TRADITIONAL AND INTEGRATIVE MEDICINE

Trad Integr Med, Volume 11, Issue 2, Spring 2026

Original Research

Effect of *Rosa canina* L. Hydroalcoholic Extract on High-Fat Diet-Induced Nonalcoholic Fatty Liver Disease in Rats

Fatemeh Afrashteh[1,2] , Shayan Eghdami[1,2], Maryam Abolhasani [3,4], Asieh Shojaii* [5,6], Manijeh Motevalian[1,7]*

[1] *Pharmacology Department, School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[2] *Student Research Committee, School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[3] *Oncopathology Research Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[4] *Department of Pathology, Hasheminejad Kidney Center (HKC), School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[5] *Institute for Studies in Medical History, Persian and Complementary Medicine, Iran University of Medical Sciences, Tehran, Iran*
[6] *Department of Traditional Pharmacy, School of Persian Medicine, Iran University of Medical Sciences, Tehran, Iran*
[7] *Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran*

Received: 20 Dec 2025 **Revised:** 31 Jan 2026 **Accepted:** 1 Feb 2026

Abstract

Non-alcoholic fatty liver disease (NAFLD) is a prevalent condition with an increasing global incidence. Given the reported anti-inflammatory, antioxidant, and lipid-lowering properties of *Rosa canina* L. (RC), this study aimed to evaluate its early-intervention effect on the laboratory and histopathological markers of NAFLD in a rat model. Thirty-six rats were divided into six groups (n=6): a control group on a regular diet, and five groups on a high-fat diet (HFD). The HFD groups received either normal saline (N/S), atorvastatin (10 mg/kg), or RC extract at doses of 300, 500, or 700 mg/kg. After 9 weeks, lipid profiles, liver enzymes (AST, ALT), and histopathological examination of liver biopsies were assessed. Total phenolic content of the extract was also determined. Total cholesterol (TC) levels were significantly reduced in the group receiving 500 mg/kg RC compared to the HFD+N/S group. AST levels were lower in the 300 mg/kg and 500 mg/kg RC groups than in the 700 mg/kg RC and atorvastatin groups. Histopathological analysis revealed ballooning scores of 55-60% in the HFD+N/S group, 30-35% in the atorvastatin group, 65-70% in the 300 mg/kg RC group, 30% in the 500 mg/kg RC group, and 45-55% in the 700 mg/kg RC group. Overall, the findings were generally positive, although the effects differed across the tested doses. Notably, the 500 mg/kg/day dose was associated with more favorable histopathological observations. RC demonstrates significant effects on lipid profile and liver enzymes comparable to atorvastatin in preventing NAFLD. These findings suggest that RC is a promising early-intervention agent for the prevention of NAFLD.

Keywords: Lipid profile; Liver enzymes; NAFLD; Rosa canina; Phenolic compound; Persian Medicine

http://doi.org/10.18502/tim.v11i2.22055

Citation: Afrashteh F, Eghdami S, Abolhasani M, Shojaii A, Motevalian M**. Effect of Rosa canina L. Hydroalcoholic Extract on High-Fat Diet-Induced Nonalcoholic Fatty Liver Disease in Rats.** Trad Integr Med 2026;11(2):170-180. http://doi.org/10.18502/tim.v11i2.22055

*Corresponding Authors: Asie Shojaii
Institute for Studies in Medical History, Persian and Complementary Medicine, Iran University of Medical Sciences, Tehran, Iran
Email: Shojaii.a@iums.ac.ir
Manijeh Motevalian
Razi Drug Research Center, Department of Pharmacology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
Email: motevalian.m@iums.ac.ir

Introduction

Non-alcoholic fatty liver disease (NAFLD), recently reclassified as metabolic dysfunction-associated steatotic liver disease (MASLD), is a prevalent hepatic disorder characterized by steatosis in over 5% of hepatocytes. Its development is strongly associated with metabolic syndrome, type 2 diabetes mellitus (T2DM), insulin resistance, and high-fat diets, rather than significant alcohol consumption [1, 2]. The disease spectrum ranges from simple steatosis (NAFL) to non-alcoholic steatohepatitis (NASH), a more severe form marked by inflammation, hepatocellular ballooning, and fibrosis, which occurs in approximately 10% of patients [3]. Progression to cirrhosis, an end-stage liver disease treatable only by transplantation, occurs in a significant portion of NASH cases, with cirrhotic patients facing an annual hepatocellular carcinoma risk of 1-4% [4]. The second leading cause of liver transplantation in the United States is NAFLD [5-7]. As the second leading cause of liver transplantation in the United States, NAFLD imposes a substantial burden on global healthcare systems and adversely affects patient quality of life [8]. The progression of NAFLD leads to increased liver-related mortality, substantial healthcare resource utilization, and reduced quality of life [9].

Despite its high prevalence, estimated at 6–35% worldwide and 32% in the Middle East, no pharmacotherapy is currently FDA-approved for NAFLD treatment [3]. Management strategies primarily involve lifestyle modifications; while investigational agents include vitamin E, insulin sensitizers, thyroid hormone receptor β (THR-β) agonists, and fibroblast growth factor analogs [3,10,11]. Due to the potential side effects and drug interactions associated with these synthetic compounds, there is growing interest in the therapeutic potential of herbal medicines for NAFLD, a trend supported by increasing global consumption and scientific validation of traditional remedies [12]. Today, the consumption of traditional herbal medicines has increased in many countries in Asia, America and Europe, and many studies have confirmed the effectiveness of traditional herbal medicines on NAFLD [7,13,14].

Dog rose (*Rosa canina* L.) is an important species in genus *Rosa* L. which is a member of Rosaceae family and rose hip is the fruit of *Rosa canina* (RC). The genus *Rosa* L. grow in areas of Asia, Middle East, Europe and North America [15]. The shrub of this plant has 1-3 m height which is resistant to hard environmental conditions and typically grows in rocky, low soil and water conditions [16]. The flowers are fragrant and the petals are white or pink [17]. The fruit is round or oval-shaped, elongated, smooth with a bright red color and the seeds are inside [18-20].

Rose hip is a rich source of vitamin C (250 to 2700 mg per100 g), minerals, tannins, carotenoids, polyphenolic compounds, and polyunsaturated fatty acids (such as ω3 and ω6: 13.67–24.75% and 45.38–54.58%, respectively) [21,22]. The most important carotenoid compounds of rose hip are lycopene 11.1 and β-carotene 7.2 mg per 100 g [23,24].

Several studies have shown the effectiveness of RC extract on treatment of different diseases. RC was used for liver disease in Persian medicine. The effect of RC fruit extract on reducing inflammation, cellular oxidation, blood glucose, blood lipids, body weight, and lipid accumulation in adipose tissues has been reported [25-27]. RC fruit extract has been used traditionally in the treatment and prevention of diseases such as hemorrhoids, diabetes, influenza and gallstones and has also shown a beneficial effect on depression and increase the density of neurons in the hippocampus [18,28].

