Fumaria parviflora Lam. Effect on Serum Levels of Glucose and Lipids in Streptozocin- Induced Diabetic Rats

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A B S T R A C T

Background and Objective: Lowering serum glucose and lipid levels in diabetic patients by using natural materials is of great importance. In this study, the effect of oral consumption of *Fumaria Parviflora Lam*was was assessed on serum glucose and lipid levels in streptozocin diabetic rats.

Materials and Methods: In this experimental study, 32 male Wistar rats were divided into four groups of control, control under the treatment of *F. Parviflora L.*, diabetic and diabetic under the treatment of *F. Parviflora L.*. *F. Parviflora L.* was administered orally (6.25%) after injection of streptozocin for five weeks. Serum levels of glucose, triglyceride, total cholesterol, HDL and LDL were evaluated before and three and six weeks after the treatment.

Results: Regarding glucose level, there was no significant difference between diabetic rats treated with *F. Parviflora L.* and diabetic rats at third and sixth weeks. However there was a significant decrease in triglyceride level in *F. Parviflora L.* treated group as compared to diabetic rats at third and sixth weeks. Regarding serum total cholesterol, *F. Parviflora L.* treated group did not show a significant decrease at third week, but this difference was significant at sixth week. Regarding HDL cholesterol, there was no significant increase in *F. Parviflora L.* treated group as compared to diabetic group at third week, while this difference was significant at sixth week.

Conclusion: Oral administration of *F. Parviflora L.* to streptozocin-induced diabetic rats improved triglyceride, total cholesterol and HDL serum levels, but no significant effect on serum glucose and LDL.

Key Words:
Fumaria Parviflora Lam
Diabetes Mellitus
Serum glucose
Serum Lipids

1. Introduction

Diabetes mellitus is a cluster of metabolic disorders with a common characteristic of hyperglycemia phenotype (1). Diabetes etiologies include decrease in insulin secretion, decrease in glucose consumption and increased glucose production (2). Two major types of diabetes are type 1 and type 2 (3). Acute complications of diabetes include hypoglycemia, diabetic ketoacidosis, non-ketotic hyperosmolar syndrome, and chronic complications include macrovascular and microvascular events (1, 3).

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While the major component of diabetes mellitus treatment is using insulin and hypoglycemic agents, but these medications have side effects such as increased fat storage, wasting fat tissue at the site of injection, and hypoglycemic shock, and although do not have any effect on long term diabetes debilitating complications. Due to increasing human kind knowledge about this disorder, there is a need to find some effective agents with minimum side effects in the treatment of diabetes and its complications (4). In the recent years, anti-oxidants effects have been identified in different plants, indicating the paramount role of plants in the treatment of diabetes. Currently, medicinal plants are widely used due to their less side effects in the treatment of diseases in developing countries (5). *Fumaria Parviflora Lam* belongs to Fumariaceae family and Fumaria genus (6). This plant grows in wide regions of humid and semi-humid areas of northern Iran. *F. Parviflora L.* medicinal effects include blood purification, antibilious, and appetizing and its effect is almost on the liver and urinary system (7). Because oxidative stress is one of the causative mechanisms of diabetes, and due to anti-oxidative effects of this plant (8), here we investigated its effect on serum levels of glucose and lipids in diabetic rats.

2. Materials and Methods

In this experimental study, 32 male Wistar rats (Razi Institute, Karaj, Iran) with a weight range of 200-250 grams were investigated. Rats were kept at 21-23 ^{0}C in cages with 3 to 4 rats per each. Rats were given ad libitum access to tap water and especial food (Pars Animal food Co., Karaj) or food mixed with *F. Parviflora L.* powder (6.25%) for six weeks. A single dose of intraperitoneal streptozocin dissolved in normal saline (60 mg/kg) was injected to induce diabetes in rats. *F. Parviflora L.* was identified and approved by the Biology Department of Shahid Beheshti University and then grinded. The powder was mixed with standard rat food at a weight proportion of 6.25%, and then the animal food was prepared (9). Non-fasting serum glucose level in these rats was below 250 mg/dL. Rats were randomly divided into four groups of control, control under the treatment of *F. Parviflora L.*, diabetic and diabetic under the treatment of *F. Parviflora L.*. Treatment course lasted for five weeks. Blood samples were taken by using capillary tubes from the retro-orbital plexus. Serum glucose level, total cholesterol, triglyceride and HDL were assessed by enzymatic method (ZistChem kits, Tehran, Iran) according to the manufacturer instructions before and at 3rd & 6th weeks after the intervention. Digital spectrophotometer (Spectronic 20, USA) was used for the measurements. Besides, LDL was calculated by using the Friedewald formula as follows:

LDL cholesterol= Total cholesterol-HDL cholesterol-(TG/5)

2.1. Statistical analysis

All results were presented as mean ± standard deviation. After identifying data distribution, ANOVA with repeated measures was used to compare the results of each parameter in different groups before and after the intervention. One-way ANOVA and Tukey`s tests were also used to compare the groups at different time points. $P<0.05$ was considered significant in all the analyses.

