol*, **2014**, 3(1): 15-19