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Comparing the effects of aqueous extract of *cumin* and Lovastatin on serum lipids in hyperlipidemic rat

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ABSTRACT

Several different drugs are used for reduction of blood lipids in hyperlipidemic patients which are associated with side effects. This study investigated the effect of aqueous cumin extract on serum lipids of hyperlipidemic rat. This study is performed on 40 male adult Wister rats (200-250 g). The animals were randomly assigned to five groups: receivers of standard food, high cholesterol food with cumin extract simultaneously, high cholesterol treated with normal saline, high cholesterol treated with lovastatin, and high cholesterol treated with cumin extract. At the end, serum samples were collected and lipids were measured by routine methods. Data analyses were performed with SPSS and through application of ANOVA and Tukey tests. P<0.05 was considered as significant. Data analyses showed that the consumption of aqueous cumin extract was able to significantly reduce the levels of Tri-glyceride, cholesterol and low-density lipoprotein compared to hyperlipidemic group. In addition, the simultaneous uptake of cumin extract and high cholesterol food prevented occurrence of hyperlipidemia among subjects. Furthermore, the level of high-density lipoprotein was significantly increased after consumption of cumin extract in comparison with the hyperlipidemic group. The prescription of cumin extract led to a significant reduction in LDL/HDL and Cholesterol/HDL ratios. In this study, the consumption of cumin extract has shown to have preventive and therapeutic effects in of dyslipidemia among hyperlipidemic animals and these effects are comparable with effects of lovastatin. Therefore, further studies are required to determine the mechanism for the effect of cumin.

Keywords: *Cumin, lovastatin, Hyperlipidemia, rat*

INTRODUCTION

Plasma lipids, at any time, may be considered to represent the balance between the production, consumption and storage of fats. Elevated plasma lipids in blood can lead to disorders, which may result in several different diseases such as atherosclerosis. A high level of serum cholesterol is an important risk factor associated with ischemic heart diseases and heart attacks [1]. Abnormality in metabolism of lipids plays a major role in occurrence of atherosclerosis and chronic Heart Disease (CHD). There is a direct relation between high levels of cholesterol and myocardial infractions [2]. In addition, the deposit of cholesterol in some cases occurs with damages to endothelial cells, which are the obvious part of atherosclerosis traumas [3].

Nowadays, different chemical drugs such as lovastatin, Clofibrate and cholestyramine are used for the treatment of dyslipidemia; however, the consumption of these drugs is under debate. These drugs are associated with several different side effects such as the occurrence of Myopathy, rhabdomyolysis, hepatic disorders, myasthenia Gravis, nausea, dizziness and digestive problems. On this basis, in terms of clinical practices, consumption of these drugs is limited [2]. On the other hand, as a result of improper consumption and overuse of chemical drugs, mankind has

been seeking natural substitutes since they are more available, affordable and more important with little side effects. One of the side effects of lipid reduction drugs such as lovastatin is their effect on gastrointestinal secretion [4]. In a review study, the effectiveness and safety of natural drugs were tested. In this study, the treatment of blood fat with capsules containing 53 different plants led to reduction of total cholesterol (TC) and Low density lipoprotein (LDL) [5].

Cumin (*Cuminum Cyminum*) is an annual plant belonging to the family of Apiaceae and has been reported to emerge from Mediterranean areas; however, it is currently cultivated in different areas such as India, Turkey, Egypt and Iran [6]. This odorous plant has several cookery and medicinal applications worldwide. Also, in terms of traditional medicine, it is used as an anti-obesity, anti-convulsion and anti-epileptic drug. In addition, in some studies, it has been recently announced as an anti-diabetic drug [7]. Furthermore, *cumin* has an anti-oxidant effect and probably it can reduce the oxidation of lipids [8]. Previous researches have shown that flavonoids are one of cumin's effective compounds in the prevention or treatment of cancer. This prevention or treatment is probably carried out through reduction in the number of free radicals [6]. On this basis, it seems that the existing flavonoid compounds in *cumin* also lead to reduction of oxidized LDL. Due to the fact that literature of studies in the context of effects of *cumin* on levels of blood lipid among hyperlipidemia patients is insufficient, this study was carried out to investigate the effects of aqueous *cumin* extract on levels of serum lipids among hyperlipidemic male rats.

