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Original article

Allium affine Extract Improves Dexamethasone-Induced Hyperlipidemia in Rats

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Abstract

Background and objectives: Various *Allium* plants were found to improve blood lipid profile. The present investigation explored the anti-hyperlipidemic potential of *A. affine* in a rat model of hyperlipidemia induced by glucocorticoid. **Methods:** Hydroalcoholic extract was prepared by maceration method and assessed for total phenolic content. Forty-eight male Wistar rats in eight groups were studied. Group I received vehicle; group II was treated only with 400 mg/kg *A. affine* orally; group III was subcutaneously injected with 10 mg/kg/day dexamethasone; group IV as the reference group received dexamethasone and 40 mg/kg atorvastatin orally; groups V-VIII were treated with dexamethasone and simultaneously with 50, 100, 200 or 400 mg/kg of *A. affine* extract orally. All treatments were done over a period of seven days. Blood levels of glucose, lipid profile, liver enzymes and malondialdehyde (MDA) were assessed in over-fasted rats. Liver tissues were weighed and evaluated for histopathological alterations. **Results:** The amount of total phenolics content of *A. affine* extract was 11.24 ± 1.7 mg/g as gallic acid equivalent. Administration of *A. affine* extract significantly lowered the blood levels of triglycerides, total cholesterol, low-density lipoprotein (LDL)-cholesterol, very low-density lipoprotein (VLDL)-cholesterol, blood sugar, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and MDA. However, there was no significant effect on high-density lipoprotein (HDL)-cholesterol level. *A. affine* improved hepatic steatosis resulted from dexamethasone. **Conclusion:** These findings suggest potential of *A. affine* for preventing and managing hyperlipidemia. However, more trials are needed concerning its clinical efficacy and identifying its bioactive phytochemicals and mechanisms participated in the lipid-lowering action.

Keywords: *Allium*; dexamethasone; hyperlipidemia; lipid peroxidation; rats

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Introduction

Hyperlipidemia is a condition characterized as hypercholesterolemia or hypertriglyceridemia and mainly caused by idiopathic, genetic factors or acquired diseases [1].

Development of atherosclerotic plaques in vasculature especially in the coronary arteries is a consequence of increased blood concentrations of total cholesterol, low-density lipoprotein (LDL)-cholesterol, and low concentrations of high-density lipoprotein (HDL)-cholesterol and considered as an important reason of death worldwide [2]. Several factors can raise the risk of atherosclerosis including dyslipidemia, high blood pressure, diabetes, smoking, family history

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of coronary heart disease at a young age and low physical activity [3].

Oxidative stress which occurs due to the overproduction of reactive oxygen species (ROS) and weakening of antioxidant system has a great impact on dyslipidemia. Various data have shown the significant relationship between blood concentrations of oxidative stress markers and atherogenic lipoproteins in cardiovascular disorders [4].

There is an ongoing interest in herbal and complementary medications for discovering novel effective hypolipidemic drugs since conventional medicines cannot treat some diseases like atherosclerosis effectively and have some side effects [5]. Several phytochemicals and herbal medicines have been described for their potential in the management of hyperlipidemia since ancient time [6].

Allium is a well-known genus in Amaryllidaceae family. More than 800 species from this genus have been recognized worldwide. There is a long history of edible or medicinal uses for some *Allium* plants like onion and garlic. *Allium* vegetables produce different active chemicals such as sulfur-containing compounds, saponins and flavonoids with many pharmacological activities especially beneficial effects against cardiovascular disorders through affecting blood glucose and blood pressure levels, lipid profile, coagulation and oxidative stress status [7,8].

Allium affine Ledeb. is an *Allium* plant which is found in Western Asian areas including the Caucasus, Lebanon, southern and eastern Turkey, Iraq, and western and central Iran. This perennial plant is harvested from the wild and used as a food [9].

Little information has been reported about the biological effects of *A. affine* extract including cytotoxic activity against breast and ovarian cancer cells, fibrinolytic and antioxidant properties [10,11]. To our knowledge, there is no data investigating the impact of *A. affine* on hyperlipidemia.