So far, studies have underpinned the antidiabetic, antihyperglycemia, anti-obesity, antihyperlipidemia, and pancreatic β-cell proliferative effect of RC [29-31]. While a limited number of studies have explored the effects of RC on NAFLD, the prophylactic potential of RC extract remains insufficiently investigated. Therefore, this study aims to evaluate the early-intervention effect of a hydroalcoholic extract of RC on high-fat diet-induced NAFLD in a rat model [32-34].

Materials and Methods

Animals

A total of thirty-six 10-week-old male Wistar albino rats (weight range: 240-320 g) were obtained from Iran University of Medical Sciences (Tehran, Iran). The animals were housed under controlled temperature (26 °C) and a 12-hour light/dark cycle with *ad libitum* access to food and water.

All animals were fed a high-fat diet (HFD) for two weeks except for six rats that considered as the healthy control group. The composition of a high-fat diet was (in 100 g): 15 g pellet, 15 g dried milk (Nestle), 15 g plain flour, 7 g solid oil from animal source, 19 g fructose, 6 g sucrose, 8 g liquid oil from corn, 6 g yolk, and 18 g high-fat milk.

Ethics

All animal practices were performed base on the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health which were approbated by ethical committee of Iran University of Medical Sciences. (Ethical code: IR.IUMS.FMD.REC.1399.082). This study was designed and reported in accordance with the ARRIVE guidelines 2.0 [35].

Preparation of RC extract

Dried fruits of RC were purchased from a herbal market in Tehran, Iran. The plant material was authenticated by a botanist at the Faculty of Pharmacy, Tehran University of Medical Sciences, and a voucher specimen (No.: PMP-636) was deposited in the faculty's herbarium for future reference. A hydroalcoholic extract was prepared from

the dried and ground plant material using 70% ethanol as the solvent via maceration. The resulting extract was filtered, and the filtrate was concentrated under reduced pressure using a rotary evaporator. The concentrated extract was then lyophilized or oven-dried to obtain a dry powder. The extraction yield was calculated to be 31% (w/w).

Determination of total phenolic content

The total phenolic content (TPC) of RC was determined using the Folin-Ciocalteu method. A standard curve was prepared with gallic acid solutions at concentrations of 75, 100, 150, and 200 µg/mL. For both the standards and the sample (10 mg/mL), 1 mL of the solution was mixed with 5 mL of a 10% (v/v) Folin-Ciocalteu reagent. After 3 minutes, 4 mL of a 75 mg/mL sodium carbonate (Na_2CO_3) solution was added. The reaction mixture was incubated in the dark for 30 minutes, and the absorbance was measured at 765 nm. The TPC was determined from the gallic acid standard curve and expressed as milligrams of gallic acid equivalent per gram of sample (mg GAE/g) [36].

Experimental groups

The animals were divided in to six groups and each group had six rats. Following groups were considered: HFD+ normal saline (N/S) (receiving normal saline through gavage), control (pellet diet without treatment), HFD + 300 mg/kg RC daily, HFD+500 mg/kg RC daily, HFD+700 mg/kg RC daily, HFD+ 10 mg/kg atorvastatin daily. The groups received the treatments for six weeks. Normal saline, RC extract and atorvastatin was given orally by gavage daily. The animals weighed weekly and their weight was recorded. The whole study was conducted 9 weeks. The doses of RCs extract (300, 500, and 700 mg/kg/day) were selected to explore potential dose-dependent effects in NAFLD. These doses were chosen to fall within the range commonly used in previous animal studies, allowing assessment of both lower and higher dose effects.

At the end of the nine-week experimental period, the rats were sacrificed. Blood samples were collected via cardiac puncture and centrifuged at 3000 *g* for 15 minutes to obtain serum. The serum was analyzed for levels of total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP).

Liver biopsies (1 cm × 1 cm) were harvested from the left lobe of each rat and fixed in 10% formalin. The tissue samples were then processed, embedded in paraffin, sectioned, and stained with both Hematoxylin and Eosin (H&E) and Masson's Trichrome stain. A blinded pathological assessment was performed on all liver sections. The severity of nonalcoholic fatty liver disease (NAFLD) was evaluated using a standardized histological scoring system [37].

Statistical analysis

Data were analyzed by SPSS26 (SPSS Inc., Chicago, Ill., USA). Results are reported as mean ± standard deviation (SD). One-way ANOVA followed by Tukey post hoc test was used for multiple comparisons between groups. The p values less than 0.05 were considered significant.

Results

Total phenolic content

The TPC was estimated by gallic acid and expressed as mg gallic acid equivalent (GAE)/g of extract . The TPC of RC extract was 96.15±0.1 mg GAE/g of extract.

Pharmacological studies

The weight of each rat was measured every week. The mean weight gain after 9 weeks is shown in figure 1. Although the control group exhibited the lowest weight gain, there were no statistically significant differences between between the groups.

Lipid profile (TG, TC, LDL, and HDL) was also demonstrated in figure2. The atorvastatin group had significantly lower TG levels compared to the control (p=0.014), HFD+N/S (p=0.014), and 700 mg/kg RC (p=0.044) groups.

TC levels were significantly lower in the control group compared to the HFD+N/S group (p=0.020). Furthermore, the group receiving 500 mg/kg RC showed a significant reduction in TC compared to the HFD+N/S group (p=0.008).

LDL levels were significantly lower in the control group than in the 300 mg/kg RC (p=0.034) and atorvastatin (p=0.006) groups. No significant differences in HDL levels were observed among the groups.

Liver enzymes, also were measured in the blood samples. Figure 3 depicts the levels of ALT, AST, and ALP in all groups.

ALT levels were significantly elevated in the HFD+N/S, 300 mg/kg RC, 500 mg/kg RC, and 700 mg/kg RC groups compared to the control group (p=0.008, p=0.045, p<0.001, and p=0.045, respectively). The 500 mg/kg RC group also had significantly higher ALT than the atorvastatin group (p=0.008).

AST levels in the 300 mg/kg RC group were significantly lower than in the 700 mg/kg RC (p=0.008) and atorvastatin (p=0.008) groups. Similarly, the 500 mg/kg RC group had lower AST levels than the 700 mg/kg RC (p=0.008) and atorvastatin (p=0.008) groups. The control group also showed significantly lower AST levels compared to the 700 mg/kg RC (p=0.008) and atorvastatin (p=0.008) groups.

ALP, the last measured enzyme was significantly higher in the atorvastatin (p=0.019) and HFD+N/S (p=0.001) groups compared to the control group. The RC treatment groups did not show significant differences in ALP levels compared to either the control or atorvastatin groups.

Histopathological assessment

A blinded pathological evaluation of liver biopsies assessed inflammation, ballooning, and necrosis and scoring was performed by comparing the slides with previously available samples and control specimens, as a qualitative and semi-quantitative evaluation. The findings are summarized in figures 4-9 and table 1. HFD+N/S group showed 55-60% ballooning and 20% of hepatocytes necrosis. The 300, 500, and 700 mg/kg RC treated groups showed 65-70%, 30%, and 45-55% of ballooning, respectively. The hepatocytes necrosis in the 300, 500, and 700 mg/kg RC treated groups were 15%, 5-10%, and 5-10%, respectively. Indeed, the atorvastatin group showed 30-35% of ballooning and 5% of hepatocytes necrosis. The control group had 5% ballooning, no necrosis, and no lobular inflammation. No fibrosis was observed in any of the groups.