MATERIALS AND METHODS

This experimental study was performed on 40 mature male Wister-Albino rats having a weight range of 200-250 g. The animals were kept in separate cages and remained under controlled condition of 12:12 h dark/light cycle, 24 ± 2^0C, and they were provided with full access to water and food. The ethical protocol of working with lab animals was considered at all levels of tests and the procedure of completion of this research was approved by the ethics committee of Zahedan University of Medical Sciences, Iran. Pure Cholesterol (produced by Sigma corp.) and Lovastatin (achieved from Pasture institute, Iran) were used. The daily consumption of water and food was recorded. After a week of compatibility, the subjects were randomly assigned to 5 groups (8 subjects in each group) as follows:

The group which received standard diet (control group); a group which received high cholesterol diet (2%) with aqueous *cumin* extract (0.4 g/kg) for 41 days (HCD + Ext.41); a group which received high cholesterol diet (2%) for 20 days and then received normal saline for three weeks (HCD + ns); a group which received high cholesterol diet (2%) for twenty days and then received Lovastatin (0.2 g/kg) for three weeks (HCD + Lovastatin) and a group which received high cholesterol diet (2%) for twenty days and then received aqueous *cumin* extract (0.4 g/kg) for three weeks (HCD + Ext.21).

1.1. Preparation of aqueous *cumin* extract

After the confirmation of visual health and scientific validation by botanical experts, the seeds of *cumin* were sieved in order to separate the seeds from any undesirable and additional particles. Afterwards, seeds were powdered in an electrical mill and were extracted using the German Soxhlet device. Then, 20 g of *cumin* powder was mixed with 300 ml of distilled water and the mixture was then put in the device for 24 hours. After leaching, the mixture was poured in a plate and afterwards, the plate containing the mixture was put in an oven at temperature of 37 ^{o}C. The yielded extract was kept under suitable conditions until used [9].

1.2. Preparation of high fat diet

For preparation of high-fat diet, 20 g of pure cholesterol powder (produced by Sigma corp.) was mixed with 5 ml of warmed olive oil and the yielded mixture was subsequently mixed with one kilogram of normal rat diet. Afterwards, the water of food was extracted and the food was turned into paste. More so, the yielded paste was then dried and turned into pellets. This food was prepared and dried in oven based on a daily schedule.

On the final day of test, body weights were measured and then, animals were made unconscious with ether. Blood samples were collected from carotid artery and placed in 10 ml tubes. After coagulation, blood samples were centrifuged at 3500 rpm for ten minutes. Serums were taken and kept at temperature of -70^OC, and then the entire studied parameters were measured using routine laboratory kits (produced by Pars Azmoon corp.).

1.3. Data analysis

Data were analyzed with SPSS v17.0 using one way analysis of variance (one-way ANOVA) and subsequent Tukey test. The obtained results were expressed as Mean ± SEM and P<0.05 was significantly considered.

RESULTS

The average of Triglyceride (figure 1) showed a significant difference between studied groups in that the consumption of high cholesterol diet was able to significantly increase the level of Triglyceride when compared with the control group. Also, the prescription of lovastatin and aqueous *cumin* extract was able to significantly decrease the amount of triglyceride in hyperlipidemic rats (P<0.01).

