

## Original Article

# *Effects of Hydroalcoholic Lavender Extract on Lipid Profiles and Liver Enzymes in Rats Fed a High-Fat Diet*

Seyed Javad Davari\_Sani<sup>1</sup>, MD; Seyed Mehdi Beheshti-Nasr<sup>2</sup>, PhD; Akbar Pejhan<sup>3</sup>, PhD; Seyede Zeynab Seyedi<sup>1</sup>, MD; Ali Abedi<sup>4\*</sup>, MS

### ABSTRACT

**Background:** In light of the antioxidant properties of lavender and the role of antioxidant capacity in blood lipid metabolism and reducing the risk factors for cardiovascular disease, this study aimed to evaluate the effect of hydroalcoholic lavender extract on the lipid profiles of rats fed a high-fat diet (HFD).

**Methods:** In this experimental study, 50 male Wistar rats were randomly divided into 5 equal groups. The rats were fed an HFD daily for 30 days. The first group received a normal diet without the extract. Groups 2 to 5 were administered saline (1 mL/kg) and lavender extract (200, 400, and 600 mg/kg) by oral gavage, respectively, 60 minutes before the HFD daily. Weight change, lipid profiles, and liver enzymes were measured and compared with the relevant control groups. Data analysis was conducted using ANOVA and Tukey's test at a significance level of  $P < 0.05$ .

**Results:** HFD feeding led to a significant increase in body weight, plasma lipid profiles, and liver enzymes compared with the control group. Lavender administration significantly decreased TG and TC parameters in the 400 mg/kg ( $P < 0.05$ ) and 600 mg/kg ( $P < 0.001$ ) groups compared with the HFD group. The LDL/HDL ratio in the 400 and 600 mg/kg groups significantly decreased compared with the HFD group ( $P < 0.001$ ). ALP, ALT, and AST levels in the 600 mg/kg group were significantly reduced by 50.5% ( $P < 0.001$ ), 20.25% ( $P < 0.001$ ), and 12.34% ( $P < 0.01$ ) compared with the HFD group, respectively.

**Conclusions:** The results demonstrated that hydroalcoholic lavender extract reduced the lipid profiles and liver enzymes in rats fed an HFD. Consequently, these findings suggest that lavender may possess protective properties against cardiovascular disease. (*Iranian Heart Journal 2024; 25(4): 43-50*)

**KEYWORDS:** Lavender, Cardiovascular disease, High-fat diet, Hypercholesterolemia, Hyperlipidemia, Liver Enzymes, Rat

<sup>1</sup> Atherosclerosis Research Center, Baqiyatallah University of Medical Sciences, Tehran, IR Iran.

<sup>2</sup> Cellular and Molecular Research Center, Sabzevar University of Medical Sciences, Sabzevar, IR Iran.

<sup>3</sup> Cellular and Molecular Research Center, Department of Physiology and Pharmacology, Faculty of Medicine, Sabzevar University of Medical Sciences, Sabzevar, IR Iran.

<sup>4</sup> Department of Nursing, School of Nursing and Midwifery, North Khorasan University of Medical Sciences, Bojnourd, IR Iran.

\*Corresponding Author: Ali Abedi, MD; Department of Nursing, School of Nursing and Midwifery, North Khorasan University of Medical Sciences, Bojnourd, IR Iran.

Email: abedia1371@gmail.com

Tel: +985831550634

Received: February 3, 2024

Accepted: June 2, 2024

**H**yperlipidemia is a major risk factor for the development of cardiovascular disease.<sup>1, 2</sup> The search for new medications capable of decreasing and regulating serum triglyceride and cholesterol levels has gained significant momentum in recent years, leading to numerous reports on the substantial activities of natural agents.<sup>3</sup>

Plants serve as a critical source for novel therapeutic drug leads; thus, plant-derived products are generally regarded as less toxic and less prone to side effects than synthetic agents. These properties of plants have facilitated the discovery of new therapeutic agents, such as hypoglycemics, antioxidants, and hypolipidemics, demonstrating the potential of plant-based products to reduce the risk of cardiovascular disease.<sup>4-7</sup>

Lavender, a perennial shrub belonging to the *Lamiaceae* family, is well-known as a potent aromatic and medicinal herb. It is employed in complementary therapy across various regions for its anti-inflammatory, anti-stress,<sup>8</sup> anti-depression,<sup>9</sup> learning,<sup>10</sup> and memory-enhancing<sup>10</sup> effects.