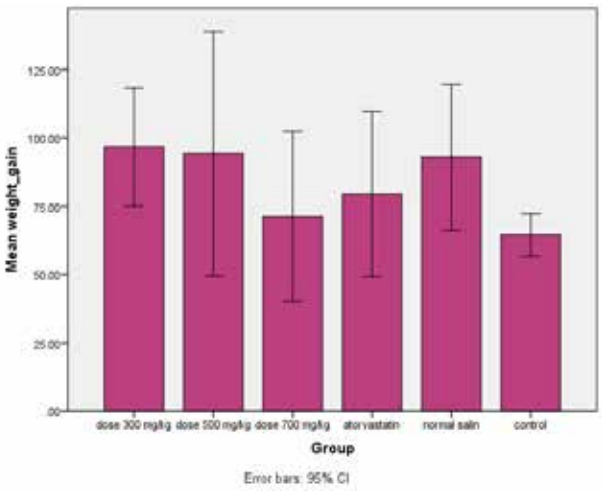


Figure 1. The mean weight gain of each group from week 1 to week 9.

Discussion

NAFLD is the most common chronic liver disease in the world and its global burden has increased due to the increasing prevalence of obesity. The disease is frequently associated with comorbidities such as type 2 diabetes,

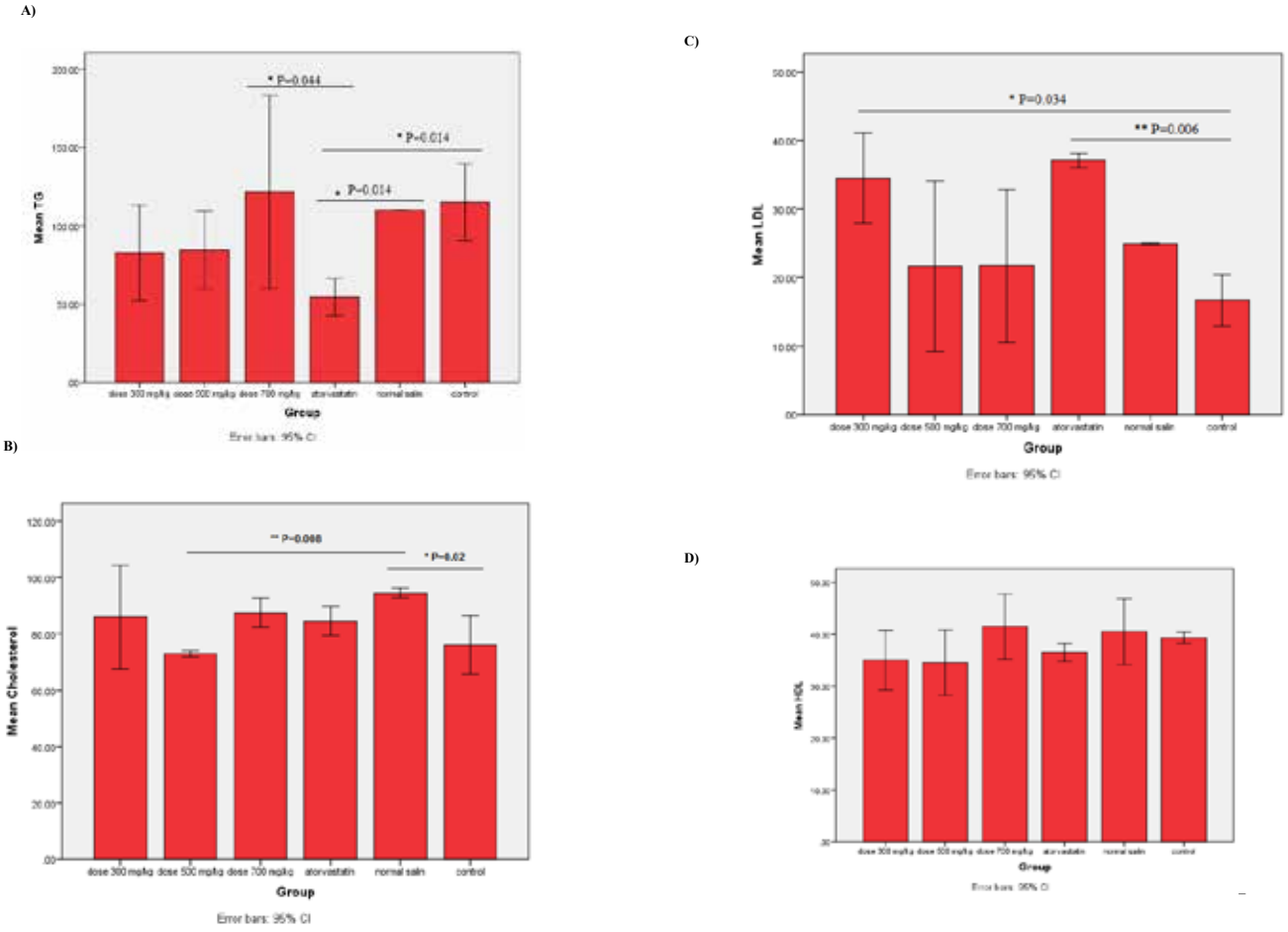
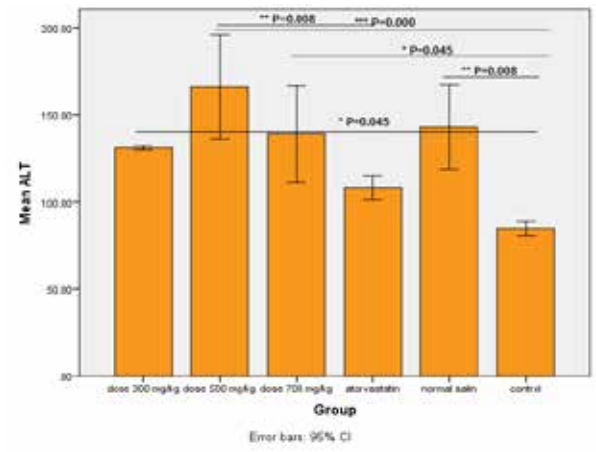
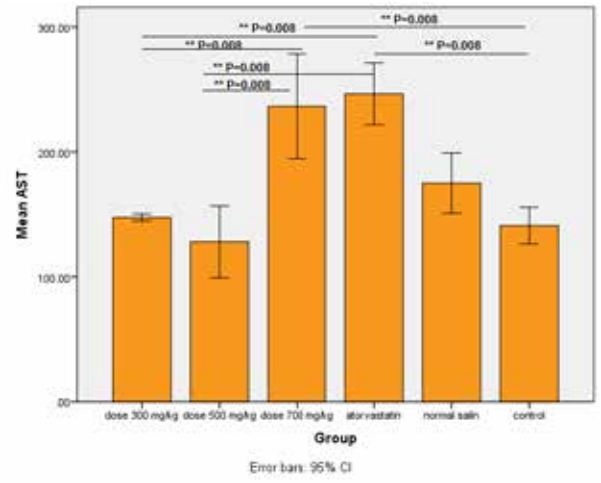