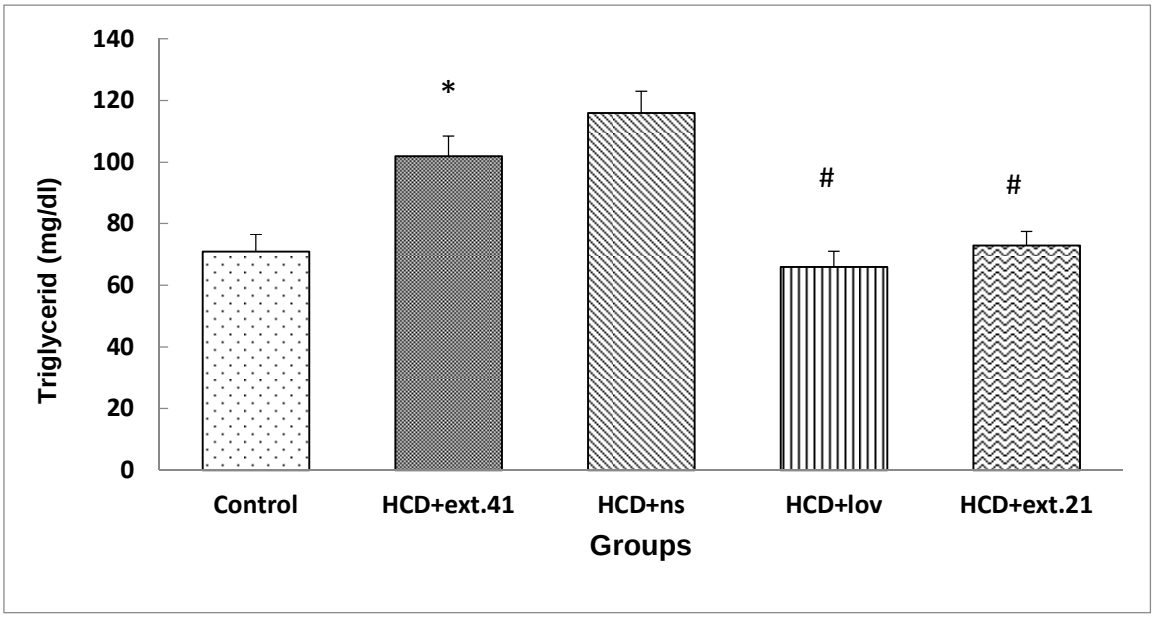

Fig. 1) Compare of Triglyceride value (mg/dl) in different groups, * P<0.05 in compare to control group, # P<0.01 in compare to high cholesterol diet group, n=8. HCD: High Cholesterol Diet, ext.41: extract use for 41 days, ns: normal saline, lov: lovastatin, ext.21: extract use for 21 days

The average of cholesterol level (Figure 2) showed a significant difference between studied groups in that the consumption of high cholesterol diet with *cumin* extract (HCD+ext.41 group) was unable to impose any significant increase in cholesterol when compared with the control group. However, the prescription of aqueous *cumin* extract, similar to lovastatin; was able to impose a significant reduction on cholesterol among hypercholesterolemic rats (P<0.01).

