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# Amelioration of Glucocorticoid-Induced Dyslipidemia by Allium affine Extract in a Rat Model

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## ABSTRACT

Several species of the genus *Allium* have been shown to exert beneficial effects on serum lipid parameters. This study aimed to evaluate the antihyperlipidemic activity of *Allium affine* in a glucocorticoid-induced hyperlipidemia model in rats. A hydroalcoholic extract of *A. affine* was prepared using the maceration technique, and its total phenolic content was quantified. Forty-eight male Wistar rats were randomly assigned to eight experimental groups. Group I received the vehicle alone, while Group II was administered *A. affine* extract (400 mg/kg, orally). Hyperlipidemia was induced in Group III by subcutaneous injection of dexamethasone (10 mg/kg/day). Group IV served as a positive control and received dexamethasone along with atorvastatin (40 mg/kg, orally). Groups V–VIII were treated with dexamethasone in combination with *A. affine* extract at doses of 50, 100, 200, or 400 mg/kg, administered orally. All treatments were continued for seven consecutive days. Following an overnight fast, serum levels of glucose, lipid parameters, liver enzymes, and malondialdehyde (MDA) were measured. Liver weights were recorded, and histopathological examinations were performed. The total phenolic content of the *A. affine* extract was determined to be 11.24 ± 1.7 mg gallic acid equivalents per gram of extract. Treatment with *A. affine* extract resulted in a significant reduction in serum triglycerides, total cholesterol, low-density lipoprotein (LDL)-cholesterol, very low-density lipoprotein (VLDL)-cholesterol, glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and MDA levels. In contrast, no significant changes were observed in high-density lipoprotein (HDL)-cholesterol concentrations. Histological analysis revealed that *A. affine* administration alleviated dexamethasone-induced hepatic steatosis. The results indicate that *Allium affine* possesses promising antihyperlipidemic and hepatoprotective properties. Nevertheless, further studies are required to confirm its clinical effectiveness and to elucidate the active phytochemical constituents and underlying mechanisms responsible for its lipid-lowering effects.

**Keywords:** Lipid peroxidation, Dexamethasone, Allium, Rats, Hyperlipidemia

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## Introduction

Hyperlipidemia is defined by elevated levels of cholesterol and/or triglycerides in the bloodstream and may arise from idiopathic causes, genetic predisposition, or secondary conditions and diseases [1]. Increased serum concentrations of total cholesterol and low-density lipoprotein (LDL)-cholesterol, together with reduced levels of high-density lipoprotein (HDL)-cholesterol, contribute to the formation of atherosclerotic plaques within blood vessels, particularly in the coronary arteries, and represent a major cause of mortality worldwide [2]. Multiple factors are known to increase the risk of atherosclerosis, including dyslipidemia, hypertension, diabetes mellitus, tobacco use, a family history of early-onset coronary heart disease, and physical inactivity [3].

Oxidative stress, resulting from excessive production of reactive oxygen species (ROS) and impairment of endogenous antioxidant defenses, plays a crucial role in the development of dyslipidemia. Numerous studies have

demonstrated a strong association between circulating oxidative stress biomarkers and atherogenic lipoproteins in cardiovascular diseases [4].

Due to the limitations and adverse effects associated with conventional lipid-lowering therapies, there is growing interest in herbal and complementary medicines as alternative or adjunctive approaches for the development of new hypolipidemic agents [5]. Since ancient times, various medicinal plants and phytochemical compounds have been recognized for their potential benefits in the prevention and management of hyperlipidemia [6].

The genus *Allium*, belonging to the family Amaryllidaceae, comprises more than 800 identified species distributed globally. Several *Allium* species, including garlic and onion, have been widely consumed as food and utilized in traditional medicine. These plants are rich in bioactive constituents such as sulfur-containing compounds, saponins, and flavonoids, which exhibit diverse pharmacological properties, particularly cardioprotective effects mediated through modulation of blood glucose, blood pressure, lipid metabolism, coagulation pathways, and oxidative stress [7, 8].