Figure 2. Lipid Profile of groups: A) Triglyceride (TG) (mg/dL), B) Total Cholesterol (TC) (mg/dL), C) LDL (mg/dL), and D) HDL (mg/dL)

A)



B)



C)

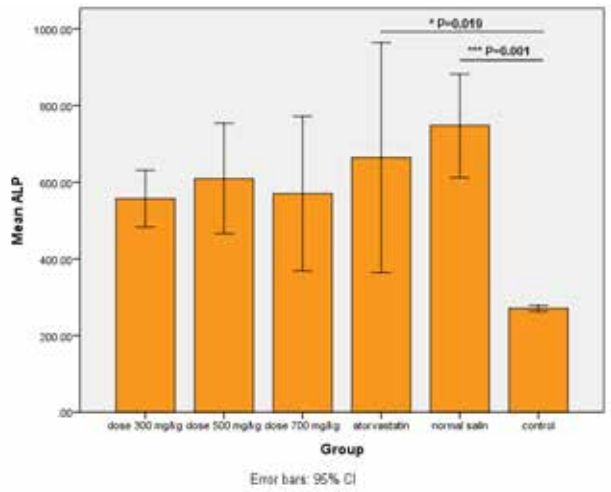


Figure 3. The level of Liver enzymes in groups: A) Alkaline phosphatase (ALP), B) Aspartate aminotransferase (AST), and C) Alanine transaminase (ALT)

dyslipidemia, and metabolic syndrome [38]. The underlying pathology of NAFLD is an increase in free fatty acids delivery to liver, cellular inflammation, cellular oxidation, and apoptosis. Herbal remedies have shown potential in ameliorating NAFLD by improving dyslipidemia, specifically by reducing levels of TG, TC, LDL, and liver enzymes (ALT, AST), while potentially increasing HDL and suppressing hepatic lipogenesis [39].

So far, studies have focused on the effects of RC extracts on reducing inflammatory and oxidative markers, as well as the lipid profile in diabetic rats [29, 30, 40].The present study investigated the early-intervention effect of three doses of RC extract on the lipid profile, liver enzymes, and liver histopathology in a HFD rat model, dose dependently.

Our findings on the lipid profile were mixed. While atorvastatin significantly lowered TG levels compared to those in the control, HFD+N/S, and 700 mg/kg RC groups, only the 500 mg/kg RC dose significantly reduced TC compared to the HFD+N/S group. Interestingly, LDL levels were lower in the healthy control group than in the atorvastatin and 300 mg/kg RC groups, and no significant differences were observed in HDL levels among the groups

Liver enzymes, particularly ALT, are key indicators of disease progression and therapeutic response in NAFLD [41, 42]. Contrary to expectations, all three RC doses resulted in significantly higher ALT levels compared to the healthy controls, with the 500 mg/kg dose also showing higher ALT than the atorvastatin group. In contrast, AST levels were significantly lower in the 300 and 500 mg/kg RC groups than in the 700 mg/kg RC and atorvastatin groups. ALP levels were unchanged across the groups, except for elevations in the HFD+N/S and atorvastatin groups compared to controls. Although RC did not show a significant effect on ALT, it demonstrated favorable effects in histopathological findings as well as in other experimental assessments. Further studies are needed to investigate an optimal dose that can exert beneficial effects on both ALT levels and histopathological outcomes.

Histopathological assessment yielded more promising results. The RC-treated groups generally exhibited reduced inflammation, ballooning, and necrosis compared to the HFD+N/S group, with the notable exception of the 300 mg/kg dose, which showed higher ballooning. Importantly, the 500 mg/kg RC group demonstrated less ballooning than the atorvastatin group, suggesting a potent protective effect at this specific dosage.

The findings of the present study, which showed mixed effects of RC extract on serum lipids and liver enzymes but promising histopathological improvements, can be contextualized by previous literature. Intraperitoneal RC fruit extract at concentrations of 50, 100,200 and 300 mg / kg for 14 days, was able to lower blood sugar, LDL, and liver enzymes (AST, ALT, and ALP) and lower HDL in diabetic rats [43]. Due to volatile, phenolic and antioxi-

dant compounds of RC, it is possible that RC is effective in the treatment of diabetes due to its antioxidant activity. In addition to RC, a study shows that 100 to 1000 mg/kg methanolic extract of the flowers of another species of rose (*Rosa damascena* Mill.) inhibits glucose uptake into the gut by inhibiting the enzyme alpha-glucoside in diabetic rats [44].

Several studies support the potential efficacy of RC extracts. For instance, Andersson et al. demonstrated that a powdered RC supplement administered over 20 weeks—a considerably longer period than our 9-week study—effectively reduced insulin resistance, prevented weight gain, and improved lipid profiles (reduced TC and LDL, increased HDL) in HFD-fed mice [45]. Reduction of lipid accumulation in liver by the down-regulated expression of lipogenic proteins like peroxisome proliferator-activated receptor (PPAR) γ2, fatty acid-binding protein 4 (aP2), stearoyl-CoA desaturase-1 (SCD-1), diacylglycerol acyltransferase 1 (DGAT2), and AMP-activated protein kinase (AMPK) were also seen [46]. We should note that the baseline and serial measurement of plasma parameters were not done in our study which could give us the better judgment of the early-intervention effect of RC in NAFLD on lipid and enzyme profiles. No difference in weight gain was observed in all groups and this could be the result of shorter duration of our study compared to other similar studies.

Consumption of HFD with 1% of RC extract could reduce the accumulation of visceral fat and liver fat in eight weeks by suppressing the expression of PPARγ in mice. However they found RC extract was able to reduce weight gain in mice, blood glucose, TG, and leptin were not significantly different compared to controls, although serum insulin and adiponectin levels were increased [47]. In an *in vitro* research, the aqueous extract of RC reduced the amount of malondialdehyd (MDA) in cell samples compared to samples did not contain antioxidants, and the 100% and 25% aqueous extract had the lowest and highest toxicity to the cells, respectively [48]. The anti-inflammatory and antioxidant effects are due to the significant amount of phenol in RC, which can reduce or prevent the inflammatory process in NAFLD. These results showed that lipid peroxidation could be reduced by RC extract [15,48].