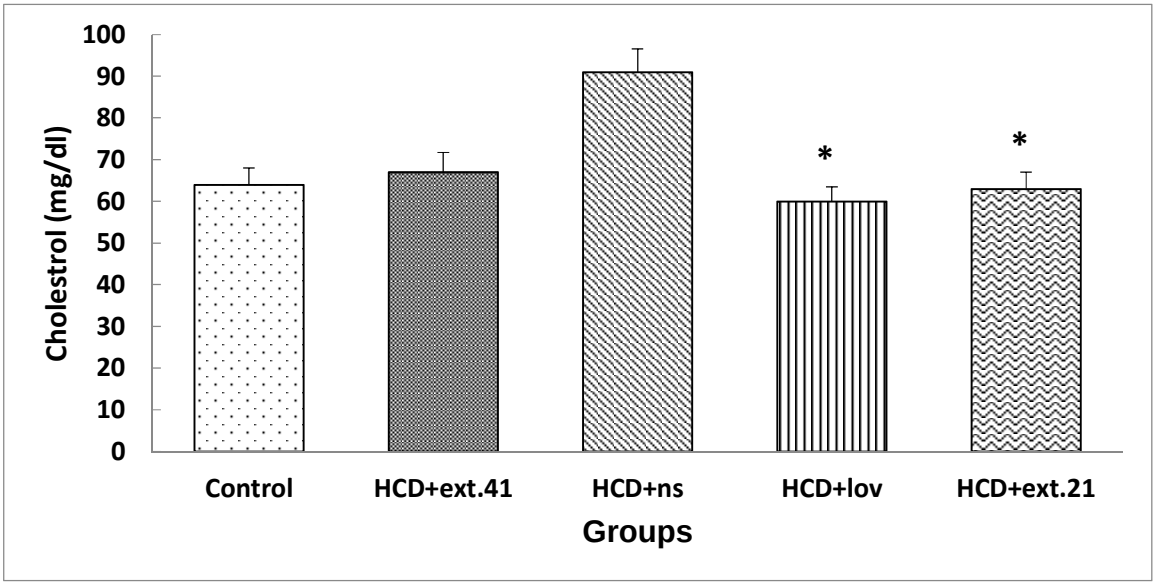

Fig. 2) Compare of total cholesterol value (mg/dl) in different groups, * P<0.01 in compare to high cholesterol diet group, n=8. HCD: High Cholesterol Diet, ext.41: extract use for 41 days, ns: normal saline, lov: lovastatin, ext.21: extract use for 21 days

The average of LDL (Figure 3) indicated a significant difference between the studied groups. The consumption of high cholesterol diet with *cumin* extract (HCD+ext.41 group) was unable to impose a significant increase on LDL when compared with the control group. However, the prescription of aqueous *cumin* extract; similar to lovastatin was able to impose a significant decrease on LDL in hypercholesterolemic animals (P<0.001).

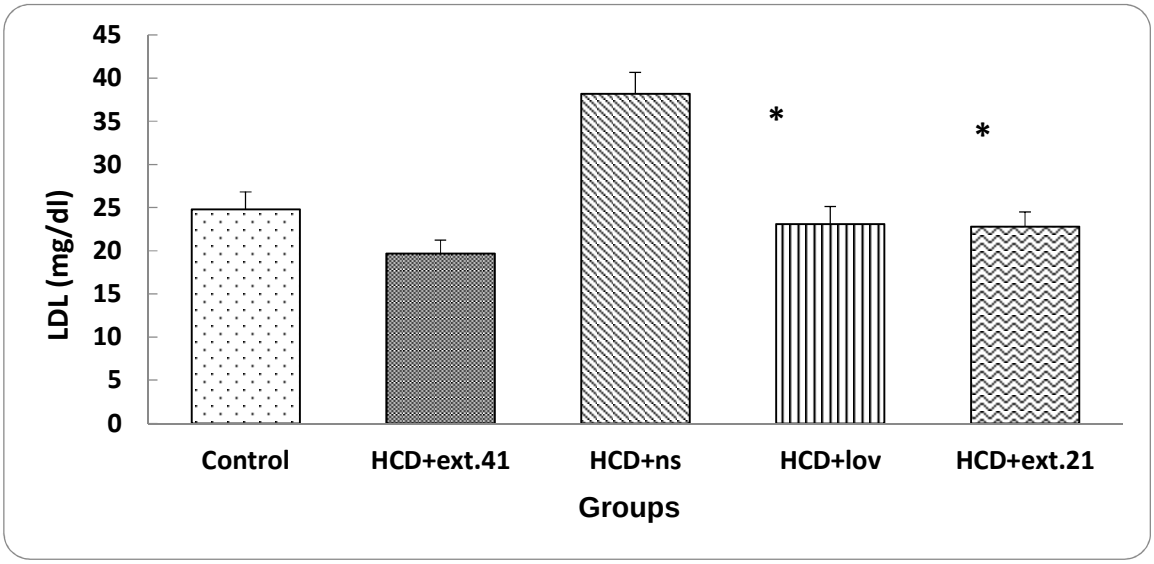

Fig. 3) Compare of LDL value (mg/dl) in different groups, * P<0.01 in compare to high cholesterol diet group, n=8. HCD: High Cholesterol Diet, ext.41: extract use for 41 days, ns: normal saline, lov: lovastatin, ext.21: extract use for 21 days