The primary objective of this study was to assess the impact of hydroalcoholic lavender extract on lipid profiles and liver enzymes in rats fed a high-fat diet (HFD).

## METHODS

### Plant Material and Extract Preparation

Lavender is widely cultivated across various regions of Iran. For this study, the aerial parts of lavender were collected from the countryside of Isfahan in 2014 and subsequently identified by the Department of Biology, Faculty of Sciences, University of Isfahan. The collected plants were divided into various parts and dried at room temperature, away from sunlight. The dried plant samples were then pulverized and stored at 4 °C for future use.<sup>11</sup>

### Animals

In this experimental study, 50 male Wistar rats, weighing 150 to 180 g, were randomly assigned to 5 equal groups. The animals were housed in a temperature and light-controlled room (22 °C, 12-h cycle starting at 08:00 h). The rats had free access to water and either a normal or an HFD.

The Ethics Committee of Sabzevar University approved all animal experiments (reference number: IR.MEDSAB.REC.1398.057).

### HFD

The HFD was composed of the following: normal pulverized chow (47%), cholesterol (2%), sodium cholate (1%), dextrose (40%), olive oil (10%), and water (15%). The food mixture was cut into pieces and dried at room temperature for 3 days.<sup>12</sup>

### Body Weight and Diet Intake Measurement

The animals' daily diet intake and body weights were recorded before the administration of the plant extract and then once a week throughout the extract administration.

### Animal Grouping and Treatment

The rats were randomly assigned to 5 equal groups. The first group received a normal diet without the extract. Groups 2 to 5 received saline (1 mL/kg) 60 minutes before HFD, followed by lavender extract (200, 400, and 600 mg/kg) administered through oral gavage daily for 30 consecutive days. Blood samples were collected from rats at 0, 7, and 17 days via cardiac puncture and centrifuged at 3000 rpm, 4 °C for 15 minutes. The rats were fasted overnight and then euthanized under diethyl ether anesthesia.

### Biochemical Analysis and Atherogenic Coefficient Calculation

Glucose, lipid profiles (triglyceride [TG], total cholesterol [TC], high-density lipoprotein [HDL], and low-density

lipoprotein [LDL]), and liver enzymes (alkaline phosphatase [ALP], aspartate aminotransferase [AST], and alanine transaminase [ALT]) were measured using enzymatic kits (Pars Azmoon, Iran) and then compared with the relevant control groups.

The atherogenic coefficient was calculated as follows:  $(\text{Total cholesterol} - \text{HDL cholesterol}) / \text{HDL cholesterol}$   $(\text{TC} - \text{HDL-c}) / \text{HDL-c}$ .<sup>13</sup>

### Statistical Analysis

Data were expressed as mean  $\pm$  standard deviation (SD). Statistical analyses were conducted using SPSS software, version 22. ANOVA and Tukey's post-hoc test were employed for data comparison. A *P* value of less than 0.05 was considered statistically significant.

## RESULTS

No significant differences in lipid profiles and hepatic enzymes were observed between the control groups before and after the normal diet period (Table 1).

### Effects of lavender extract on animal weight

Animals fed the HFD exhibited increased weight gain from the second week compared to the control group ( $P < 0.001$ ). The administration of the lavender extract alongside the diet led to a moderation in weight gain. Notably, a significant decrease in weight was observed with the 600 mg/kg dose in the second week ( $P < 0.001$ ) and fourth week ( $P < 0.01$ ) compared with the HFD group, with weight changes similar to the control group ( $P > 0.05$ ).

### Effects of lavender extract on blood glucose levels

A significant increase in blood glucose levels was observed in the HFD control

group ( $P < 0.001$ ). Compared with the HFD group, the lavender extract administration at doses of 400 mg/kg ( $P < 0.05$ ) and 600 mg/kg ( $P < 0.001$ ) resulted in a significant decrease in blood glucose levels (Fig. 1A).