3. Results

3.1. Body weight

In control group, there were 19.1% and 33.07% increase in body weight at third and sixth weeks as compared to the first week of study; this increase was statistically significant($p<0.05$, and $p<0.01$). In the group under the treatment of *F. Parviflora L.*, the increase rates were 23% and 40.5% at third and sixth weeks, which were statistically significant ($p<0.05$, and $p<0.01$). In diabetic group, their weight was decreased by 21.61% at third week, and significantly decreased ($p<0.05$) by 26.85% at sixth week as compared to the first week. In diabetic group under the treatment of *F. Parviflora L.*, their weights decreased by 21.73% and 17.06% at third and sixth weeks as compared to the first week; the decrease was only significant at third week ($p<0.05$). Moreover, weights of diabetic group under the treatment of *F. Parviflora L.* at third and sixth weeks did not have a significant difference with diabetic group at the same weeks (Figure 1).

3.2. Serum glucose level

There was no significant difference between the third and sixth weeks in control and control under the treatment of *F. Parviflora L.* In diabetic group, serum glucose level was increased by 275.26% and 266.07% at third and sixth weeks, which both were statistically significant (p<0.0005).Glucose level in diabetic group under the treatment of *F. Parviflora L.* was also increased at third and sixth weeks (270% and 261.81%), which both were statistically significant (P<0.0005). Moreover, serum glucose level in diabetic rats under the treatment of *F. Parviflora L.* was not statistically different from diabetic group at third and sixth weeks (Figure 2).

3.3. Triglyceride level

In control group, there was no statistically significant difference between triglyceride level at first of study and third and sixth weeks of study. In control group under the treatment of *F. Parviflora L.*, there was a 39.2% decrease at third week compared to the first of study, which was statistically significant (p<0.05), while its decrease at sixth week (17.55%) was not statistically significant. In diabetic rats, triglyceride level was increased at third and sixth weeks compared to the first of study (51.41% and 153.47), which both were statistically significant (p<0.01 and p<0.001). Triglyceride level in diabetic group under the treatment of *F. Parviflora L.* in third and sixth weeks did change as compared to the first of study. Although, triglyceride level at third and sixth weeks in diabetic group under the treatment of *F. Parviflora L.* decreased as compared to diabetic groups at these weeks (34.61% and 58.3%), which were statistically significant (p<0.01, and p<0.005) (Figure 3).

3.4. Serum Total Cholesterol

There was no significantdifference in control and control under the treatment of *F. Parviflora L.* groups at third and sixth weeks compared to the first of study regarding the level of serum total cholesterol. Serum total cholesterol was increased in diabetic group at third and sixth weeks (51.13% and 44.16%), compared to the first of study, which was statistically significant(P<0.01). Serum total cholesterol increased by 30.37% in diabetic group under the treatment of *F. Parviflora L.* at third week compared to the first of study, which was statistically significant(P<0.05).While, increase of serum total cholesterol at sixth week (6.96%) was not statistically meaningful. Serum total cholesterol in diabetic group under the treatment of *F. Parviflora L.* was decreased at third and sixth weeks (8.39% and 26.03%) compared to the diabetic group, which was not statistically significantat third week but significantat sixth week (p<0.05)(Figure 4).

3.5. Serum HDL Cholesterol

There was no significant change regarding the level of HDL cholesterol in control and control under the treatment of *Fumaria Parviflora Lam* groups at third and sixth weeks. HDL cholesterol was decreased by 18.42% and 46.96% in diabetic group at third and sixth weeks as compared to the first of study, which was statistically significant at sixth week (p<0.01). HDL cholesterol level in diabetic group under the treatment of *F. Parviflora L.* at third and sixth weeks did not change significantly as compared to initial values. HDL cholesterol was increased by 43.98% in diabetic group under the treatment of *F. Parviflora L.* as compared to the diabetic group at third week, which was statistically significant (p<0.05), although increased level of serum HDL cholesterol at sixth week by 61.46% between these groups was statistically significant (p<0.01) (Figure 5).