The average of HDL (Figure 4) indicated a significant difference between the studied groups. The consumption of high cholesterol diet with *cumin* extract (HCD+ext.41 group) was unable to impose significant changes in the level of HDL when compared with the control group. However, the prescription of aqueous *cumin* extract; similar to lovastatin was able to impose a significant increase on HDL in hypercholesterolemic rats (P<0.001).

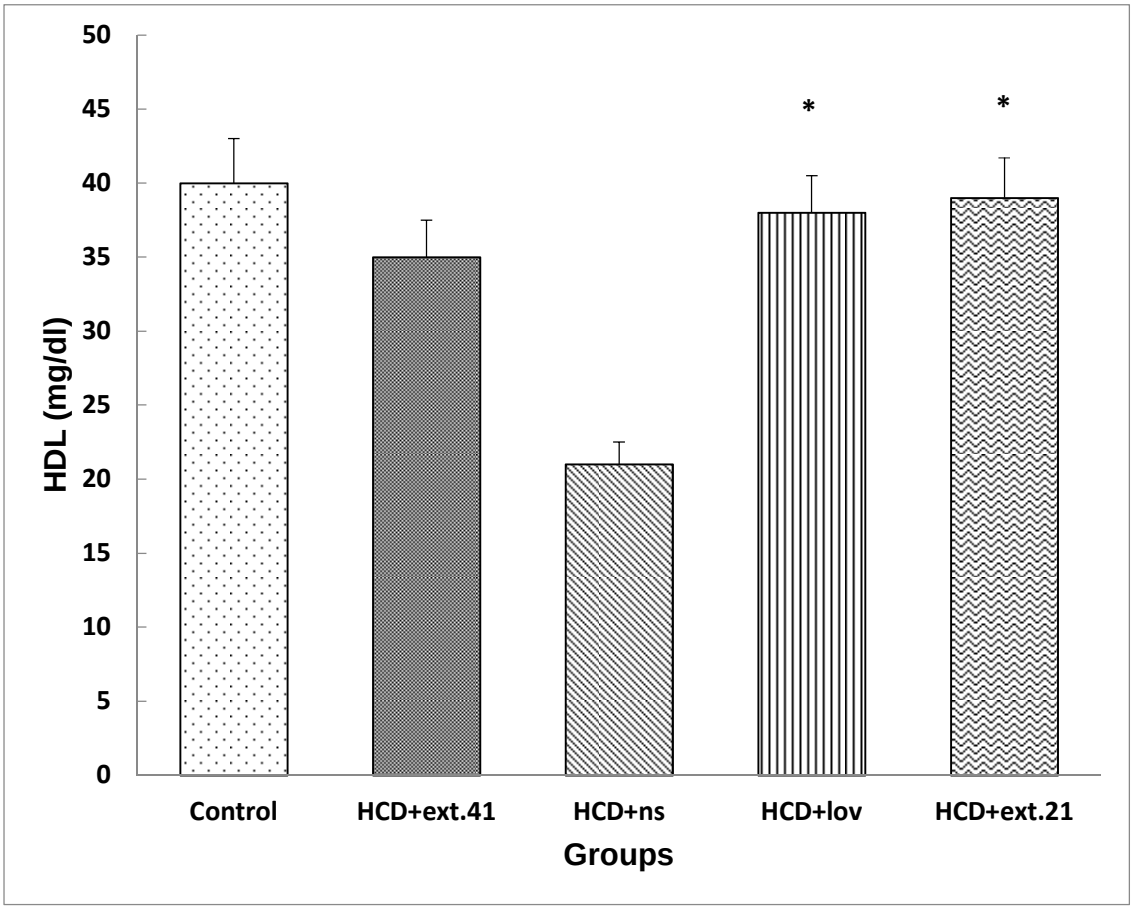

Fig. 4) Compare of HDL value (mg/dl) in different groups, * P<0.001 in compare to high cholesterol diet group, n=8. HCD: High Cholesterol Diet, ext.41: extract use for 41 days, ns: normal saline, lov: lovastatin, ext.21: extract use for 21 days

Figure 5 shows a comparison between LDL/HDL ratio. In the group that received high cholesterol diet, this ratio showed a significant increase when compared with the