*Allium affine* Ledeb. is a perennial species native to Western Asia, with a geographical distribution encompassing the Caucasus, Lebanon, southern and eastern regions of Turkey, Iraq, and western and central parts of Iran. This plant is commonly collected from natural habitats and traditionally used as a food source [9].

Limited studies have examined the biological activities of *A. affine* extract, with reported effects including cytotoxic activity against breast and ovarian cancer cell lines, as well as fibrinolytic and antioxidant properties [10, 11]. However, to date, no investigations have addressed its potential effects on hyperlipidemia.

Considering the presence of multiple bioactive compounds in *A. affine* and the documented lipid-lowering effects observed in other *Allium* species, the present study aimed to evaluate the impact of a hydroalcoholic extract of *A. affine* in a rat model of glucocorticoid-induced hyperlipidemia. Dyslipidemia is a well-recognized metabolic side effect of glucocorticoid therapy and closely resembles the lipid abnormalities observed in metabolic syndrome [12]. In metabolic syndrome, atherogenic dyslipidemia is strongly associated with chronic complications and increased mortality [13]. Given the substantial global prevalence of metabolic syndrome—affecting approximately 3% of children and 5% of adults—and its role as a major risk factor for atherosclerotic cardiovascular diseases [13], dexamethasone-induced hyperlipidemia was selected as the experimental model in this study.

## Materials and Methods

### *Ethical approval*

The study protocol received formal approval from the Research Ethics Committee of Isfahan University of Medical Sciences (Approval code: IR.MUI.RESEARCH.REC.1400.332). All animal experiments were carried out in strict accordance with internationally recognized standards governing the ethical use and care of laboratory animals.

### *Reagents and chemicals*

Dexamethasone was obtained from Darou Pakhsh Pharmaceutical Company (Iran), and atorvastatin was supplied by Abidi Pharmaceutical Laboratories (Iran). Commercial assay kits for the determination of serum triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were purchased from Pars Azmoon (Iran). Measurement of malondialdehyde (MDA) levels was performed using a kit provided by Hakiman Shargh Research Company (Iran). All other laboratory reagents, including Folin–Ciocalteu reagent, gallic acid, and formalin, were of analytical grade and sourced from Merck (Germany).

### *Collection and preparation of plant material*

The aerial portions of Allium affine were collected in April 2019 from local vendors in Borujen, a city located in Chaharmahal and Bakhtiari Province in southwestern Iran. Taxonomic authentication was conducted by a pharmacognosy specialist, and a reference specimen was archived at the Herbarium of the Department of Pharmacognosy, Isfahan University of Medical Sciences (voucher number: 3403). The harvested plant material was dried under ambient conditions and mechanically ground to obtain a uniform powder. Extraction was performed by soaking the powdered material in 70% ethanol using the maceration method for 72 hours at room temperature, with the procedure repeated three times to ensure maximum yield. The combined extracts were

filtered, concentrated under reduced pressure at 50 °C using a rotary evaporator, and subsequently freeze-dried to obtain a dry extract. The final extract was stored at 4 °C until use. For animal treatment, the dried extract was freshly dissolved in normal saline and administered orally using a gastric gavage tube.

*Assessment of total phenolic constituents*

Quantification of phenolic compounds present in the hydroalcoholic extract of *Allium affine* was carried out using the Folin–Ciocalteu colorimetric procedure, which is commonly applied for phytochemical standardization [14]. In brief, test solutions containing either the plant extract or reference standards were sequentially reacted with 20% sodium bicarbonate solution and diluted Folin–Ciocalteu reagent. The reaction mixtures were maintained at ambient temperature for a period of 120 minutes to allow chromogenic development. Absorbance readings were subsequently obtained at a wavelength of 765 nm using a UV–visible spectrophotometer. A calibration curve was constructed employing known concentrations of gallic acid, and this curve was used to determine phenolic content in the extract samples. Final values were expressed as milligrams of gallic acid equivalents (GAE) per gram of dried extract [15].