3.6. LDL Cholesterol Level

In control and control under the treatment of *F. Parviflora L.*, no difference was observed in the level of LDL cholesterol at third and sixth weeks. LDL cholesterol in diabetic group was increased by 317.68% and 120.86% at third and sixth weeks as compared to the first of study, which was statistically significant (P<0.005, P<0.05). LDL cholesterol level in diabetic rats under the treatment of *F. Parviflora L.* increased by 241.18% and 101.51% at third and sixth weeks, which was statistically significant at third week (p<0.01), but not significant at sixth week. In addition, LDL cholesterol level of diabetic group under the treatment of *F. Parviflora L.* did not change meaningfully at third and sixth weeks compared to the diabetic group (Figure 6).

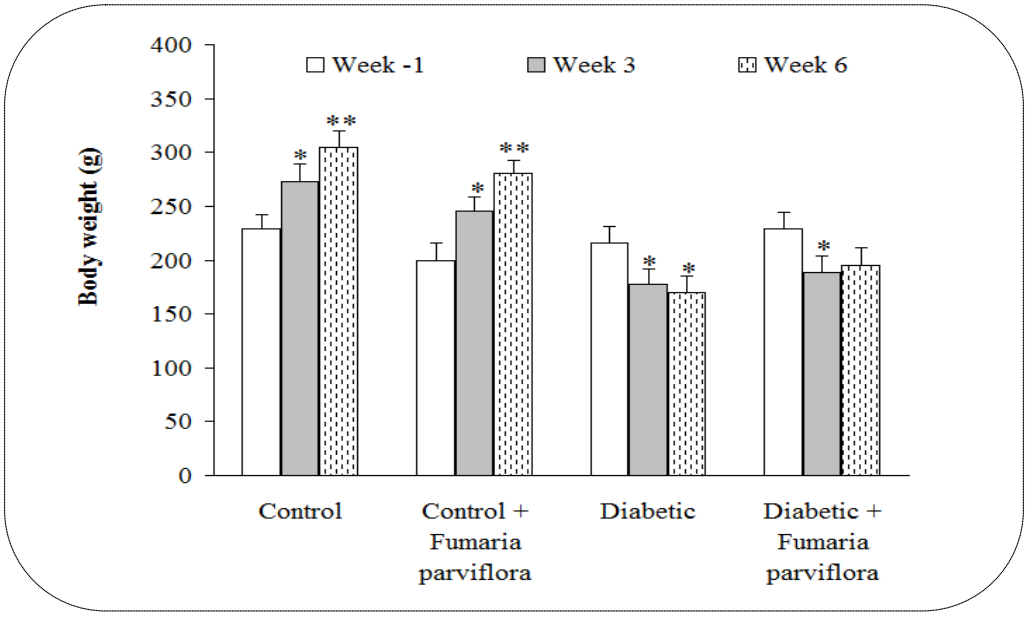

Figure 1. Body weight at Different Weeks in Control and Diabetic Rats Under the Treatment of *Fumaria Parviflora Lam*
* P<0.05, ** P<0.01 (as compared to basal value of the same group)