### Effects of lavender extract on lipid profiles

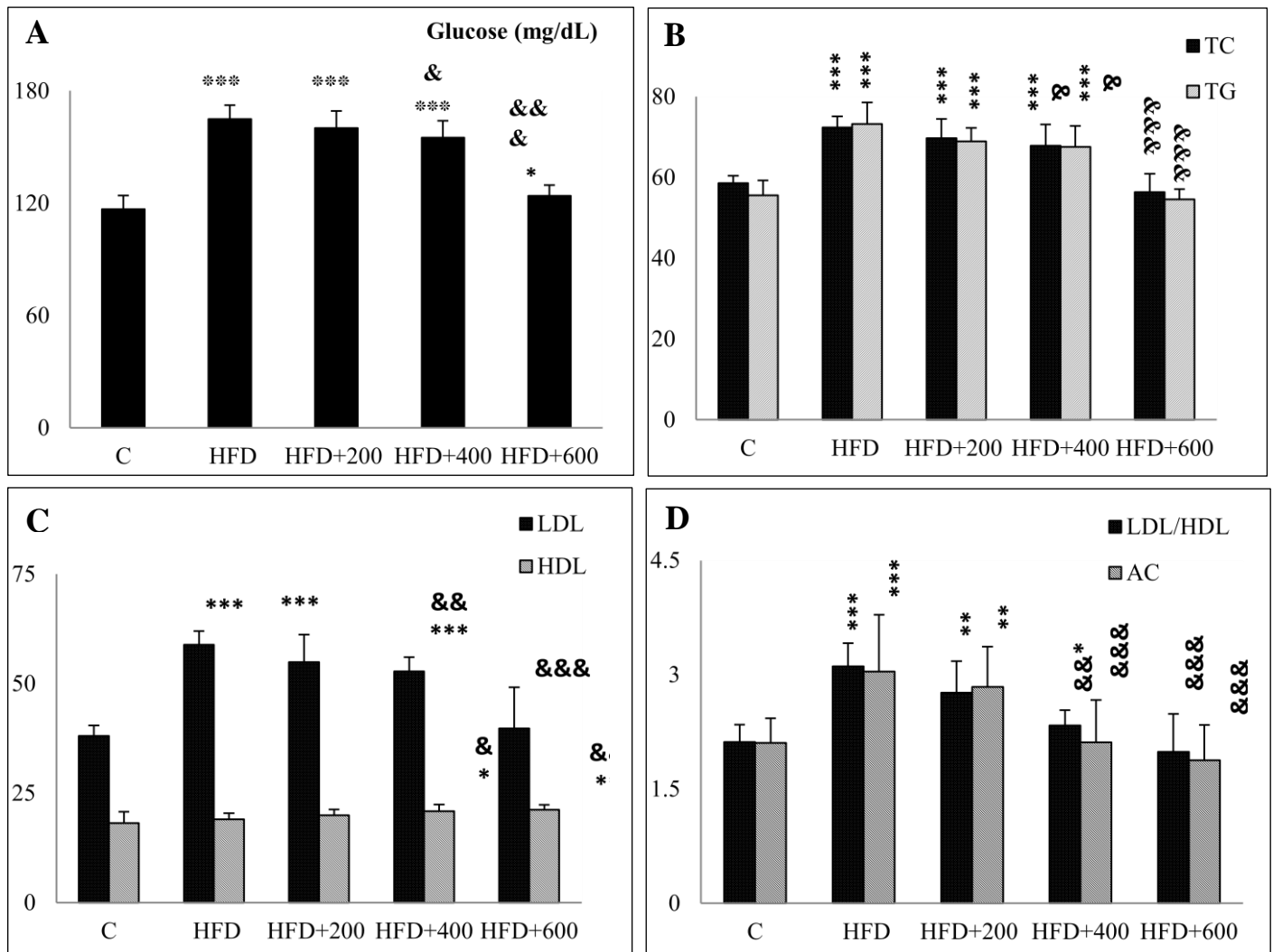
A 1-month HFD led to a significant increase in these parameters in the HFD groups compared with the control group ( $P < 0.001$ ). These changes were not observed in the group administered 600 mg/kg of the extract. The administration of 400 mg/kg ( $P < 0.05$ ) and 600 mg/kg ( $P < 0.001$ ) doses resulted in a significant decrease in these parameters compared with the HFD group without the extract (Fig. 1B). Pearson's correlation coefficient between TC and TG was 0.878, indicating a significant ( $P < 0.01$ ), strong, and positive correlation between these 2 parameters, suggesting that an increase in one of the parameters leads to a rise in the other.

In the HFD group, excluding the 600 mg/kg dose, a significant increase in this parameter was observed compared with the control group ( $P < 0.001$ ). The administration of 400 mg/kg ( $P < 0.01$ ) and 600 mg/kg ( $P < 0.001$ ) doses of the extract led to a significant decrease in these parameters compared with the HFD group without the extract (Fig. 1C).