Regarding the presence of many effective compounds with possible useful effects on blood lipid profile and the evidence of hypolipidemic activities in various *Allium* species, the aim of this study was to investigate the effect of hydroalcoholic extract of *A. affine* in a model of glucocorticoid-induced hyperlipidemia in rats. Development of dyslipidemia is one of the metabolic adverse effects of glucocorticoids and is similar to what happens in metabolic syndrome [12]. In metabolic syndrome, atherogenic dyslipidemia is linked with chronic problems and mortality [13]. Regarding the high prevalence of metabolic syndrome (about 3% of children and 5% of adult) worldwide and its role as an important risk factor for atherosclerotic cardiovascular disorders [13], we used hyperlipidemia model caused by dexamethasone in this investigation.

Material and Methods

Ethical considerations

The research procedures was approved by the Institutional Research Ethics Committee of Isfahan University of Medical Sciences with ethic approval ID: IR.MUI.RESEARCH.REC.1400.332. The animal experimental practice was performed in accordance with the international guidelines for laboratory animal use and care.

Chemicals

Dexamethasone was prepared from Darou Pakhsh Pharmaceutical Co. (Iran). Atorvastatin was obtained from Abidi Pharmaceutical Laboratories Co. (Iran). The assay kits for evaluation of serum levels of triglycerides, total cholesterol, high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were purchased from Pars Azmoon Co. (Iran). The kit for malondialdehyde (MDA) assay was purchased from Hakiman Shargh Research Co. (Iran). All other chemicals including Folin-Ciocalteu reagent, gallic acid and formalin were obtained from Merck Co. (Germany).

Plant material

Aerial parts of *A. affine* were collected during the month of April 2019 from the local sellers at Borujen (Chaharmahal and Bakhtiari Province) in the southwestern part of Iran. The plant was authenticated with a voucher specimen (No. 3403) stored at the Herbarium of the Department of Pharmacognosy, Isfahan University of Medical Sciences. The dried *A. affine* aerial parts were pulverized followed by hydroalcoholic extraction with 70% ethanol by maceration technique for 72 h, three times at room temperature. The extract was filtered and ethanol was removed by rotary evaporation at 50 °C and then subjected to freeze

drying. The obtained powder was kept at 4 °C. For oral administration in animals, the extract powder was dissolved in normal saline and administered using an intra-gastric tube.

Determination of total phenolics content

Folin-Ciocalteu method was used for estimation of the amount of total phenolic compounds in the hydroalcoholic extract of *A. affine* as a common assay for standardizing of the extracts [14]. In this spectrophotometrical test, the extract or standard samples were mixed with sodium bicarbonate (20%) and then with diluted Folin-Ciocalteu reagent. After 120 min incubation at room temperature, the absorbance was measured by an ultraviolet (UV)-visible spectrophotometer at 765 nm using. A standard curve was depicted by different concentrations of gallic acid and was used for quantitation of total phenolics content in the samples. The results were specified in terms of mg of gallic acid equivalents (GAE)/g of dried extract [15].

Animals

Forty-eight male Wistar rats (230-250 g) were attained from the animal house of the School of Pharmacy and Pharmaceutical Sciences (Isfahan, Iran). They were housed under standard laboratory condition including room temperature of 20-25 ºC and a daily routine with 12 h of light; standard diet and water were provided. The animals were acclimatized for one week prior to experimentation.

Induction of hyperlipidemia

The glucocorticoid-induced hyperlipidemia model was developed using the subcutaneously (s.c.) administration of dexamethasone 10 mg/kg for seven days in rats [16]. Animals were weighed at the start of the experiment ant then on every other day. At the end of the study period, all rats were kept fasting during overnight and the blood samples were taken by retro-orbital technique from the anesthetized animals. The serum samples were used for biochemical evaluations. Moreover, the liver samples were collected from from rats which were sacrificed with exposure to CO_2. Livers were weighed and immersed in 10% formalin solution and used for histopathological analysis after additional processing.

Experimental protocol

Rats were randomly divided into 8 groups, each comprising of 6 rats as follows: The first group as the normal control received daily injection of normal saline (1 ml/kg, s.c.) and oral administration of the vehicle. The second group as the extract control, received only *A. affine* hydroalcoholic extract orally at the dose of 400 mg/kg. In the third group as the hyperlipidemic control group, dexamethasone (10 mg/kg/day, s.c.) was administered. Group IV as the reference group received dexamethasone and atorvastatin (40 mg/kg, orally) [17]. In groups V-VIII as the test groups, rats were treated with dexamethasone and simultaneously with 50, 100, 200 or 400 mg/kg of *A. affine* hydroalcoholic extract orally. Different doses of *A. affine* hydroalcoholic extract were selected based on the previous study confirming their safety and efficacy [10]. All treatments were done over a period of seven days.