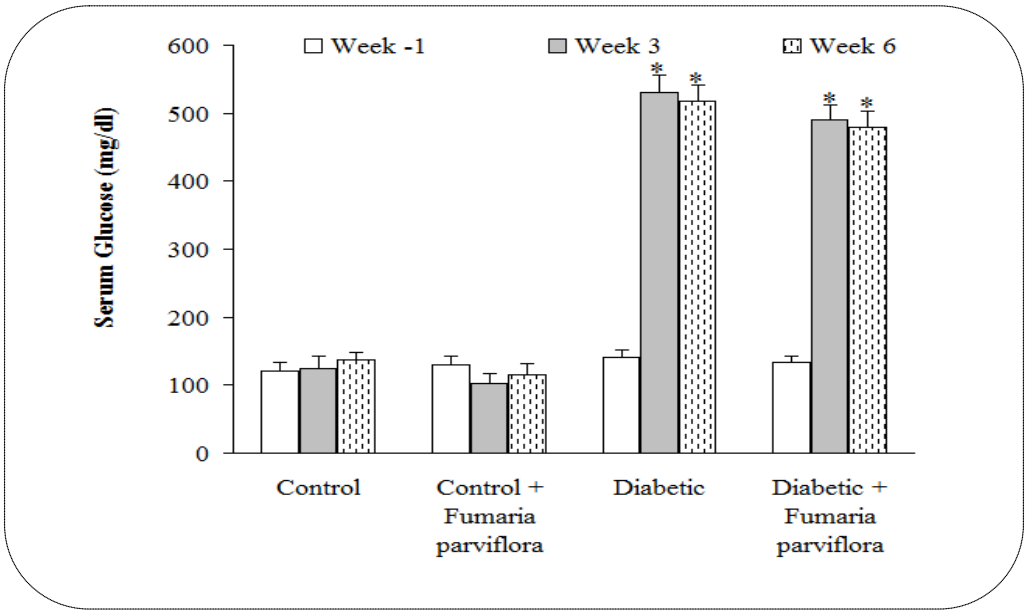

Figure 2. Serum Glucose Level at Different Weeks in Control and Diabetic Rats Under the Treatment of *Fumaria Parviflora Lam*
* P<0.0005 (as compared to the week before treatment)

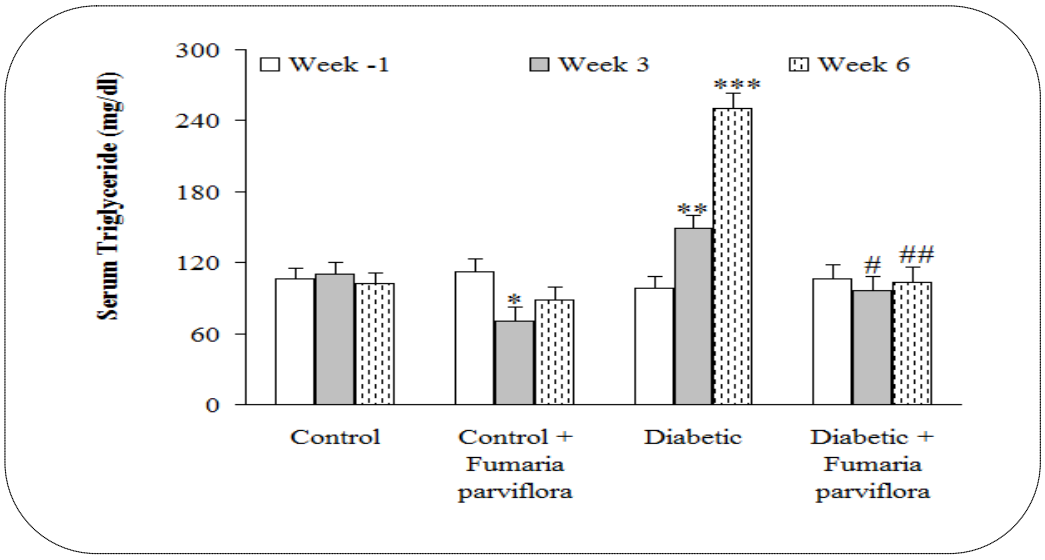

Figure 3. Serum Triglyceride Level at Different Weeks in Control and Diabetic Rats Under the Treatment of *Fumaria Parviflora Lam*
* P<0.05, ** P<0.01, *** P<0.005 (as compared to the basal value of the same group)
# P<0/01, ## P<0/005(as compared to the basal value of the same group)