The protective effect of RC extract on the liver toxicity has been investigated in several studies. RC extract at doses of 500 and 750 mg/kg can reduce carbon tetrachloride-induced hepatotoxicity in rats by reducing levels of ALT, AST, ALP and MDA in serum [49]. Another study showed that RC extract at a dose of 100 mg/kg for eight weeks along with aerobic training can prevent increasing or elevation of liver enzymes and MDA after an acute aerobic exercise because of its antioxidant effect [50]. Also in other studies, the doses of 250 and 500 mg/kg in four or six weeks were able to reduce the liver toxicity caused by diabetes by reducing the liver enzymes (ALT, AST and ALP) in rats [51,52].

In general, due to the rich antioxidant compounds in RC fruit such as flavonoid, carotenoids and vitamin C, it can increases the total antioxidant capacity of liver cells, which prevents oxidative stress in liver cells and as a result, it prevents the increase of MDA in the liver tissue and the release of liver enzymes into the serum [17, 53]. The discrepancy between our findings and previous studies reporting stronger hepatoprotective effects of RC may be due to differences in chemical composition profiles between whole Rose hip fruit and the RC extract used in this study, as the extraction process may reduce or eliminate certain components which are liver protective. Furthermore, a longer duration for monitoring ALT levels may have been necessary to detect the hepatoprotective effects.

In a randomized control trial on NAFLD patients who received isolated polysaccharide from RC for 90 days, the reduction of weight gain, liver enzymes, and grade of the disease were seen [32].

From all the findings, it can be concluded that the effect of RC extract on blood lipid profile is dependent on the dose used and especially the duration of consumption of the extract. Although in our study lipid profile results were controversial among the groups, the pathologic observations showed promising results. The prominent results were about 500 mg/kg of RC which showed the better results in pathology findings even more than atorvastatin. This dose of RC was the only dose that could reduce the TC compared to rats with HFD +N/S. The non-linear dose–response observed in the present study may indicate a hormetic effect of RC, in which moderate doses may exert beneficial effects; while higher doses may result in reduced efficacy. Toxicological evaluation

Table 1. The histopathological test results in RC and atorvastatin treated and control groups

	Ballooning	Necrosis	Inflammation	Fibrosis
RC 300 mg/kg	65-70%	15%	2/x10	-
RC 500 mg/kg	30%	5-10%	1/x10	-
RC 700 m/kg	45-55%	5-10%	1/x10	-
Atorvastatin	30-35%	5%	1/x10	-
HFD	55-60%	20%	2/x10	-
Controls	5%	0%	0	-

RC: *Rosa canina*, HFD: High-fat diet

represents a limitation and warrants further investigation in future studies.

This study comprised some limitations. The lack of baseline and serial measurements of plasma parameters prevents a clear understanding of the temporal fluctuations in lipid and enzyme profiles. While a sample size of six animals per group is commonly used in animal studies, it may have contributed to some of the inconsistent statistical findings observed in this study. Moreover, the absence of baseline measurements of liver enzymes and lipid profiles prior to begin HFD may have affected the statistical outcomes. Future studies should incorporate a larger sample size, a longer intervention period, and different doses of RC, preferably using standardized extracts. More precise molecular investigations into antioxidant (e.g., MDA, total antioxidant capacity) and anti-inflammatory markers are needed to elucidate the exact mechanisms of action.

Conclusion

In this study we found that 500 mg/kg of RC extract could benefit NAFLD in reducing cholesterol and pathologic findings. However, the pathology findings suggested the desirable early-intervention effect of RC in other doses compared to HFD treated with normal saline. Among these results, 500 mg/kg/day of RC showed even better results than atorvastatin in liver biopsies. Despite the promising findings, the laboratory assessments, especially ALT, showed some inconsistency. Additional studies are recommended to determine the optimal dosage that can exert consistent beneficial effects on both biochemical and histopathological parameters in NAFLD.

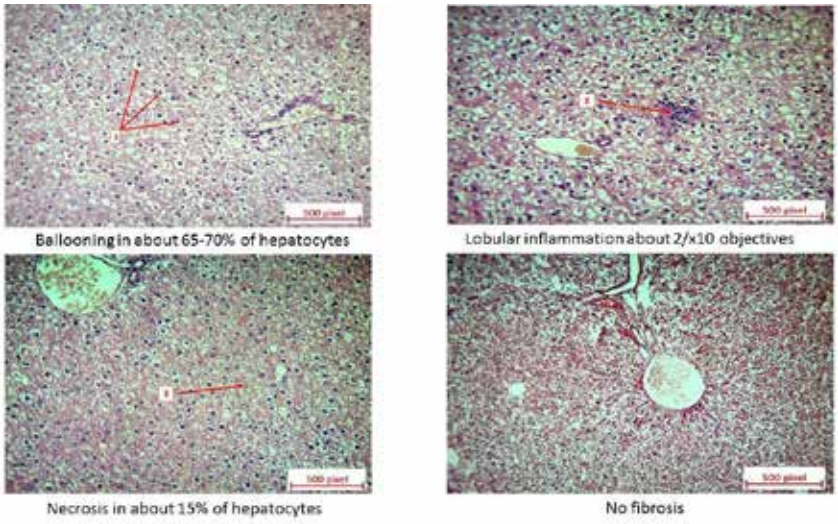


Figure 4. Pathology findings of liver biopsy from 300 mg/kg RC group (×10 objective)

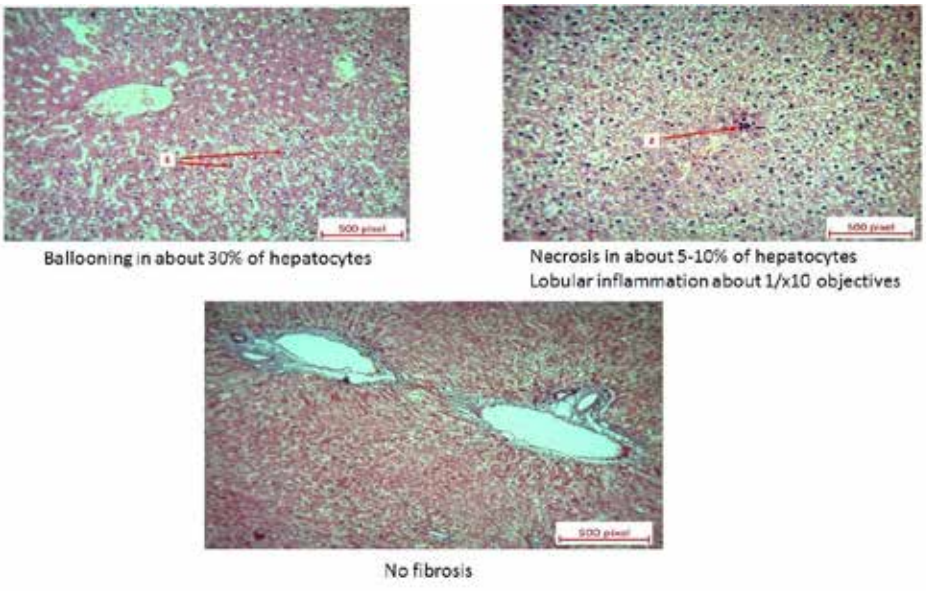


Figure 5. Pathology findings of liver biopsy from 500 mg/kg RC group (x10 objective)