Biochemical analysis

The commercial biochemical kits were used for assessment of the serum levels of blood glucose, total cholesterol, HDL, LDL, triglyceride, aspartate aminotransferase (AST) and alanine aminotransferase (ALT). The intra- and inter-assay coefficients of variation were 1.50% and 0.90% for glucose and the kit had assay sensitivity of 5 mg/dL. The intra-assay coefficients of variation were 0.95%, 0.78%, 1.60%, 2.0% and 2.54% for total cholesterol, HDL, triglycerides, ALT and AST, respectively. The inter-assay coefficients of variation were 1.09%, 1.8%, 1.23%, 2.01% and 3.61% for total cholesterol, HDL, triglycerides, ALT and AST, respectively. The assay sensitivities of kits were 5 mg/dl, 1 mg/dl, 5 mg/dl, 4 IU/L, and 2 IU/L for total cholesterol, HDL, triglycerides, ALT and AST, respectively. Very low-density lipoprotein (VLDL)-cholesterol was calculated through dividing the triglyceride value by 5 [18].

The serum malondialdehyde (MDA) levels were estimated to evaluate the development of lipid peroxidation using a standard kit based on thiobarbituric acid reactive substances technique [19]. The intra- and inter-assay coefficients of variation were 4.1% and 7.2% for MDA. The detection range for MDA assay was 2.92-40 µM with sensitivity of 1.13 µM.

Histopathological analysis

After cutting in small pieces, the liver tissues were immersed in neutral buffered formalin for 24 h. The fixed specimens were subjected to

processing through sequential steps including dehydrating in ascending grades of alcohol and then embedding in paraffin, sectioning at 5 μm thickness, deparaffinization, rehydrating and finally staining with hematoxylin and eosin. The liver sections were detected microscopically for histopathological alterations [20].

Statistical analysis

Data were presented as mean ± standard deviation (SD) and subjected to Shapiro-Wilk normality test and one-way analysis of variance (ANOVA) followed by Tukey post-hoc test using the statistical package for the social sciences (SPSS software version 18.0). The p value <0.05 was considered as significant level.

Results and Discussion

In this animal study, the effects of hydroalcoholic extract of *A. affine* as an *Allium* vegetable with limited pharmacological data were investigated in a rat model of hyperlipidemia caused by dexamethasone.

The yield of *A. affine* extraction was 27.5% (w/w). Measurement of total phenolics content indicated 11.24 ± 1.7 mg GAE/g of dried aerial parts of *A. affine* extract. In the study of Chang et al., evaluation of hydroalcoholic extract of different plant tissues of *A. sativum* for total phenolics showed a variety from 82.86 to 182.60 mg GAE/g [21]. However, Beato et al. reported total phenolic contents of 3.4 - 10.8 mg GAE/g in different cultivar of dried garlic [22]. Plants of *Allium* have shown wide variations in the amount of phenols and flavonoid constituents in various surveys depending on the cultivar, place of growth, parts of plant tissues and type of extraction [23].

In the present investigation, dexamethasone-induced hyperlipidemia was used for estimation of anti-hyperlipidemic potential of *A. affine* extract. Dexamethasone is a corticosteroid hormone with strong glucocorticoid activities. Despite the wide clinical applications in relieving inflammation and allergies, preventing graft rejection and also treating certain types of cancers by glucocorticoids, many harmful side effects may occur by their long-term use. Dexamethasone disturbs the fat metabolism and increases blood sugar which may result in illnesses like hyperlipidemia, diabetes and metabolic syndrome [18].

In glucocorticoids-induced dyslipidemia, the amount of serum fatty acids and lipids are amplified due to the increased lipolysis in adipose tissue and more synthesis of fatty acid and VLDL in liver tissue, and also due to the decreased clearance of lipoproteins in circulation through affecting lipoprotein receptors and apolipoprotein genes [24]. Dexamethasone reduces the activity of lecithin cholesterol acetyl transferase and down regulates the LDL receptor and subsequently inhibits the uptake and catabolism of LDL which finally leads to an increase in total serum cholesterol [25,26]. Glucocorticoids cause more lipid and fatty acids synthesis and less production of triacylglycerol through motivation of adenosine monophosphate (AMP)-activated protein kinase in the liver. Moreover, decreased activity of hepatic lipoprotein lipase, augmented lipogenesis as a result of increases in the activity of acetyl-coenzyme A (CoA) carboxylase and fatty acid synthase are contributed in the development of glucocorticoids-induced fatty liver [27,28].