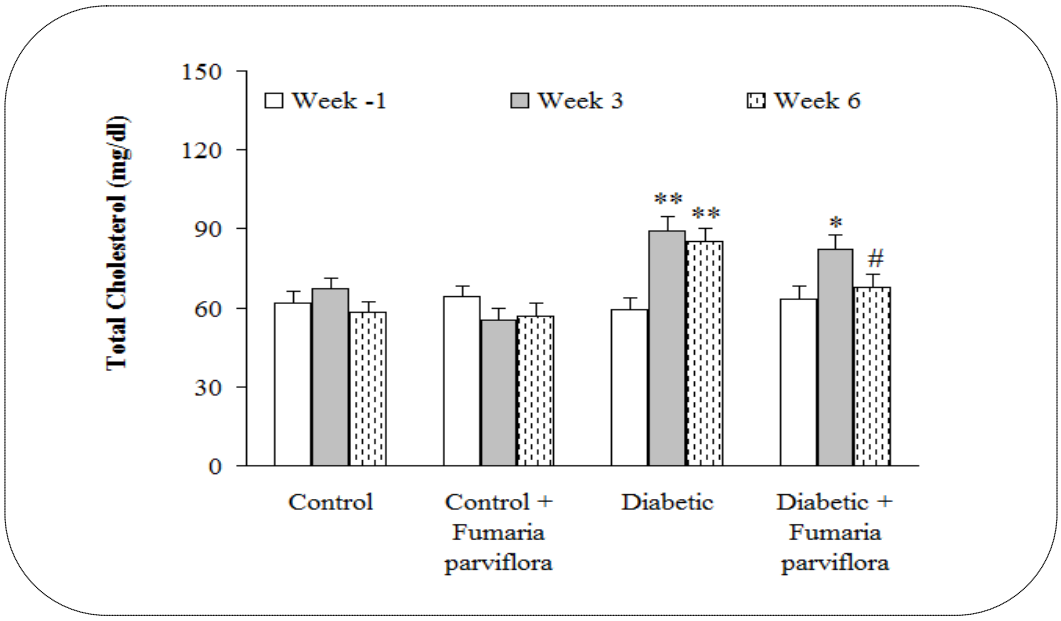

Figure 4. Serum Total Cholesterol Level at Different Weeks in Control and Diabetic Rats Under the Treatment of *Fumaria Parviflora Lam*
* P<0.05, ** P<0.01 (as compared to the basal value of the same group)
# P<0.05 (as compared to the diabetic group at the same week)

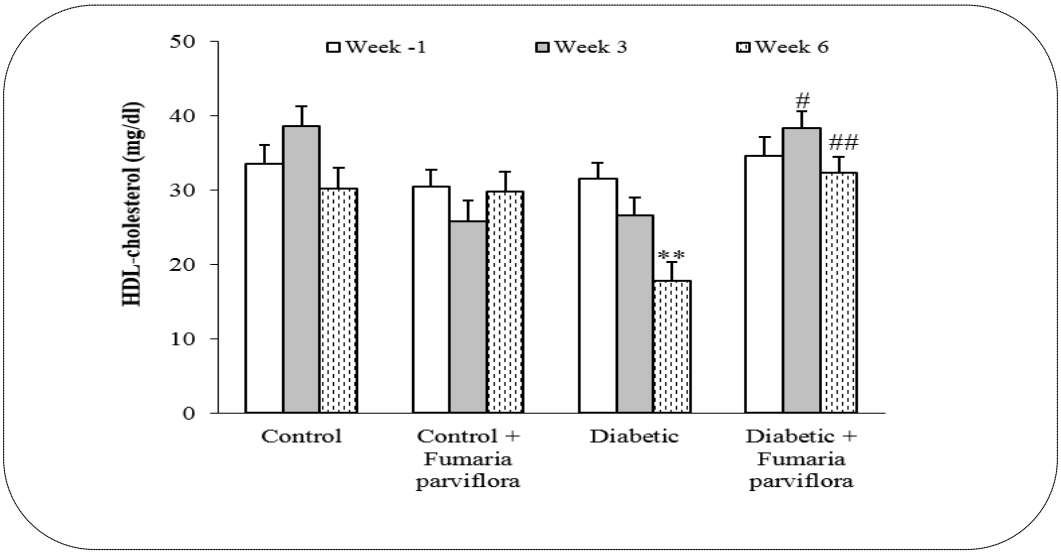

Figure 5. Serum HDL Level at Different Weeks in Control and Diabetic Rats Under the Treatment of *Fumaria Parviflora Lam*
** P<0.01 (as compared to the basal value of the same group)
# P<0.05, ## P<0.01 (as compared to the diabetic group at the same week)