*Experimental animals*

Male Wistar rats (n = 48), weighing 230–250 g, were supplied by the animal facility of the School of Pharmacy and Pharmaceutical Sciences, Isfahan, Iran. Animals were housed under controlled environmental conditions, including a temperature range of 20–25 °C and a fixed 12-hour light/dark cycle. Access to standard pellet diet and water was unrestricted. Prior to initiation of experimental procedures, all rats were allowed to adapt to laboratory conditions for seven days.

*Establishment of hyperlipidemia model*

To induce hyperlipidemia, rats were administered dexamethasone subcutaneously at a dose of 10 mg/kg once daily for seven consecutive days, following a validated glucocorticoid-based protocol [16]. Body weight measurements were obtained at baseline and at alternate intervals throughout the experimental period. At study termination, animals underwent overnight fasting. Blood samples were then collected via the retro-orbital sinus under anesthesia, and serum was separated for biochemical testing. Following blood collection, animals were euthanized by carbon dioxide exposure. Liver tissues were excised immediately, weighed, and preserved in 10% formalin for histological processing.

*Treatment allocation and study design*

Animals were randomly assigned to eight groups, each containing six rats. The normal control group (Group I) received daily subcutaneous injections of physiological saline (1 ml/kg) along with oral vehicle administration. Group II served as the extract-only control and was given *A. affine* hydroalcoholic extract orally at a dose of 400 mg/kg. Hyperlipidemia control animals (Group III) were treated exclusively with dexamethasone (10 mg/kg/day, s.c.). Group IV functioned as the positive control and received dexamethasone in combination with atorvastatin (40 mg/kg, orally) [17]. Experimental treatment groups (Groups V–VIII) received dexamethasone alongside *A. affine* extract at oral doses of 50, 100, 200, or 400 mg/kg. Dose selection for the plant extract was based on earlier investigations confirming its safety and biological activity [10]. All interventions were maintained for a duration of seven days.

*Biochemical evaluations*

Serum biochemical parameters, including glucose, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, aspartate aminotransferase (AST), and alanine aminotransferase (ALT), were analyzed using validated commercial diagnostic kits in accordance with manufacturer protocols. For glucose determination, intra-assay and inter-assay variability were reported as 1.50% and 0.90%, respectively, with a minimum detectable concentration of 5 mg/dL. Intra-assay coefficients of variation for total cholesterol, HDL, triglycerides, ALT, and AST were 0.95%, 0.78%, 1.60%, 2.0%, and 2.54%, respectively, while inter-assay coefficients were 1.09%, 1.8%, 1.23%, 2.01%, and 3.61%. Assay sensitivities were 5 mg/dL for total cholesterol, 1 mg/dL for HDL, 5 mg/dL for triglycerides, 4 IU/L for ALT, and 2 IU/L for AST. Serum very-low-density lipoprotein (VLDL) cholesterol concentrations were calculated mathematically by dividing triglyceride values by five [18].

Oxidative lipid damage was assessed by determining serum malondialdehyde (MDA) concentrations using a thiobarbituric acid reactive substances–based assay kit [19]. The method demonstrated intra-assay and inter-assay coefficients of variation of 4.1% and 7.2%, respectively, with a detection range of 2.92–40 µM and an analytical sensitivity of 1.13 µM.

*Histological examination of liver tissue*

Excised liver samples were sectioned into small fragments and fixed in neutral buffered formalin for 24 hours. Standard histological processing was performed, including dehydration through graded ethanol solutions, paraffin embedding, microtome sectioning at 5 µm thickness, and subsequent deparaffinization and rehydration. Tissue sections were stained using hematoxylin and eosin and examined under light microscopy to identify structural and pathological changes [20].

*Statistical processing*

Experimental results were reported as mean ± standard deviation (SD). Data normality was assessed using the Shapiro–Wilk test. Group comparisons were performed using one-way analysis of variance (ANOVA), followed by Tukey's multiple comparison post hoc test. Statistical analyses were conducted using SPSS software (version 18.0), and statistical significance was defined as $p < 0.05$.