Dexamethasone also persuades hyperglycemia and insulin resistance through hindering glucose uptake by peripheral tissues and disturbing insulin signaling pathway [29]. In our study, seven-days exposure of rats to the high dosage of dexamethasone led to significant rise in blood concentrations of total cholesterol ($p<0.05$), LDL ($p<0.05$), VLDL ($p<0.001$), triglyceride ($p<0.001$) and fasting blood sugar ($p<0.05$), and a notable decrease in HDL value ($p<0.05$) in comparison with the normal values in control group (Table 1).

As presented in Table 1, oral administration of hydroalcoholic extract of *A. affine* at all doses (100, 200 and 400 mg/kg) caused prominent reduction in serum levels of triglycerides, LDL and VLDL. It showed anti-hypercholesterolemic effect at the doses of 200 and 400 mg/kg. *A. affine* extract had no meaningful effect on HDL level. The high dose of *A. affine* extract resulted in an important reduction of 56.83% in LDL, 51.92% in VLDL, 28.87% in total cholesterol, 43.18% in triglycerides, and 26.98% in fasting blood glucose levels in dexamethasone-induced hyperlipidemic animals. However, no significant result was detected on HDL value. In this study, atorvastatin was used as a standard anti-hyperlipidemic agent and improved dyslipidemia by significant reduction in serum levels of triglycerides by 57.72% ($p<0.01$), total cholesterol by 22.83% ($p<0.01$), LDL by 49.51% ($p<0.001$) and VLDL by 64.23% ($p<0.001$), and notable elevation in HDL level by 50.00%

($p<0.05$) without any change in fasting blood sugar (FBS) (Table 1).

Many surveys have presented beneficial effects for various *Allium* plants in improving the blood glucose and lipid profile, and subsequently preventing cardiovascular disorders. After treatment with *A. sativum* (garlic) for 90 days, a major decrease in LDL by 37.7%, in total cholesterol by 33.2%, and a 12.6% elevation in HDL concentrations were reported in an animal model of hyperlipidemia [30]. *Allium cepa* (onion) also exhibited 23% reduction in cholesterol and 37% decrease in LDL in rats with high serum cholesterol levels [31]. Moreover, clinical investigations have shown the potential of garlic on improving serum lipid profile by declining serum cholesterol and triglyceride levels [32]. According to a meta-analysis, garlic consumption for 60 days has a great impact on serum lipids that reduces cholesterol and LDL concentrations (by 17±6 and 9±6 mg/dL, respectively) as well as somewhat raises in HDL levels, with no result on triglycerides value [33].

Allium spp. may exert their hypolipidemic properties through a variety of mechanisms such as stimulating insulin release, regulating the genes that control glucose and lipid metabolism, preventing the gastrointestinal absorption of cholesterol and its biosynthesis by the liver and conversely increasing its clearance [34,35].

A recent animal study has revealed the hypolipidemic activity for polyphenols-rich *A. cepa* extract through up regulation of LDL receptor and down regulation of 3-hydroxy-3-methylglutaryl (HMG) -CoA reductase [36]. In our previous investigation, *A. affine* exhibited fibrinolytic and antioxidative effects which may contribute to its anti-atherosclerotic activity [10].

The cardiovascular protective properties of the *Allium* spp. are due to their major compounds including polyphenolics like quercetin, saponin or triterpene glycosides and sulfur-containing compounds [26]. *Allium affine* has been found to contain polyphenolics, organo-sulfuric compounds, steroidal saponin and sapogenins including diosgenin, tigogenin and ruscogenin [37]. Potent anti-hyprlipidemic activity has been reported for saponins via reducing absorption of cholesterol and regulating cholesterol turnover [38].