In comparison with the control group, LDL/HDL was significantly increased in the group receiving the diet without the extract ( $P < 0.001$ ) and the diet with 200 mg/kg and 400 mg/kg doses of the extract ( $P < 0.01$ ). The 600 mg/kg dose of the extract significantly decreased this ratio compared with the group receiving the diet without the extract ( $P < 0.001$ ), bringing it close to the control group ( $P < 0.001$ ). Notably, these changes were not significant when compared with the control group (Fig. 1D).

**Table 1:** Parameters of Lipid Profiles and Hepatic Enzymes in the Control Group Before and After 4 Weeks of Experiments With a Normal Diet

Parameters	Pre-period	Post-period	P value
Glucose, mg/dL	5.63± 117.78	7.25± 116.72	0.31
Total cholesterol, mg/dL	2.9± 56.6	1.73± 58.6	0.07
Triglycerides, mg/dL	3.75± 54.55	3.7± 55.56	0.71
Low-density lipoprotein, mg/dL	3.82± 36.04	2.39±38.03	0.24
High-density lipoprotein, mg/dL	3.11± 19.02	2.58± 18.18	0.84
Alkaline phosphatase, IU/l	12.27± 281.34	11.22± 284.11	0.65
Alanine transaminase, IU/l	6.09± 69.01	3.54± 69.93	0.72
Aspartate aminotransferase, IU/l	3.40± 125.97	5.31± 127.95	0.65



**Figure 1:** The images demonstrate the impact of hydroalcoholic lavender extract on glucose, total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), LDL/HDL ratio, and atherogenic coefficient (AC). The graphs show that a high-fat diet (HFD) led to increased lipid profiles and AC in comparison to the control group. The administration of hydroalcoholic lavender extract effectively mitigated these effects.

Values are expressed as mean ± SD in each group.

\*, \*\*, and \*\*\* respectively show  $P < 0/05$ ,  $P < 0.01$ , and  $P < 0.001$  in comparison with the control group.

&, &&, and &&& respectively represent  $P < 0.05$ ,  $P < 0.01$ , and  $P < 0.001$  compared with the HFD group (n=8).

### Effects of lavender extract on hepatic enzymes

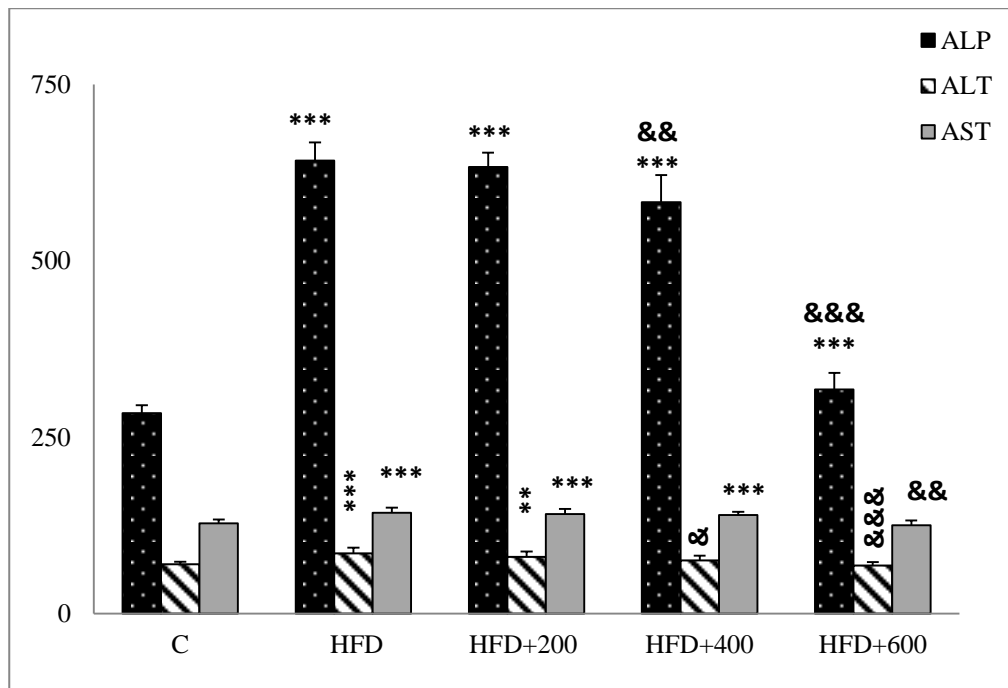
ALP levels increased by 125.95% in the HFD group without the extract compared with the control group. The administration of the extract at doses of 400 mg/kg and 600 mg/kg led to a significant decrease in this enzyme by 9.17% ( $P < 0.01$ ) and 50.50% ( $P < 0.001$ ), respectively, compared with the HFD group without the extract (Fig. 3).