**Results and Discussion**

The present in vivo investigation examined the biological activity of the hydroalcoholic extract of *Allium affine*, an edible *Allium* species for which pharmacological evidence remains scarce, using a dexamethasone-induced hyperlipidemic rat model.

Extraction of the aerial parts of *A. affine* yielded 27.5% (w/w). Quantitative analysis of phenolic compounds revealed a total phenolic content of 11.24 ± 1.7 mg gallic acid equivalents (GAE) per gram of dried extract. Previous studies have reported considerable variability in phenolic levels among *Allium* species. For example, Chang *et al*. observed phenolic contents ranging from 82.86 to 182.60 mg GAE/g in hydroalcoholic extracts of different tissues of *Allium sativum* [21], whereas Beato *et al*. reported markedly lower values (3.4–10.8 mg GAE/g) across various dried garlic cultivars [22]. Such discrepancies are likely attributable to differences in plant genotype, geographic origin, harvested plant parts, and extraction techniques, all of which have been shown to influence phenolic and flavonoid composition in *Allium* plants [23].

In this study, a glucocorticoid-induced hyperlipidemia model was employed to assess the lipid-lowering potential of *A. affine*. Dexamethasone, a synthetic corticosteroid with potent glucocorticoid activity, is widely prescribed for inflammatory and allergic conditions, prevention of transplant rejection, and certain malignancies. However, prolonged exposure to glucocorticoids is associated with multiple metabolic disturbances, including impaired lipid and glucose homeostasis, leading to hyperlipidemia, diabetes, and metabolic syndrome [18].

Glucocorticoid-induced dyslipidemia is characterized by elevated circulating fatty acids and lipids, primarily resulting from enhanced lipolysis in adipose tissue, increased hepatic synthesis of fatty acids and very-low-density lipoproteins (VLDL), and reduced lipoprotein clearance due to alterations in lipoprotein receptors and apolipoprotein gene expression [24]. Dexamethasone further suppresses lecithin–cholesterol acyltransferase activity and downregulates LDL receptors, thereby limiting LDL uptake and catabolism and ultimately increasing serum cholesterol levels [25, 26]. In addition, glucocorticoids promote hepatic lipid accumulation by stimulating lipogenesis through activation of acetyl-coenzyme A (CoA) carboxylase and fatty acid synthase, reducing lipoprotein lipase activity, and modulating AMP-activated protein kinase signaling pathways, all of which contribute to fatty liver development [27, 28].

Dexamethasone also induces hyperglycemia and insulin resistance by inhibiting glucose uptake in peripheral tissues and disrupting insulin signaling cascades [29]. Consistent with these mechanisms, seven-day administration of dexamethasone at a high dose in the present study resulted in a significant elevation of serum total cholesterol ($p < 0.05$), LDL-cholesterol ($p < 0.05$), VLDL-cholesterol ($p < 0.001$), triglycerides ($p < 0.001$), and fasting blood glucose ($p < 0.05$), accompanied by a marked reduction in HDL-cholesterol ($p < 0.05$), compared with the normal control group **(Table 1).**

As shown in **Table 1**, concurrent oral treatment with *A. affine* extract at doses of 100, 200, and 400 mg/kg significantly reduced serum triglycerides, LDL, and VLDL concentrations in hyperlipidemic rats. A significant

cholesterol-lowering effect was observed at doses of 200 and 400 mg/kg. No statistically significant change in HDL levels was detected following extract administration. At the highest dose tested, *A. affine* extract reduced LDL by 56.83%, VLDL by 51.92%, total cholesterol by 28.87%, triglycerides by 43.18%, and fasting blood glucose by 26.98% in dexamethasone-treated animals, while HDL concentrations remained unaffected.