control group (P<0.001). In addition, in group that received *cumin* extract; similar to lovastatin group, a significant decrease was observed when compared with the hypercholesterolemic animals (P<0.001).

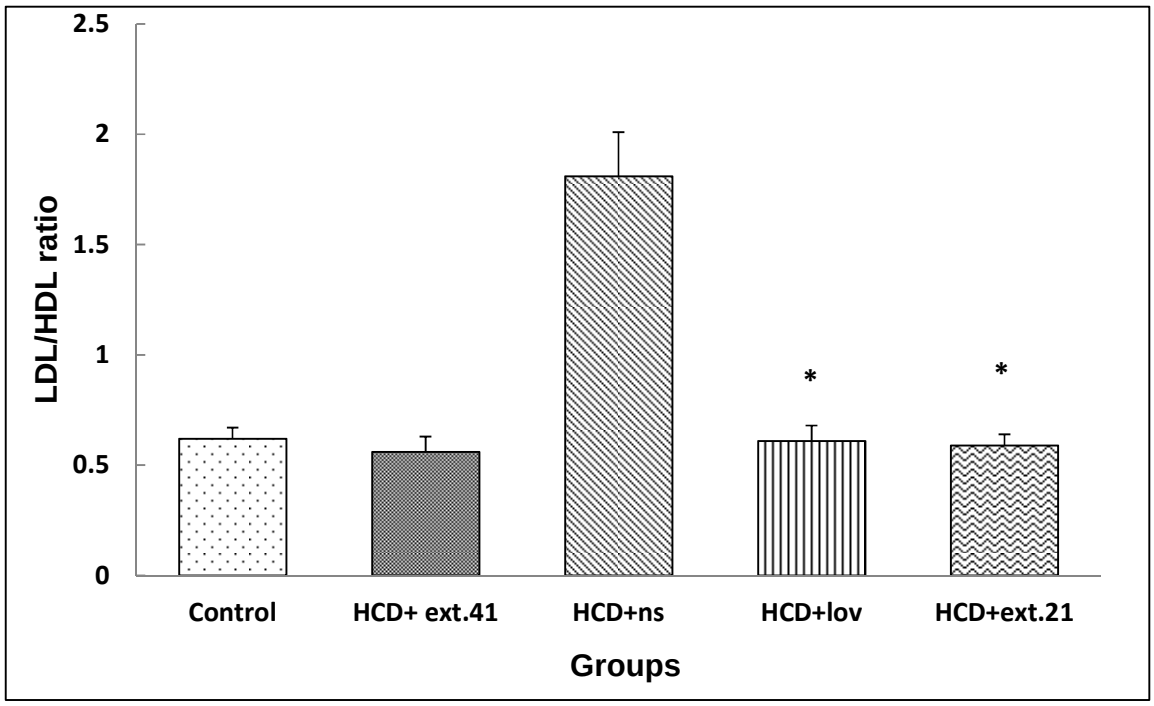

Fig. 5) Compare of LDL/HDL ratio in different groups, * P<0.001 in compare to high cholesterol diet group, n=8. HCD: High Cholesterol Diet, ext.41: extract use for 41 days, ns: normal saline, lov: lovastatin, ext.21: extract use for 21 days

Furthermore, the comparison between Cholesterol/HDL ratio showed in Figure 6. In the group that received high cholesterol diet, this ratio showed a significant increase when compared with the control group (P<0.001). Moreover, in the group that received *cumin* extract; similar lovastatin, a significant decrease in this ratio was observed when compared with the Hypercholesterolemic subjects (P<0.001).