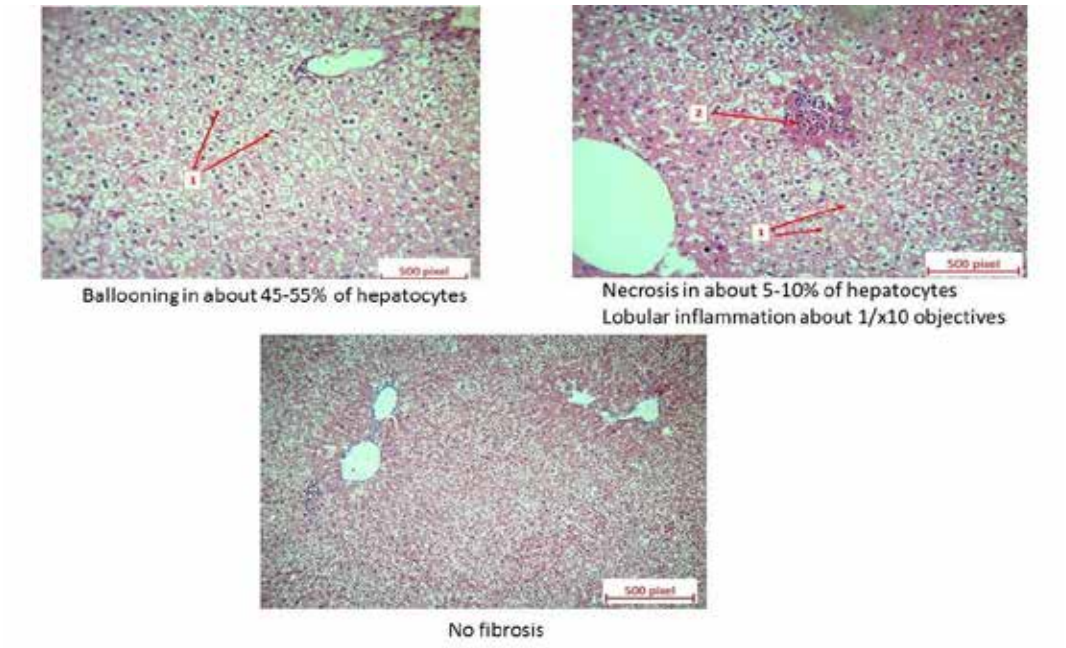


Figure 6. Pathology findings of liver biopsy from 700 mg/kg RC group (x10 objective)

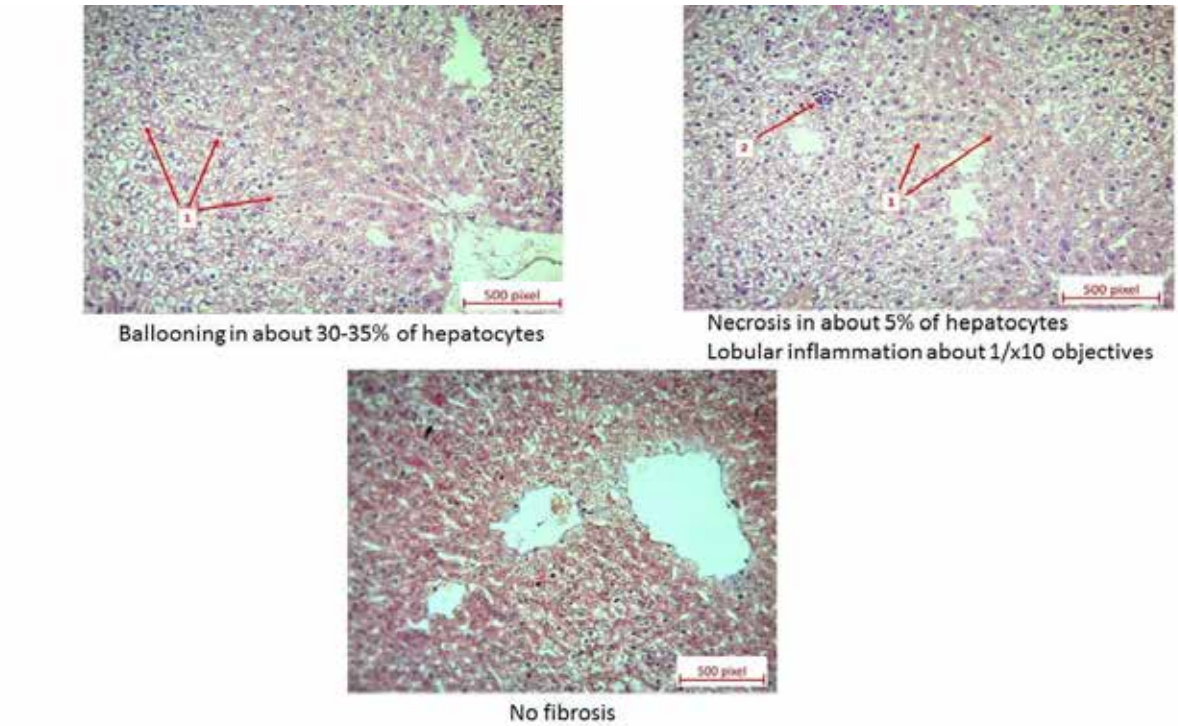


Figure 7. Pathology findings of liver biopsy from atorvastatin group (x10 objective)

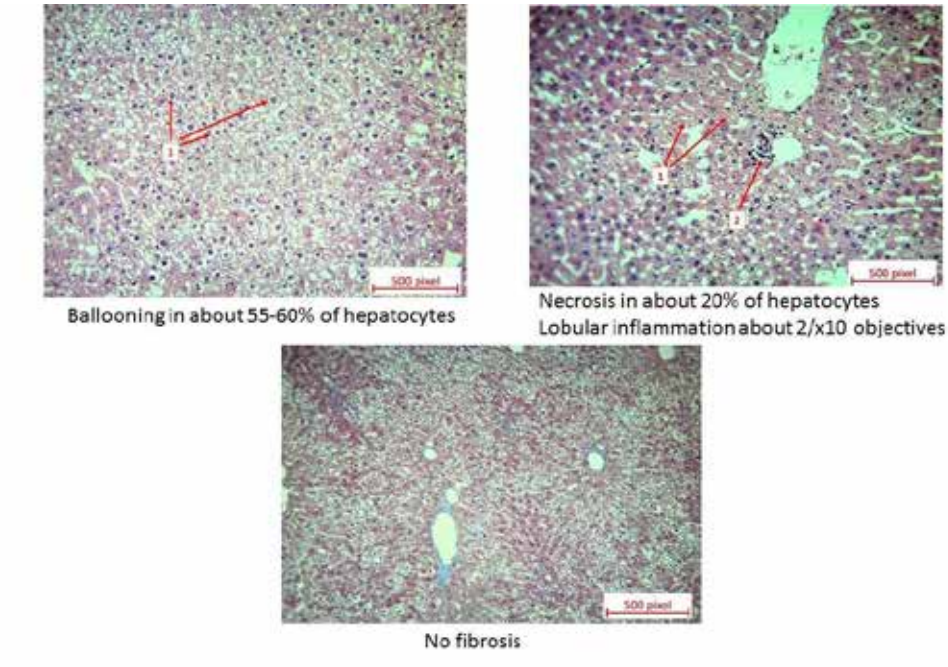


Figure 8. Pathology findings of liver biopsy from HFD+N/S group (×10 objective)