Atorvastatin, used as a standard hypolipidemic agent, effectively corrected dyslipidemia, producing significant reductions in serum triglycerides (57.72%, $p < 0.01$), total cholesterol (22.83%, $p < 0.01$), LDL (49.51%, $p < 0.001$), and VLDL (64.23%, $p < 0.001$), along with a notable increase in HDL levels (50.00%, $p < 0.05$), without influencing fasting blood glucose concentrations **(Table 1).**

Extensive evidence supports the beneficial role of *Allium* species in improving lipid and glucose metabolism and reducing cardiovascular risk. Administration of *Allium sativum* for 90 days in a hyperlipidemic animal model resulted in substantial reductions in LDL (37.7%) and total cholesterol (33.2%), alongside a 12.6% increase in HDL levels [30]. Similarly, *Allium cepa* demonstrated cholesterol- and LDL-lowering effects of 23% and 37%, respectively, in hypercholesterolemic rats [31]. Clinical studies have further confirmed the lipid-modulating effects of garlic, particularly in lowering serum cholesterol and triglycerides [32]. A meta-analysis reported that garlic supplementation for approximately 60 days significantly reduced total cholesterol and LDL levels, modestly increased HDL concentrations, and exerted no significant effect on triglycerides [33].

The hypolipidemic actions of *Allium* species are believed to involve multiple mechanisms, including enhancement of insulin secretion, modulation of genes governing lipid and glucose metabolism, inhibition of intestinal cholesterol absorption, suppression of hepatic cholesterol biosynthesis, and facilitation of cholesterol clearance from circulation [34, 35]. Supporting this, a recent animal study demonstrated that a polyphenol-rich *A. cepa* extract improved lipid profiles through upregulation of LDL receptors and downregulation of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase expression [36].

In earlier work, *A. affine* exhibited notable fibrinolytic and antioxidant activities, which may contribute to its anti-atherosclerotic potential [10]. The cardiovascular benefits attributed to *Allium* species are largely associated with their major bioactive constituents, including polyphenolic compounds such as quercetin, steroidal saponins and sapogenins, triterpene glycosides, and organosulfur compounds [26]. Phytochemical analyses have identified polyphenols, organosulfur compounds, and steroidal saponins—including diosgenin, tigogenin, and ruscogenin—in *A. affine* [37]. Saponins, in particular, have been reported to exert strong lipid-lowering effects by reducing cholesterol absorption and enhancing cholesterol turnover [38].

In the present study, dexamethasone administration caused a significant reduction in body weight compared with the normal control group ($p < 0.001$). This observation is consistent with previous reports indicating that dexamethasone decreases body weight by lowering the body weight set point [39]. Due to the pronounced weight loss observed, neither *A. affine* extract nor atorvastatin was able to reverse dexamethasone-induced weight reduction **(Table 2).** Additionally, dexamethasone significantly increased the relative liver weight (liver-to-body weight ratio) in hyperlipidemic rats ($p < 0.01$); however, treatment with *A. affine* extract or atorvastatin did not significantly alter this parameter **(Table 2).**

**Table 1.** Effects of Allium affine hydroalcoholic extract on serum biochemical indices in rats with dexamethasone-induced hyperlipidemia

| Experimental Group | Total Cholesterol (mg/dL) | Triglycerides (mg/dL) | VLDL-C (mg/dL) | LDL-C (mg/dL) | HDL-C (mg/dL) | Fasting Blood Glucose (mg/dL) | ALT (IU/L) | AST (IU/L) |
|---|---|---|---|---|---|---|---|---|
| Normal control | 100.5 ± 7.3 | 115.2 ± 17.9 | 22.0 ± 8.9 | 30.5 ± 3.6 | 60.2 ± 8.7 | 100.2 ± 8.1 | 131.2 ± 20.5 | 95.7 ± 28.6 |
| Dexamethasone-treated hyperlipidemic control | 120.9 ± 9.1# | 235.8 ± 43.7### | 53.3 ± 5.5### | 41.2 ± 8.0# | 46.5 ± 4.2# | 126.2 ± 26.2# | 275.2 ± 72.3### | 260.0 ± 88.0### |
| A. affine control (400 mg/kg) | 98.2 ± 8.9 | 105.6 ± 11.5 | 21.3 ± 5.2 | 31.0 ± 6.3 | 54.9 ± 8.9 | 91.5 ± 8.5 | 162.3 ± 28.1 | 118.5 ± 39.1 |