Our data showed a noticeable reduction in body weight of animals receiving dexamethasone in comparison with normal control rats ($p<0.001$). Dexamethasone has caused significant decrease in the animal body weights in some experimental models due to the lowering the body weight set point [39]. However due to the severe body weight declining in the current study, treatment with *A. affine* extract and atorvastatin was not able to improve body weight loss stimulated by dexamethasone (Table 2). Dexamethasone also promoted significant increase in the relative liver weight (liver/body weight ratio) in hyperlipidemic rats ($p<0.01$); however, no significant effect was found after administration of various doses of *A. affine* extract and atorvastatin in this glucocorticoid-induced complication (Table 2).

Table 1. Effect of hydroalcoholic extract of *Allium affine* on serum biochemical parameters in dexamethasone-induced hyperlipidemia

Groups	TG (mg/dL)	TC (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)	HDL (mg/dL)	FBS (mg/dL)	AST (IU/L)	ALT (IU/L)
Normal control	115.2 ±17.9	100.5 ± 7.3	30.5 ± 3.6	22.0 ± 8.9	60.2 ± 8.7	100.2 ± 8.1	95.7 ± 28.6	131.2 ± 20.5
***A. affine* control (400 mg/kg)**	105.6 ±11.5	98.2 ± 8.9	31.0 ± 6.3	21.3 ± 5.2	54.9 ± 8.9	91.5 ± 8.5	118.5 ±39.1	162.3 ± 28.1
Dex-induced hyperlipidemic control	235.8±43.7$^{###}$	120.9 ± 9.1$^{\#}$	41.2 ± 8.0$^{\#}$	53.3±5.5$^{###}$	46.5 ± 4.2$^{\#}$	126.2±26.2$^{\#}$	260±88.0$^{###}$	275.2±72.3$^{###}$
Dex+Atorvastatin (40 mg/kg)	93.3±10.1***	93.3 ± 5.2**	20.7±4.5***	18.9 ± 6.0*	64.1 ± 8.9*	106.3 ±11.4	127.7±47.5*	134.3 ±41.5**
Dex + *A. affine* (50 mg/kg)	211.3 ± 45.9	111.2 ± 6.4	32.2 ± 7.1	40.2 ± 9.1	49.2 ± 11.7	116.7 ±13.0	259.7±54.1	181.5 ± 35.7
Dex + *A. affine* (100 mg/kg)	168.0 ± 54.1*	103.4 ±13.9	22.4±2.3***	34.6 ± 9.5*	57.3 ± 5.7	92.5 ± 9.8	215.3 ±73.2	182.0 ± 50.2
Dex + *A. affine* (200 mg/kg)	129.3±22.6***	97.7±14.53*	21.9±4.5***	25.8±7.4***	60.1 ± 7.4	107.2 ±14.8	176.3 ±52.4	150.1 ± 38.4*
Dex + *A. affine* (400 mg/kg)	125.2±31.7***	86.3±10.1***	17.7±6.3***	25.1±7.1***	54.7 ± 8.5	102.5±16.4*	112.7±40.3**	113.7±34.8***

Values are means ± SD (n=6); Tukey post hoc analysis, $^{\#}p<0.05$ and $^{###}$ $p<0.001$ versus normal control, and $^{*}p<0.05$, $^{**}p<0.01$ and $^{***}p<0.001$ versus Dex control; ALT: alanine aminotransferase, AST: aspartate aminotransferase, Dex: dexamethasone, FBS: fasting blood sugar, HDL: high-density lipoprotein-cholesterol, LDL: low-density lipoprotein-cholesterol, TC: total cholesterol, TG: triglycerides, VLDL: very low-density lipoprotein-cholesterol

Table 2. Effect of hydroalcoholic extract of *Allium affine* on body and liver weight in dexamethasone-induced hyperlipidemia

Groups	Initial body weight (g)	Final body weight (g)	Relative liver weight (%)
Normal control	248.0 ± 7.9	262.9 ± 8.8	4.3 ± 0.9
***Allium affine* control (400 mg/kg)**	244.3 ± 9.5	249.9 ± 7.3	4.0 ± 0.8
Dex-induced hyperlipidemic control	250.3 ± 13.1	209.2 ± 6.9$^{###}$	5.5 ± 0.4$^{##}$
Dex + Atorvastatin (40 mg/kg)	241.5 ± 6.9	206.5 ± 9.1$^{###}$	4.6 ± 0.4
Dex + *Allium affine* (50 mg/kg)	253.7 ± 14.3	211.3 ± 10.4$^{###}$	5.4 ± 0.2$^{#}$
Dex + *Allium affine* (100 mg/kg)	242.4 ± 8.2	205.5 ± 9.9$^{###}$	5.1 ± 0.4
Dex + *Allium affine* (200 mg/kg)	252.0 ± 7.8	211.2 ± 9.3$^{###}$	4.8 ± 0.3
Dex + *Allium affine* (400 mg/kg)	241.0 ± 10.4	204.1 ± 11.2$^{###}$	4.9 ± 0.2