ALT levels significantly increased only in the HFD group without the extract ( $P < 0.001$ ) and the HFD group with the extract ( $P < 0.01$ ) compared with the control group. A 1-month administration of the extract at doses of 400 mg/kg and 600 mg/kg led to a significant elevation in ALT levels by 11.65% ( $P < 0.05$ ) and ( $P < 0.001$ ),

respectively, compared with the HFD group without the extract (Fig. 3).

AST levels significantly increased in all HFD groups except for the group receiving the 600 mg/kg dose of the extract ( $P < 0.001$ ). The 600 mg/kg dose of the extract brought AST levels down from  $127.95 \pm 25.31$  in the control group and  $143.16 \pm 7.11$  in the HFD group without the extract to  $125.48 \pm 6.48$ . These changes were significant only when compared with the HFD group without the extract ( $P < 0.001$ ) (Fig. 3).

Pearson's correlation coefficient between ALT and AST indicated a significant ( $P < 0.01$ ) and positive correlation between these parameters, suggesting that an increase in one is associated with an increase in the other.



**Figure 2:** The image showcases the impact of hydroalcoholic lavender extract on hepatic enzymes: alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST).

The graph illustrates that a high-fat diet (HFD) resulted in elevated levels of hepatic enzymes, including ALP, ALT, and AST, compared with the control group. The administration of hydroalcoholic lavender extract led to a significant reduction in these enzyme levels,

Values are expressed as mean  $\pm$  SD in each group.

\*\* and \*\*\* respectively show  $P < 0.01$  and  $P < 0.001$  in comparison with the control group.

&, &&, and &&& respectively represent  $P < 0.05$ ,  $P < 0.01$ , and  $P < 0.001$  compared with the HFD group (n=8).

## DISCUSSION

Lipid metabolism disorder is a major risk factor for the development of cardiovascular disease. Current hypolipidemic drugs are associated with numerous complications, which highlights the need for alternative drugs with fewer adverse effects and improved efficacy.<sup>14</sup> One potential solution is utilizing medicinal plants as valuable resources in the treatment of hyperlipidemia. In this study, a hydroalcoholic extract of lavender was investigated as a potential hypolipidemic agent. The results demonstrated that the hydroalcoholic extract of lavender reduced lipid profiles and liver enzyme levels in rats fed an HFD. Although cholesterol serves as a precursor to many essential compounds, including bile acids, steroid hormones, and vitamin D, elevated serum cholesterol levels are associated with an increased risk of cardiovascular disease.<sup>15</sup> This experimental study demonstrated that rats fed an HFD exhibited high serum TG levels. The administration of a hydroalcoholic extract of lavender effectively reduced these elevated serum TG levels. Research has established that low plasma TG levels are associated with a decreased risk of congestive heart disease.<sup>16</sup> Moreover, high plasma LDL levels have been identified as a significant risk factor for congestive heart disease.<sup>17</sup> A direct relationship between LDL and atherosclerosis has been established, indicating that reducing serum LDL levels may help decrease the risk of atherosclerosis.<sup>18, 19</sup> Our study demonstrated that the hydroalcoholic extract of lavender effectively decreased high LDL concentrations, indicating that lavender may serve as a promising treatment option for atherosclerosis by reducing serum LDL levels. A reduction in serum HDL levels is another established risk factor for atherosclerosis; therefore, increasing HDL levels can potentially mitigate the risk of atherosclerosis.<sup>20</sup> Our study revealed that the