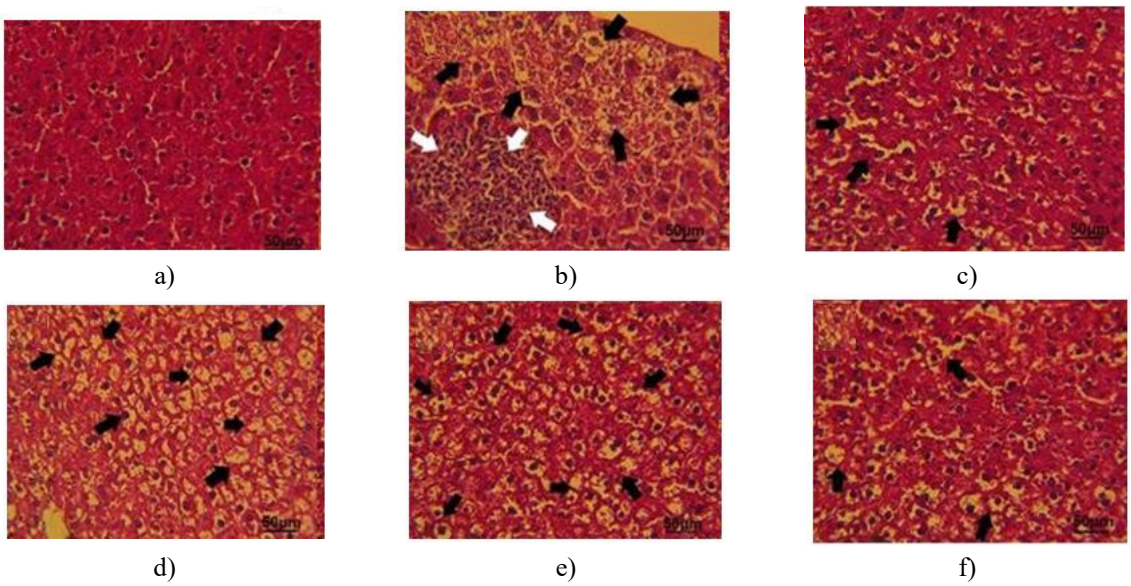
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Dexamethasone + A. affine (50 mg/kg) | 111.2 ± 6.4 | 211.3 ± 45.9 | 40.2 ± 9.1 | 32.2 ± 7.1 | 49.2 ± 11.7 | 116.7 ± 13.0 | 181.5 ± 35.7 | 259.7 ± 54.1 |
| Dexamethasone + Atorvastatin (40 mg/kg) | 93.3 ± 5.2** | 93.3 ± 10.1*** | 18.9 ± 6.0* | 20.7 ± 4.5*** | 64.1 ± 8.9* | 106.3 ± 11.4 | 134.3 ± 41.5** | 127.7 ± 47.5* |
| Dexamethasone + A. affine (100 mg/kg) | 103.4 ± 13.9 | 168.0 ± 54.1* | 34.6 ± 9.5* | 22.4 ± 2.3*** | 57.3 ± 5.7 | 92.5 ± 9.8 | 182.0 ± 50.2 | 215.3 ± 73.2 |
| Dexamethasone + A. affine (400 mg/kg) | 86.3 ± 10.1*** | 125.2 ± 31.7*** | 25.1 ± 7.1*** | 17.7 ± 6.3*** | 54.7 ± 8.5 | 102.5 ± 16.4* | 113.7 ± 34.8*** | 112.7 ± 40.3** |
| Dexamethasone + A. affine (200 mg/kg) | 97.7 ± 14.5* | 129.3 ± 22.6*** | 25.8 ± 7.4*** | 21.9 ± 4.5*** | 60.1 ± 7.4 | 107.2 ± 14.8 | 150.1 ± 38.4* | 176.3 ± 52.4 |

Data are expressed as mean ± standard deviation (SD) for six animals per group (n = 6). Statistical comparisons were performed using Tukey's post hoc test. $p < 0.05$ and ### $p < 0.001$ indicate significant differences compared with the normal control group, whereas * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$ denote significant differences relative to the dexamethasone-treated control group. ALT, alanine aminotransferase; AST, aspartate aminotransferase; Dex, dexamethasone; FBS, fasting blood glucose; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; VLDL, very-low-density lipoprotein cholesterol.