Values are means ± SD (n=6); Tukey post hoc analysis, #p<0.05, ##p<0.01, ### p<0.001 versus normal control. Dex: dexamethasone

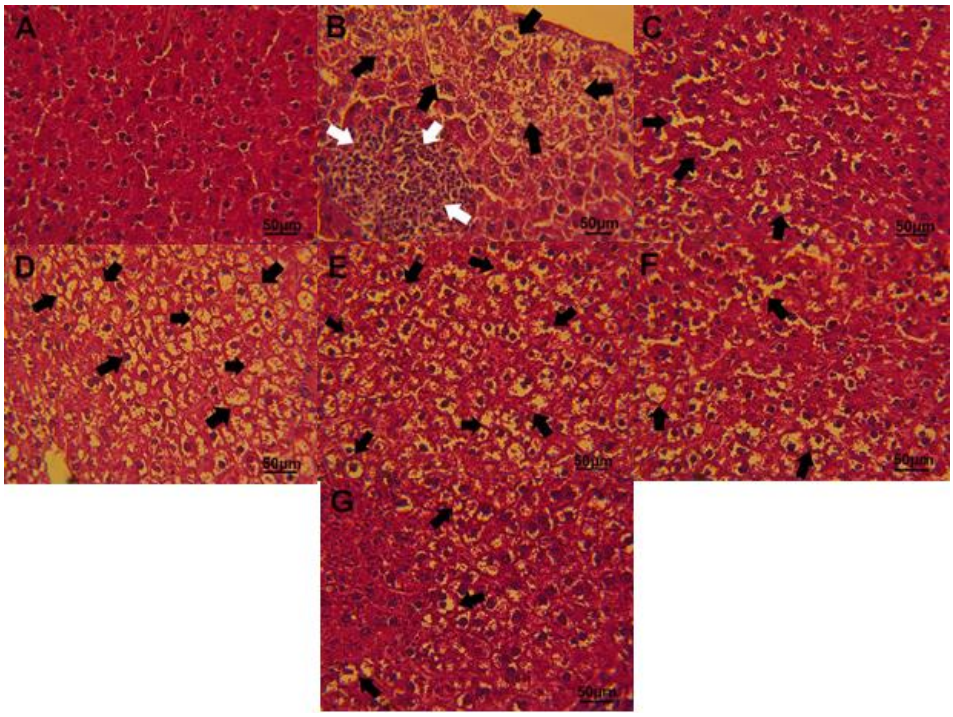

Figure 1. Representative H & E histological sections of the liver tissue of normal control group showing normal hepatocytes appearance (A); dexamethasone-induced dyslipidemic group showing diffused steatosis, fatty degeneration and cellular swelling, (B); atorvastatin treated group showing mild vesicular steatosis (C); *Allium affine* extract treated groups with doses of 50 mg/kg (D), 100 mg/kg (E), 200 mg/kg (F) and 400 mg/kg showing moderate vesicular steatosis (G), ×400 magnification; Black arrows indicate steatosis, and white arrows indicate infiltration of inflammatory cells.

Dexamethasone also caused major elevations in serum levels of AST and ALT as the biomarkers for liver damage (p<0.001). Atorvastatin and *A. affine* extract at its higher doses improved biomarkers of hepatic function (Table 1).

Assessment of the animals' hepatic tissues for histopathological changes presented infiltration of inflammatory cells, lipid accumulation and diffused steatosis of hepatic parenchymal cells after exposure to the high dose of dexamethasone in comparison with the typical feature of the normal hepatocytes (Figures 1A and 1B). Evaluation of liver tissue in atorvastatin treated rats indicated prominent decrease in steatosis (Figure 1C). Although *A. affine* extract at the dose of 50 mg/kg did not show remarkable effect (Figure 1D), it improved liver histopathological alterations at the doses of 100 mg/kg (Figure 1E), 200 mg/kg (Figure 1F) and 400 mg/kg (Figure 1G).