hydroalcoholic extract of lavender significantly increased plasma HDL levels. The atherosclerotic index, a diagnostic criterion for atherosclerosis defined as the ratio of LDL-C to HDL-C, was shown to be significantly reduced following 10 days of treatment with the lavender extract. Flavonoids, a class of antioxidant polyphenolic compounds, have been associated with a reduced risk of cardiovascular disease.<sup>21</sup> Previous studies have demonstrated that flavonoids can inhibit arachidonic acid metabolism, which may contribute to their cardioprotective effects. The presence of a 5-hydroxy group in the flavonoid structure allows for free rotation of the flavonoid  $\beta$  loop, which inhibits the 5-lipoxygenase enzyme and reduces inflammation.<sup>22</sup> Researchers have proposed several possible mechanisms for the beneficial effects of flavonoids, including diminished cholesterol acyltransferase activity in liver cells, decreased enzyme 3-hydroxy-methyl-3-glutaryl coenzyme A activity,<sup>23</sup> and increased liver receptors.<sup>24</sup> Consequently, flavonoids effectively reduce lipid profiles.<sup>7, 21</sup> In a study by Bahramikia et al,<sup>4</sup> rats fed an HFD were administered phenolic antioxidant compounds from the *Nasturtium* plant, which led to decreased serum lipid profiles. Similarly, Rabiei et al<sup>25</sup> observed a reduction in lipid profiles in rats that received lavender plants rich in phenolic antioxidant compounds. While the effects of lavender extract on serum lipid levels in rats with hyperlipidemia had not been previously measured, our study specifically examined its impact in hyperlipidemic rats. Independent studies have identified the presence of phenolic antioxidant compounds in the lavender plant.<sup>26</sup> Research has established that elevated serum cholesterol levels can lead to liver cell damage.<sup>27</sup> Our findings demonstrated that an HFD resulted in a significant elevation in serum ALT and AST levels. However, rats treated with lavender

exhibited lower serum ALT and AST levels than rats in Group II, suggesting a hepatoprotective effect for lavender.

## CONCLUSIONS

The findings of this study demonstrate that a hydroalcoholic extract of lavender effectively lowered lipid profiles and liver enzyme levels in rats fed an HFD, without causing significant adverse effects on liver function. These results suggest that lavender possesses protective properties against cardiovascular disease, making it a promising option for further research and potential therapeutic applications.

### Conflict of Interest

The authors declare no conflicts of interest.

### Funding

The project was funded by the Vice Chancellorship of Research at Sabzevar University of Medical Sciences.

### Acknowledgments

We are grateful to the Vice Chancellorship of Research at Sabzevar University of Medical Sciences and the Cellular and Molecular Research Center for their financial support of this research. We would also like to express our appreciation to all the staff members of these centers for their invaluable contributions and assistance throughout the project.

### Ethical Statement

The Ethics Committee of Sabzevar University of Medical Sciences approved the animal experiments in this study (reference number: IR.MEDSAB.REC.1398.057).

## REFERENCES

1. Fallah Huseini H, Fakhrzadeh H, Dastpak A, Azarabadi M, Mohtashami Tokabny RJJomP. Review of antihyperlipedemic herbal medicine. 2005; 3: 9-20
2. Fras Z-JAJoC. Increased cardiovascular risk associated with hyperlipoproteinemia (a) and the challenges of current and future therapeutic possibilities. 2020; 23: 60
3. Jahromi MF, Ray AB, Chansouria J. Antihyperlipidemic effect of flavonoids from *Pterocarpus marsupium*. Journal of Natural Products 1993; 56: 989-994
4. Bahramikia S, Yazdanparast RJJoe. Effect of hydroalcoholic extracts of *Nasturtium officinale* leaves on lipid profile in high-fat diet rats. 2008; 115: 116-121
5. Campos-Vega R, Oomah BD, Vergara-Castaneda HA. Food Wastes and By-products: Nutraceutical and Health Potential: John Wiley & Sons; 2020
6. Hemler EC, Hu FBjCar. Plant-based diets for cardiovascular disease prevention: all plant foods are not created equal. 2019; 21: 18
7. Russo P, Prinzi G, Lamonaca P, Cardaci V, Fini MJCmc. Flavonoids and Reduction of Cardiovascular Disease (CVD) in Chronic Obstructive Pulmonary Disease (COPD). 2019; 26: 7048-7058
8. Yousefi M, Shabunin SV, Vatikov YA, Kulikov EV, Adineh H, Hamidi MK, Hoseini SMJA. Effects of lavender (*Lavandula angustifolia*) extract inclusion in diet on growth performance, innate immunity, immune-related gene expression, and stress response of common carp, *Cyprinus carpio*. 2020; 515: 734588
9. Al-Sayari A, Ghazwani M, Alhamhoom Y, Almaghaslah D, Louis JV, Gurusamy NJBR. The antidepressant-like effect of almond oil: An additive effect with lavender oil. 2018; 29:
10. Rabiei Z, Rafieian-Kopaei M, Mokhtari S, Alibabaei Z, Shahrani M. The effect of pretreatment with different doses of *Lavandula officinalis* ethanolic extract on memory, learning and nociception. Biomedicine & Aging Pathology 2014; 4: 71-76