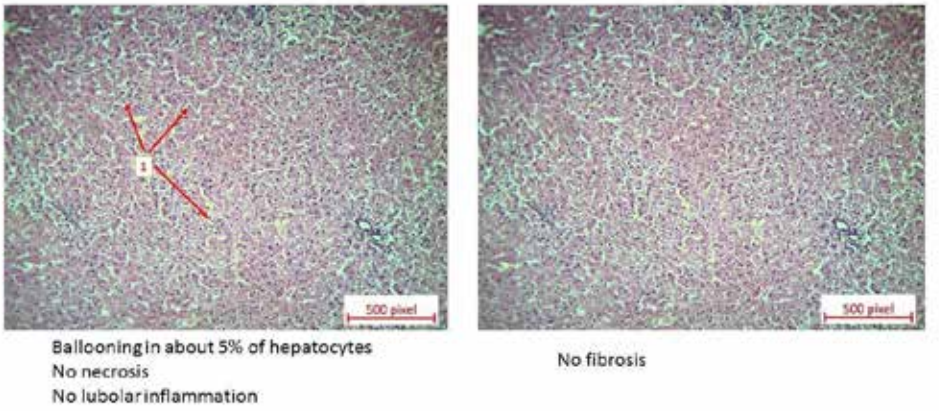


Figure 9. Pathology findings of liver biopsy from control group (×10 objective)

Funding Statement

This work has received financial support from the research deputy of Iran University of Medical Sciences, Tehran, Iran (grant number 16603).

Conflict of Interests

We have no conflict of interest to disclose.

Acknowledgements

The authors would like to thank Dr. Vosoogh and Dr. Abdollahi for their assistance.

References

[1] Sergi CM. NAFLD (MASLD)/NASH (MASH): Does it bother to label at all? a comprehensive narrative review. Int J Mol Sci 2024;25:8462.

[2] Amorim R, Magalhães CC, Borges F, Oliveira PJ, Teixeira J. From non-alcoholic fatty liver to Hepatocellular Carcinoma: A Story of (Mal) adapted Mitochondria. Biology 2023;12:595.

[3] Cobbina E, Akhlaghi F. Non-alcoholic fatty liver disease (NAFLD) - pathogenesis, classification, and effect on drug metabolizing enzymes and transporters. Drug Metab Rev 2017;49:197-211.

[4] Tapper EB, Parikh ND. Diagnosis and management of cirrhosis and its complications: a review. JAMA 2023;329:1589-1602.

[5] Yasui K, Hashimoto E, Komorizono Y, Koike K, Arii S, et al. Characteristics of patients with nonalcoholic steatohepatitis who develop hepatocellular carcinoma. Clin Gastroenterol Hepatol 2011;9:428-433

[6] Fazel Y, Koenig AB, Sayiner M, Goodman ZD, Younossi ZM. Epidemiology and natural history of non-alcoholic fatty liver disease. Metabolism Clin Experiment 2016;65:1017-1025.