It is noteworthy that hepato-protective activities have been reported for various *Allium* plants in different liver damage conditions such as diabetic hepatopathy or ethanol-induced liver toxicity by improving oxidant/antioxidant balance and increasing antioxidants including catalase, glutathione and glutathione peroxidase [40,41].

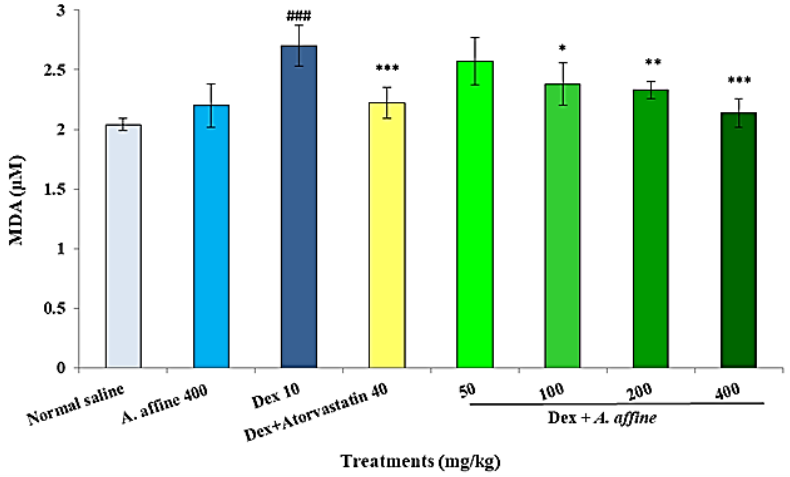

Figure 2. Effects of *Allium affine* extract (50, 100, 200 and 400 mg/kg) and atorvastatin (40 mg/kg) on serum MDA level in dexamethasone (Dex)-induced dyslipidemia; values are means ± SD (n=6); ###p<0.001 versus normal control, and *p<0.05, **p<0.01 and ***p<0.001 versus Dex control

In dexamethasone-induced dyslipidemia, oxidative damage is also participated in the pathogenesis of various complication of glucocorticoid excess [19]. Our data exhibited significant anti-lipid peroxidation effects for *A. affine* extract (100-400 mg/kg) and atorvastatin through decreasing MDA level in dyslipidemia caused by dexamethasone (Figure 2). In a previous investigation, *A. affine* extract has been recognized as a potent antioxidant like other *Allium* plants via increasing the total antioxidant power, scavenging the free radical and decreasing the hydroperoxides [10].

The main limitation of the current study included the lack of exploration of the mechanisms of antihyperglycemic and antihyperlipidemic effects of *A. affine* extract. Moreover, high doses of dexamethasone are required to induce hyperlipidemia which is associated with side effects such as skeletal muscle loss and severe body weight loss in laboratory animals [42].

Conclusion

In conclusion, our data exhibited that hydroalcoholic extract of *A. affine* aerial parts possessed blood lipid lowering activity in terms of reducing serum lipids, glucose, transaminases and lipid peroxides, and also improving liver histopathological changes in dexamethasone-induced dyslipidemic rats. Therefore, this herbal medicine may be useful as a preventive intervention for reducing the global burden of metabolic syndrome and the conditions that lead to it. However, more trials are suggested concerning the efficacy of *A. affine* in the managing of hyperlipidemia and identifying its bioactive phytochemicals and mechanisms participated in the lipid-lowering action.

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Author contributions

Leila Safaeian was responsible for the research plan, designing the animal study, supervising the investigation, analyzing the data and editing the manuscript; Masoud Sadeghi Dinani planned the herbal experiments; Moosa Mohsen and Yasaman Mohammadzamani performed the experiments, collected the data and prepared the draft of manuscript. All authors have read and agreed to the final version of the manuscript.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

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Abbreviations

ALT: alanine aminotransferase; AST: aspartate aminotransferase; Dex: dexamethasone; FBS: fasting blood sugar; GAE: gallic acid equivalents; HDL: high-density lipoprotein; LDL: low-density lipoprotein; MDA: malondialdehyde; ROS: reactive oxygen species; SD: standard deviation; TC: total cholesterol; TG: triglycerides; VLDL: very low-density lipoprotein