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

| Experimental groups | Body weight at study end (g) | Body weight at baseline (g) | Liver weight index (%) |
|---|---|---|---|
| A. affine alone (400 mg/kg) | 249.9 ± 7.3 | 244.3 ± 9.5 | 4.0 ± 0.8 |
| Healthy control | 262.9 ± 8.8 | 248.0 ± 7.9 | 4.3 ± 0.9 |
| Dexamethasone + atorvastatin (40 mg/kg) | 206.5 ± 9.1### | 241.5 ± 6.9 | 4.6 ± 0.4 |
| Dexamethasone-treated hyperlipidemic group | 209.2 ± 6.9### | 250.3 ± 13.1 | 5.5 ± 0.4## |
| Dexamethasone + A. affine (100 mg/kg) | 205.5 ± 9.9### | 242.4 ± 8.2 | 5.1 ± 0.4 |
| Dexamethasone + A. affine (50 mg/kg) | 211.3 ± 10.4### | 253.7 ± 14.3 | 5.4 ± 0.2# |
| Dexamethasone + A. affine (400 mg/kg) | 204.1 ± 11.2### | 241.0 ± 10.4 | 4.9 ± 0.2 |
| Dexamethasone + A. affine (200 mg/kg) | 211.2 ± 9.3### | 252.0 ± 7.8 | 4.8 ± 0.3 |

Values represent mean ± SD (n = 6). Group comparisons were analyzed using Tukey's post hoc procedure. $p < 0.05$, ## $p < 0.01$, and ### $p < 0.001$ indicate statistically significant differences compared with the normal control group. Dex: dexamethasone.



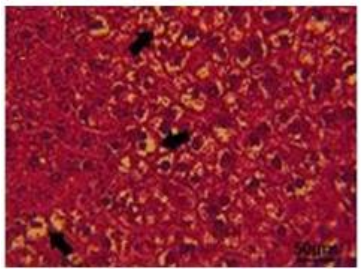


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**Figure 1.** Representative hematoxylin and eosin (H&E)–stained liver sections illustrating histological features across experimental groups. Normal control animals displayed intact hepatic architecture with healthy hepatocytes (a). Rats with dexamethasone-induced dyslipidemia exhibited widespread fatty infiltration, he patocellular swelling, and marked steatosis (b). The atorvastatin-treated group showed only mild microvesicular fat accumulation (c). Liver sections from animals receiving *Allium affine* extract at doses of 50 mg/kg (d), 100 mg/kg (e), 200 mg/kg (f), and 400 mg/kg (g) demonstrated dose-dependent improvement, with moderate vesicular steatosis observed at higher doses. All images were captured at ×400 magnification. Black arrows denote steatotic changes, while white arrows indicate inflammatory cell infiltration.

Dexamethasone administration also resulted in pronounced increases in serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT), which are established indicators of hepatic injury ($p<0.001$). Treatment with atorvastatin as well as higher doses of *A. affine* extract significantly ameliorated these liver function markers **(Table 1).**

Histopathological examination of liver samples revealed extensive lipid deposition, inflammatory cell infiltration, and diffuse steatosis in hepatic parenchymal cells following exposure to high-dose dexamethasone, compared with the normal hepatic morphology observed in control animals **(Figures 1a and 1b).** In rats receiving atorvastatin, liver architecture showed a clear reduction in steatotic changes **(Figure 1c).** While the lowest dose of *A. affine* extract (50 mg/kg) produced minimal histological improvement **(Figure 1d),** administration of 100 mg/kg **(Figure 1e),** 200 mg/kg **(Figure 1f),** and 400 mg/kg **(Figure 1g)** led to noticeable attenuation of hepatic damage.