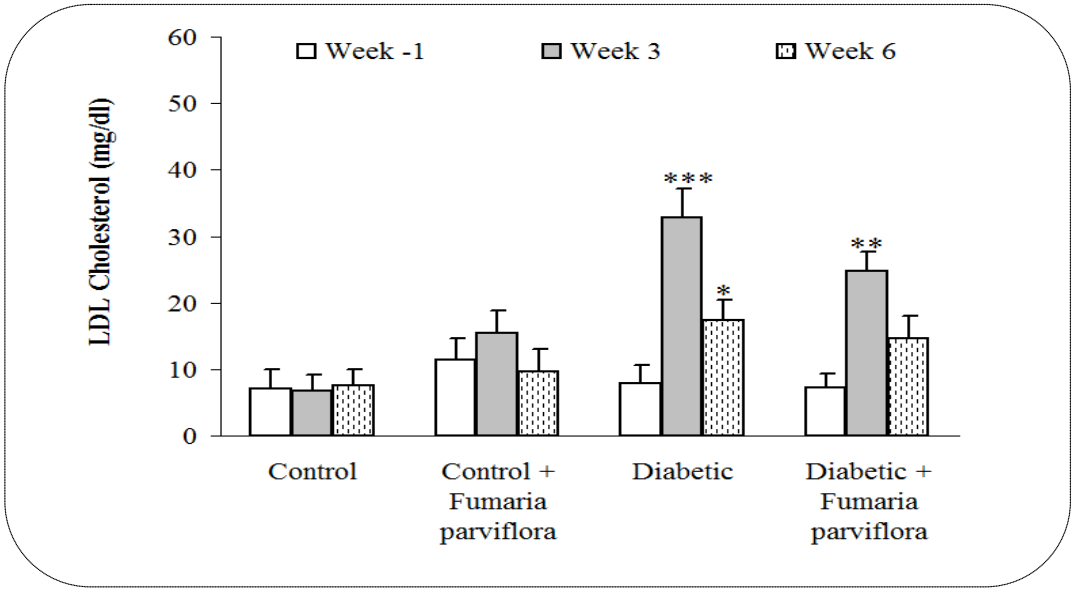

Figure 6. Serum LDL Level at Different Weeks in Control and Diabetic Rats Under the Treatment of *Fumaria Parviflora Lam*
* P<0.05, ** P<0.01, *** P<0.005 (as compared to the basal value of the same group)

4. Discussion

By inducing diabetes with streptozocin or alloxan in rodents such as laboratory rats, some significant and devastating injuries occur in pancreatic Langerhans cells, which lead to inappropriate alterations in the serum level of lipids and lipoproteins. In this regard, some of body tissues especially liver, play a significant role in releasing free fat acids and their metabolic change to other agents, increase in cholesterol synthesis and phospholipids and secretion of some lipoproteins to blood. Moreover, increased serum levels of triglyceride and cholesterol and decreased HDL cholesterol have been reported in streptozocin induced diabetic rats, which was seen in our investigation as well (10). On the other hand, increased blood sugar in streptozocin

or alloxan induced diabetic rats would indirectly increase cholesterol, triglyceride, LDL and VLDL and decrease HDL level (11), which can justify inappropriate changes in serum levels of lipids in diabetic rats in this investigation. Besides, inducing diabetes in diabetic animals accompanies with oxidative stress and lipid peroxidation in long term.

Beneficial effects of long-term oral consumption of *F. Parviflora L.* include decreasing oxidative stress and removing free O2 radicals like hydroxyl, protection of tissue cells against induced chemical injuries of toxic agents, decreasing lipid peroxidation in different tissues, and protection of tissues like liver against different chemical stresses. These effects are probably due to high amounts of antioxidants like flavonoids in this valuable plant. Therefore, consumption of this plant provides protective mechanisms for different body tissues and acts to decrease oxidative stress in diabetes mellitus (12). Furthermore, it has been found that protective and beneficial components in this plant including polyphenols and flavonoids owe protective effects against chemical injuries (8). In the present investigation, because no significant hypoglycemic effect was observed in diabetic group under the treatment of *F. Parviflora L.* compared to diabetic group, therefore beneficial effects of plant on other parameters might be due to alteration of liver enzymes activity and lipids metabolism. Although we did not measure activity of lipoprotein lipase, but since activity of this enzyme decreases in experimental model of streptozocin induced diabetes and in humans with type 1 diabetes, it is possible that our treatment has corrected the activity of this enzyme and in this way has led to desirable alterations in some serum lipid parameters in the present study. In this regard, Montazeri et al. showed that *F. Parviflora L.* plant exerts proper antioxidants property, which is seen in case of using the plant essence (13). Nonetheless, Fathi Azad and colleagues showed hypoglycemic effect of methanolic extract of *F. Parviflora L.* on streptozocin induced diabetic rats (12), hence it can be assumed that the concentration of active ingredients with hypoglycemic effect are less in case of oral consumption compared to its essence form. Therefore, no significant hypoglycemic effect was observed in this investigation. Finally Tajik et al. showed that long-term consumption of *F. Parviflora L.* essence improves serum levels of cholesterol and triglyceride (14) which is in accordance with our investigation.

5. Conclusion

Treating diabetic rats with *F. Parviflora L.* prevents their weight loss, controls dangerous factors underlying cardiovascular diseases like cholesterol and triglyceride, and prevents their significant increase in diabetic rats. Besides, increasing HDL cholesterol is another beneficial effect of *F. Parviflora L.* in diabetic rats.

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