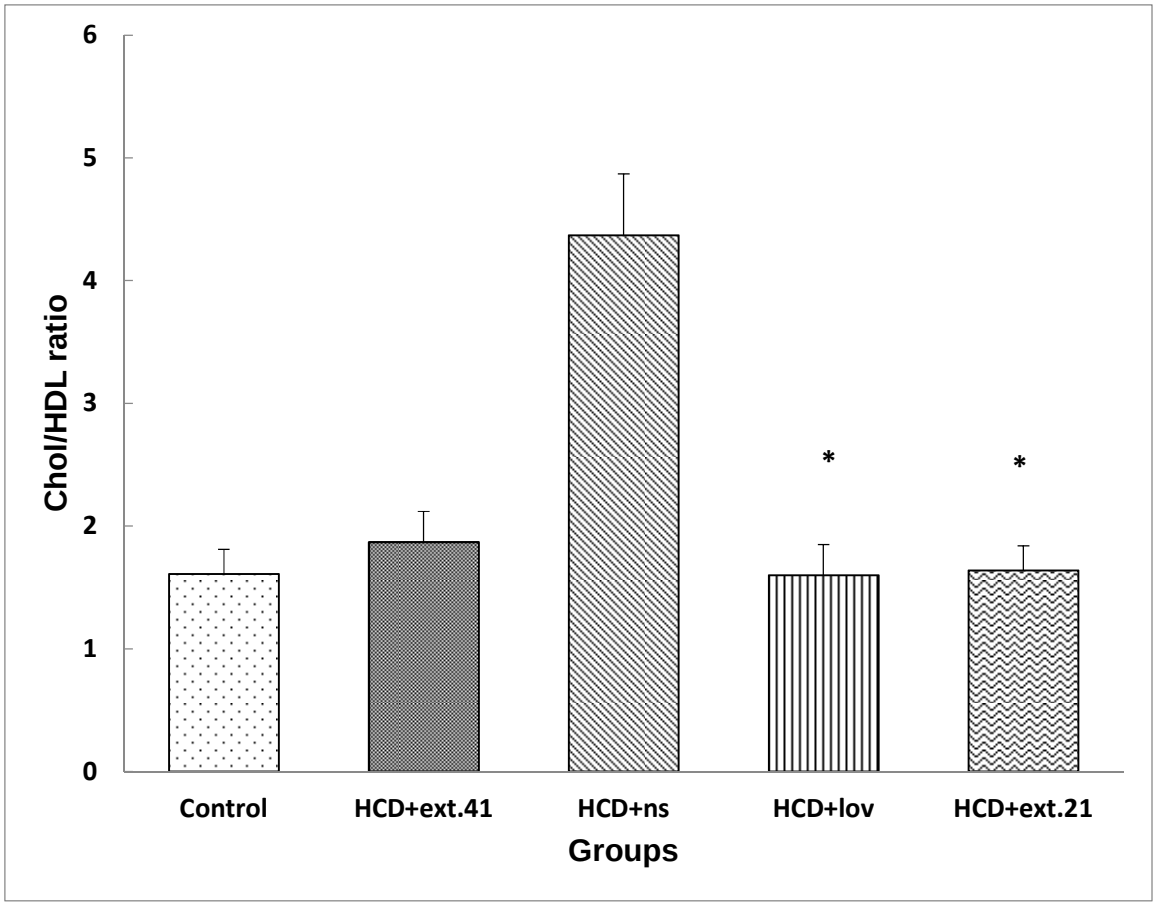

Fig. 6) Compare of Chol/HDL ratio in different groups, * P<0.001 in compare to high cholesterol diet group, n=8. HCD: High Cholesterol Diet, ext.41: extract use for 41 days, ns: normal saline, lov: lovastatin, ext.21: extract use for 21 days.