Notably, hepatoprotective effects have been documented for several *Allium* species in different experimental models of liver injury, including diabetic liver dysfunction and ethanol-induced hepatotoxicity. These protective actions have been attributed to restoration of oxidative balance and enhancement of antioxidant defenses such as catalase, glutathione, and glutathione peroxidase activities [40, 41].

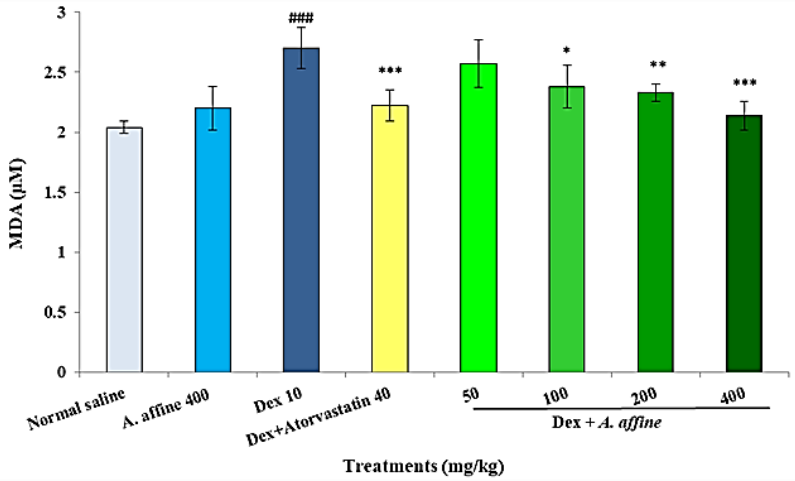


**Figure 2.** Impact of *Allium affine* extract (50, 100, 200, and 400 mg/kg) and atorvastatin (40 mg/kg) on serum malondialdehyde (MDA) concentrations in dexamethasone (Dex)-induced dyslipidemic rats. Data are expressed as mean ± SD (n=6); ###$p<0.001$ compared with normal control; *$p<0.05$, **$p<0.01$, and ***$p<0.001$ versus Dex-treated control.

Oxidative stress is known to play a critical role in the development of complications associated with glucocorticoid excess in dexamethasone-induced dyslipidemia [19]. In the present study, both *A. affine* extract (at doses of 100–400 mg/kg) and atorvastatin significantly suppressed lipid peroxidation, as evidenced by reduced serum MDA levels in dexamethasone-treated animals **(Figure 2).** Previous findings have similarly identified *A. affine* as a strong antioxidant agent, comparable to other *Allium* species, through mechanisms such as enhancement of total antioxidant capacity, free radical scavenging, and reduction of hydroperoxide formation [10].

One of the main limitations of this study was the absence of mechanistic investigations into the antihyperglycemic and antihyperlipidemic actions of *A. affine* extract. Additionally, the induction of hyperlipidemia required relatively high doses of dexamethasone, which are known to produce adverse effects in experimental animals, including pronounced body weight loss and skeletal muscle wasting [42].

## Conclusion

In conclusion, the present findings demonstrated that the hydroalcoholic extract of Allium affine aerial parts exerted hypolipidemic effects by lowering serum lipids, glucose, transaminases, and lipid peroxides, while also ameliorating histopathological alterations in the liver of rats with dexamethasone-induced dyslipidemia. Accordingly, this plant-based remedy holds potential as a preventive approach to alleviate the worldwide impact of metabolic syndrome and its associated disorders. Nevertheless, further studies are recommended to evaluate the therapeutic efficacy of A. affine in hyperlipidemia management, as well as to isolate its active phytochemical constituents and elucidate the underlying mechanisms responsible for its lipid-lowering properties.

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**Conflict of Interest:** None

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**Ethics Statement:** None

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