[7] Yan T, Yan N, Wang P, Xia Y, Hao H, et al. Herbal drug discov-

ery for the treatment of nonalcoholic fatty liver disease. Acta Pharm Sin B 2020;10:3-18.
[8] Neuschwander-Tetri BA. Non-alcoholic fatty liver disease. BMC Med 2017;15:45.
[9] Paik JM, Henry L, Younossi Y, Ong J, Alqahtani S, et al. The burden of nonalcoholic fatty liver disease (NAFLD) is rapidly growing in every region of the world from 1990 to 2019. Hepatol Commun 2023;7:e0251.
[10] Rong L, Zou J, Ran W, Qi X, Chen Y, et al. Advancements in the treatment of non-alcoholic fatty liver disease (NAFLD). Front Endocrinol 2023;13:1087260.
[11] Hegazi OE, Alalalmeh SO, Alnuaimi GRH, Shahwan M, Jairoun AA, et al. NAFLD and nutraceuticals: A review of completed phase III and IV clinical trials. Front Med 2023;10:1227046.
[12] Gong P, Long H, Guo Y, Wang Z, Yao W, et al. Chinese herbal medicines: The modulator of nonalcoholic fatty liver disease targeting oxidative stress. J Ethnopharmacol 2024;318:116927.
[13] Barghi M, Alemzadeh E. Role of herbal remedies in liver fibrosis: what is the evidence? J Fasa Uni Med Sci 2020;10:2164-2178.
[14] Latief U, Ahmad R. Herbal remedies for liver fibrosis: A review on the mode of action of fifty herbs. J Tradit Complement Med 2018;8:352-360.
[15] Javanmard M, Asadi-Gharneh HA, Nikneshan P. Characterization of biochemical traits of dog rose (Rosa canina L.) ecotypes in the central part of Iran. Nat Prod Res 2018;32:1738-1743.
[16] Selahvarzian A, Alizadeh A, Baharvand PA, Eldahshan OA, Rasoulian B. Medicinal properties of Rosa canina L. Herb Med J 2018;3:77-84.
[17] Pehlivan M, Mohammed FS, Sevindik M, Akgul H. Antioxidant and oxidant potential of Rosa canina. Eur J For Sci 2018;6:22-25.
[18] Amintaheri N, Tehranipour M, Balanezhad SZ. The Effects of aqueous extracts of Rosa canina L fruit on hippocampus neuronal density in male mouse. Pejouhesh dar Pezeshki. 2018;41:251-257
[19] Demir F, Özcan M. Chemical and technological properties of rose (Rosa canina L.) fruits grown wild in Turkey. J Food Eng 2001;47:333-336.
[20] Gruenwald J, Uebelhack R, Moré MI. Rosa canina - Rose hip pharmacological ingredients and molecular mechanics counteracting osteoarthritis - A systematic review. Phytomedicine 2019;60:152958.
[21] Popović-Djordjević J, Špirović-Trifunović B, Pećinar I, de Oliveira LFC, Krstić Đ, et al. Fatty acids in seed oil of wild and cultivated rosehip (Rosa canina L.) from different locations in Serbia. Ind Crops Prod 2023;191:115797.
[22] Mármol I, Sánchez-de-Diego C, Jiménez-Moreno N, Ancín--Azpilicueta C, Rodríguez-Yoldi MJ. Therapeutic applications of rose hips from different Rosa species. Int J Mol Sci 2017;18:1137.
[23] Wenzig EM, Widowitz U, Kunert O, Chrubasik S, Bucar F, et al. Phytochemical composition and in vitro pharmacological activity of two rose hip (Rosa canina L.) preparations. Phytomedicine 2008;15:826-835.
[24] Kılıçgün H, Altıner D. Correlation between antioxidant effect mechanisms and polyphenol content of Rosa canina. Pharmacogn Mag 2010;6:238-241.
[25] Chrubasik C, Roufogalis BD, Müller-Ladner U, Chrubasik S. A systematic review on the Rosa canina effect and efficacy profiles. Phytotherapy research. 2008;22:725-733.
[26] Ayati Z, Amiri MS, Ramezani M, Delshad E, Sahebkar A, et al. Phytochemistry, traditional uses and pharmacological profile of rose hip: a review. Curr Pharm Des 2018;24:4101-4124.
[27] Miljković VM, Nikolić L, Mrmošanin J, Gajić I, Mihajilov-Krstev T, et al. Chemical profile and antioxidant and antimicrobial activity of rosa canina l. dried fruit commercially available in Serbia. Int J Mol Sci 2024;25:2518
[28] Aghili-Khorasani MH. Makhzan al adviah. Tehran: Safir Ardehal 2015:870
[29] Rahimi M, Sajadimajd S, Mahdian Z, Hemmati M, Malekkhatabi P, et al. Characterization and anti-diabetic effects of the oligosaccharide fraction isolated from Rosa canina in STZ-Induced diabetic rats. Carbohydr Res 2020;489:107927.
[30] Fattahi A, Niyazi F, Shahbazi B, Farzaei MH, Bahrami G. Antidiabetic mechanisms of Rosa canina fruits: an in vitro evaluation. J Evid Based Complemen Alternat Med 2017;22:127-33.
[31] Sanz-Lamora H, Nicola-Llorente M, Torres-Oteros D, Pérez-Martí A, Aghziel I, et al. The antiobesity effects of Rosehip (Rosa canina) flesh by antagonizing the PPAR gamma activity in high-fat diet-fed mice. Mol Nutr Food Res 2024;68:2300539.
[32] Bahrami G, Naseri R, Khosravifar M, Sajadimajd S, Mohammadi B, et al. The safety and effectiveness of a polysaccharide extracted from rosa canina in patients with NAFLD: a randomized trial. Clin Diabetol 2022;11:239-244.
[33] Tapia G, Silva D, Romero N, Pettinelli P, Dossi CG, et al. Role of dietary α-and γ-tocopherol from Rosa mosqueta oil in the prevention of alterations induced by high-fat diet in a murine model. Nutrition 2018;53:1-8.
[34] Davoodi I, Rahimi R, Abdollahi M, Farzaei F, Farzaei, et al. Promising effect of Rosa damascena extract on high-fat diet-induced nonalcoholic fatty liver. J Tradit Complement Med 2017;7:508-514.
[35] Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, et al. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. Br J Pharmacol 2020;177:3617-3624.
[36] Hosseinzadeh H, Zarei H, Taghiabadi E. Antinociceptive, anti-inflammatory and acute toxicity effects of juglans regia L. Leaves in mice, Iran. Red Crescent Med J 2011;13:27-33.
[37] Lackner C. Hepatocellular ballooning in nonalcoholic steatohepatitis: the pathologist's perspective. Expert Rev Gastroenterol Hepatol 2011;5:223-231.
[38] Maurice J, Manousou P. Non-alcoholic fatty liver disease. Clin Med 2018;18:245-50.
[39] Xu Y, Guo W, Zhang C, Chen F, Tan HY, et al. Herbal medicine in the treatment of non-alcoholic fatty liver diseases-efficacy, action mechanism, and clinical application. Front Pharmacol 2020;11:601.
[40] Orhan N, Aslan M, Hosbas S, Deliorman OD. Antidiabetic effect and antioxidant potential of Rosa canina fruits. Pharmacogn Mag 2009;5:309-315.
[41] Ekstedt M, Franzén LE, Mathiesen UL, Thorelius L, Holmqvist M, et al. Long-term follow-up of patients with NAFLD and elevated liver enzymes. Hepatology 2006;44:865-873.
[42] Senior JR. Alanine aminotransferase: a clinical and regulatory tool for detecting liver injury-past, present, and future. Clin Pharmacol Ther 2012;92:332-339.
[43] Kavgani A, Ghorbani A, Eidi A, Sasaninejad S, Ahmarinejad A. The antidiabetic effect of Rosa canina fruit in alloxan-induced diabetic male rats. Qom Univ Med Sci J 2015;9:23-34.
[44] Gholamhoseinian A, Fallah H, Sharifi far F. Inhibitory effect

of methanol extract of Rosa damascena Mill. flowers on alpha-glucosidase activity and postprandial hyperglycemia in normal and diabetic rats. Phytomedicine 2009;16:935-941.

[45] Andersson U, Henriksson E, Ström K, Alenfall J, Göransson O, et al. Rose hip exerts antidiabetic effects via a mechanism involving downregulation of the hepatic lipogenic program. Am J Physiol Endocrinol Metab 2011;300:111-121

[46] Cavalera M, Axling U, Berger K, Holm C. Rose hip supplementation increases energy expenditure and induces browning of white adipose tissue. Nutr Metab 2016;13:91.

[47] Nagatomo A, Nishida N, Matsuura Y, Shibata N. Rosehip Extract inhibits lipid accumulation in white adipose tissue by suppressing the expression of peroxisome proliferator-activated receptor gamma. Prev Nutr Food Sci 2013;18:85-91.

[48] Farhadi J, Abdollahpour F, Ghasemi M, Kakaei Z, Karimi Z. Antioxidant and cytotoxicitic effects of aqueous and alcoholic extracts of Rose Canina fruit on on the cell line U937. Yafte 2015;17:15-25

[49] Sadeghi H, Hosseinzadeh S, Akbartabar Touri M, Ghavamzadeh M, Jafari Barmak M, et al. Hepatoprotective effect of Rosa canina fruit extract against carbon tetrachloride induced hepatotoxicity in rat. Avicenna J Phytomedicine 2016;6:181-188.

[50] Khosravi A. The simultaneous effect of eight weeks of aerobic exercise and hydroalcoholic extract of Rosa canina fruit on some serum liver enzymes and liver malondialdehyde in Wistar rats following a session of exhaustive aerobic activity. Tabriz Univ Med Sci J 2020;42:302-311.

[51] SM BK, Basirat E, Sheikhzadeh F, Hatami H. Effect of alcoholic extract of Rosa canina on hepatic tissue and hepatic enzymes activity in diabetic rats. J Ardabil Uni Med Sci 2017;17:81-89.

[52] Taghizadeh M, Rashidi AA, Taherian AA, Vakili Z, Mehran M. The protective effect of hydroalcoholic extract of rosa canina (Dog Rose) fruit on liver function and structure in streptozotocin-induced diabetes in rats. J Diet Suppl 2018;15:624-635.

[53] Orhan N, Aslan M, Hosbas S, Deliorman OD. Antidiabetic effect and antioxidant potential of Rosa canina fruits. Pharmacogn Mag 2009;5:309-315.