DISCUSSION

This study was carried out to compare the effects of aqueous *cumin* extract and lovastatin on blood lipids among hypercholesterolemic rats. It was shown that high fat diets increased the levels of LDL, TC and Triglyceride and decreased the level of HDL. The simultaneous consumption of aqueous *cumin* extract and lovastatin with high cholesterol diet prevents changes in lipid profiles, which indicate their preventive effects. In addition, the consumption of aqueous *cumin* extract and lovastatin after occurrence of hyperlipidemia results in a significant decrease in the level of TC, Triglyceride and LDL, however, the amount of HDL was significantly increased. This indicates the beneficial therapeutic effects of this extract.

Zare et al. carried out a study on 88 over-weight women and indicated that the use of *cumin* decreased the levels of cholesterol, triglyceride and LDL and also increased the level of HDL. This result is in line with the results obtained in the present study [10]. In another study by Samani et al., it was reported that the consumption of *cumin* supplement for 45 days by hypercholesterolemic patients reduced the level of oxidized LDL and fasting blood sugar. However, it increases the level of activity of Paraoxonase enzymes, although, it has no effects on Total cholesterol level and Triglyceride [11]. This result is somehow inconsistent with the outcome of the present study. The effect of *cumin* extract on the decreased oxidized LDL is one of anti-oxidant effects of *cumin*, and in the present study, it seems that the existence of flavonoids in *cumin* leads to the reduction of oxidized LDL.

In a study by Shirke et al. it was shown that the removal of ovaries in rats led to increase in blood cholesterol and treatment with alcoholic *cumin* extract directed to reduction in the level of cholesterol [12]. This outcome is

consistent with the result obtained in this study. Also, they proposed that this effect might be related to existence of epigenin and estrogenic iso-flavonoids in *cumin*.

In this study, increase in the ratios LDL/HDL, as well as CHOL/HDL among hypercholesterolemic animals was observed. The rise in these ratios increases the chances for occurrence of cholesterol plaques, arteriosclerosis and coronary arteries diseases. The prescription of *cumin* extract reduces these indices and it shows the beneficial therapeutic effects of this extract.

In previous studies, it was shown that prescription of aqueous *cumin* extract in diabetic rats led to a decrease in glucose, cholesterol, triglyceride, fatty acids and phospholipids. These facts are in consistence with the results of this study [7, 13]. It has also been shown that *cumin* contains phenols and flavonoids [6]. As regard the antioxidant role of these compounds, it seems that at least a portion of beneficial effects of *cumin* in treatment of dyslipidemia is related to existence of these materials. Routine reducing blood lipid drugs including statins, directed to reduction of cholesterol through inhibition of 3-hydroxy-3-methyl-glutaryl co-enzyme A reductase [14]. Considering the similarity of the effect of *cumin* extract with lovastatin, it seems that, at least one of effective mechanisms in beneficial effects of *cumin* might be through inhibition of this enzyme in cholesterol's biosynthesized route. Also, it has been reported that aqueous extract of *cumin* has an antioxidant effect [7, 15] which can be effective in the reduction of LDL through prescription of *cumin* extract.

CONCLUSION

Prescription of aqueous *cumin* extract is effective in treatment of hypercholesterolemia and it also can inhibit the occurrence of hypercholesterolemia induced by high cholesterol diets. This effect is comparable with lovastatin. Therefore, further studies are required to determine the mechanism of these effects.

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Conflict of Interest: The authors declare that there are no conflicts of interest.

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