11. Bahramikia S, Yazdanparast R. Effect of hydroalcoholic extracts of *Nasturtium officinale* leaves on lipid profile in high-fat diet rats. *Journal of ethnopharmacology* 2008; 115: 116-121
12. Bahramikia S, Yazdanparast R. Effect of hydroalcoholic extracts of *Nasturtium officinale* leaves on lipid profile in high-fat diet rats. *Journal of ethnopharmacology* 2008; 115: 116-121
13. Ahmadvand H, Bagheri S, Tamjidi-Poor A, Cheraghi M, Azadpour M, Ezatpour B, Moghadam S, Shahsavari G, Jalalvand M. Biochemical effects of oleuropein in gentamicin-induced nephrotoxicity in rats. *ARYA atherosclerosis* 2016; 12: 87
14. Ghatak A, Asthana OJJP. Recent trends in hyperlipoproteinemias and its pharmacotherapy. 1995; 27: 14
15. Yamamoto H, Yamanashi Y, Takada T, Mu S, Tanaka Y, Komine T, Suzuki HJMp. Hepatic Expression of Niemann-Pick C1-Like 1, a Cholesterol Reabsorber from Bile, Exacerbates Western Diet-Induced Atherosclerosis in LDL Receptor Mutant Mice. 2019; 96: 47-55
16. Ference BA, Kastelein JJ, Ray KK, Ginsberg HN, Chapman MJ, Packard CJ, Laufs U, Oliver-Williams C, Wood AM, Butterworth ASJJ. Association of triglyceride-lowering LPL variants and LDL-C-lowering LDLR variants with risk of coronary heart disease. 2019; 321: 364-373
17. Navar AMJJ. The evolving story of triglycerides and coronary heart disease risk. 2019; 321: 347-349
18. Ross R. Atherosclerosis — An Inflammatory Disease. 1999; 340: 115-126
19. Shah PKJRicm. Emerging non-statin LDL-lowering therapies for dyslipidemia and atherosclerosis. 2019; 4: 136-141
20. Xepapadaki E, Zvintzou E, Kalogeropoulou C, Filou S, Kypreos KEJA. The Antioxidant Function of HDL in Atherosclerosis. 2020, DOI: 0003319719854609
21. Shahrani M, Pilehvarian AA, Kheyri S, Asgari A, Farokhi E, Parvin N, Rafieian-Kopaei MJJoSUoMS. Effects of *Kelussia odoratissima* Mozaffarian (KOM) extract on blood lipid in Balb/c mice. 2009; 10:
22. Burnett B, Jia Q, Zhao Y, Levy RJJomf. A medicinal extract of *Scutellaria baicalensis* and *Acacia catechu* acts as a dual inhibitor of cyclooxygenase and 5-lipoxygenase to reduce inflammation. 2007; 10: 442-451
23. Dávalos A, Fernández-Hernando C, Cerrato F, Martínez-Botas J, Gómez-Coronado D, Gómez-Cordovés C, Lasunción MAJTJon. Red Grape Juice Polyphenols Alter Cholesterol Homeostasis and Increase LDL-Receptor Activity in Human Cells In Vitro, 2. 2006; 136: 1766-1773
24. Adebawo O, Salau B, Ezima E, Oyefuga O, Ajani E, Idowu G, Famodu A, Osilesi OJLih, disease. Fruits and vegetables moderate lipid cardiovascular risk factor in hypertensive patients. 2006; 5: 14
25. Rabiei Z, Rafieian-Kopaei M, Mokhtari S, Shahrani MJJoprI. Effect of dietary ethanolic extract of *Lavandula officinalis* on serum lipids profile in rats. 2014; 13: 1295
26. Kıvrak ŞJIC, Products. Essential oil composition and antioxidant activities of eight cultivars of Lavender and Lavandin from western Anatolia. 2018; 117: 88-96
27. Al-Mesaibih MA, Khalifa SA, Hakami AHJEJoPHS. The impact of high cholesterol on the liver of both male rabbits and rats. 2019