Comparative Clinical Pathology (2019) 28:963–969
https://doi.org/10.1007/s00580-018-2853-8

ORIGINAL ARTICLE

Hepatoprotective potential of aqueous extract of *Allium eriophyllum* Boiss in high-fat diet-induced fatty liver diseases

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Received: 16 October 2018 / Accepted: 30 October 2018 / Published online: 6 November 2018

Abstract

In recent years, Iranian traditional medicine has been used to control, prevent, and treat various diseases such as fatty liver. One of these plants is *Allium eriophyllum* Boiss. In this research, we assessed the potential of aqueous extract of *A. eriophyllum* in the treatment of fatty liver disease in Wistar male rats. At beginning of the study, a total of 10 rats were selected as the negative control, and 50 rats were treated with a high-fat diet for 4 months. Then, the animals were randomly divided into six subgroups, including negative healthy control, untreated negative control, and four groups receiving the aqueous extract of *A. eriophyllum* at 25, 50, 100, and 200 mg/kg concentrations. After 2 months, the rats were sacrificed, and blood and liver samples were collected. The data were analyzed by SPSS 21 software. All groups of *A. eriophyllum* (especially A200) could significantly ($p \leq 0.05$) decrease the raised weights of body and liver and the concentrations of ALP, AST, ALT, GGT, cholesterol, LDL, triglyceride, total and conjugated bilirubin, glucose, and GR and increase the concentrations of HDL, total protein, albumin, SOD, CAT, and GPx as compared to the untreated group. Also, *A. eriophyllum* (especially A200) decreased the degree of hepatic steatosis as compared to the untreated group. In finally, it appears that the aqueous extract of *A. eriophyllum* can treat the fatty liver disease in rats.

Keywords Aqueous extract · *Allium eriophyllum* Boiss · Fatty liver disease

Introduction

The fatty liver disease as a metabolic disorder is usually followed by extreme obesity and increased blood lipid (Day 2011; Ganz et al. 2014; Jacobs et al. 2002). Studies have revealed that a high-fat diet leads to fatty liver disease (Ganz et al. 2014; Jacobs et al. 2002). It is characterized by the accumulation of triglycerides in liver cells due to stratification of glycerol and free fatty acids. It is accompanied by a series of histopathologic changes varying from steatosis to cirrhosis (Flora et al. 1998; Haga et al. 2015; Shaker et al. 2010; Tamayo and Diamond 2007). In any case, it is evident now that fatty liver is dependent upon factors such as vulnerable oxidative stress and can lead to steatohepatitis, which is characterized by inflammation, necrosis, fibrosis, and cirrhosis (Bosisio et al. 1992). The possible pharmacologic treatments include insulin sensitizers, antioxidants, hepatic protectors, or lipid-reducing factors (Bundy et al. 2008). Since there are numerous pharmaceutical plants with antioxidant and anti-inflammatory properties, their application can be impressive in the inhibition and treatment of steatohepatitis in high-fat diet cases (Yao et al. 2016).

In Iranian traditional medicine, plants have been the foundation of inhibition and treatment of several diseases (Ghashghaii et al. 2017; Hagh-Nazari et al. 2017; Hamelian

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et al. 2018; Zhaleh et al. 2018). One of the most important herbal medicines which are widely used in Iranian traditional medicine for the treatment of fatty liver disease is *Allium eriophyllum* Boiss. The plant is widely distributed in the western parts of Asia such as in Iraq, Turkey, and Iran (Foroughi et al. 2016; Mozafari et al. 2015). *A. eriophyllum* is a good source of low-cost food and is a perfect part of the Iranian diet. It has been used as a medicinal plant for its antimicrobial, antioxidant, anti-inflammatory, antidiabetic, and antihypertensive effects (Foroughi et al. 2016; Janahmadi et al. 2015; Mozafari et al. 2015). High prevalence of fatty liver disease in the whole world has drawn the attention of researchers in finding remedial and preventive methods to control and treat this disease. In this regard, we attempted to study the potentials of aqueous extract of *A. eriophyllum* on the treatment of fatty liver disease in rats.

Materials and methods

Animal

This study was conducted on 60 Wistar male rats with the weight of 205 ± 5 g that were kept in individual cages for 7 days to adapt to the environment.

Plant collection and extraction

A. eriophyllum was collected from Kermanshah City west of Iran. The leaves of the plant were dried in shadow, and after grinding, each time 150 g of the obtained powder was dissolved in 1500 cc of distilled water and put in a Soxhlet extractor for 8 h. The collected extract was filtered by Whatman filter paper no. 1 and steamed into a glass container at the solvent temperature. The remaining dried extract was poured into a glass container and weighed. The powder of the obtained extract was weighed as required depending on the dose and dissolved in normal saline (Zangeneh et al. 2018b, c; Moradi et al. 2018). It was then administered to the rats by the oral catheter.

In vivo design

In this study, a total of 10 rats were selected as the negative control, and the rest of them were treated with a high-fat diet for 4 months. The rats with fatty liver were then divided into five groups, 10 rats in each group: I, fatty diet; II, fatty diet plus 25 mg/kg of aqueous extract of *A. eriophyllum*; III, fatty diet plus 50 mg/kg of aqueous extract of *A. eriophyllum*; IV, fatty diet and 100 mg/kg of aqueous extract of *A. eriophyllum*; and V, fatty diet and 200 mg/kg of aqueous extract of *A. eriophyllum*. Different concentrations of extract were administered via gavage for 2 months. To consider gavage stress, distilled water was administered to the control group every day. After 2 months of gavage, the rats were sacrificed.

Fatty diet preparation

Rats diet powder (28%), butter, (28%), egg yolk (19%), sucrose (14%), and egg white (11%) were mixed to prepare the fatty diet. The obtained powder was dried in 100 °C oven for 30 min and was given to the rats as the pellet. The fatty diet was prepared weekly and stored in the refrigerator.

Histopathological assay

The histopathological changes were rated based on fat accumulation in liver: 0 = no steatosis, 1 = steatosis in less than 25% of hepatocytes, 2 = steatosis in 26–50% of hepatocytes, 3 = steatosis in 51–75% of hepatocytes, and 4 = steatosis in more than 75% of hepatocytes (Mohammadifar et al. 2018).

Statistical analysis

The quantitative data were analyzed by SPSS 21 software using one-way ANOVA followed by Duncan test. To determine the normality of data, the Kolmogorov-Smirnov test was applied. To analyze the histopathological data, the Kruskal-Wallis test was run. $P \leq 0.05$ was considered significant.

Results

Effect of aqueous extract of *A. eriophyllum* on the weights of body and liver

The weights of body and liver increased significantly ($p \leq 0.05$) in untreated rats as compared to the control ones (Figs. 1 and 2). Consumption of aqueous extract of *A. eriophyllum* at all doses could significantly ($p \leq 0.05$) reduce above weights in comparison with the untreated group. Administration of A200 could significantly ($p \leq 0.05$) reduce the body weight similar to the control group. No remarkable changes ($p \leq 0.05$) were found between A25 and A50.

Effect of aqueous extract of *A. eriophyllum* on the degree of hepatic steatosis

As revealed in Table 1, the degree of hepatic steatosis raised in untreated rats as compared to the control ones. But, all doses of aqueous extract of *A. eriophyllum* could reduce it. Consumption of A200 could significantly ($p \leq 0.05$) reduce the degree of hepatic steatosis similar to the control group. No remarkable changes were found among A25, A50, and A100 groups.

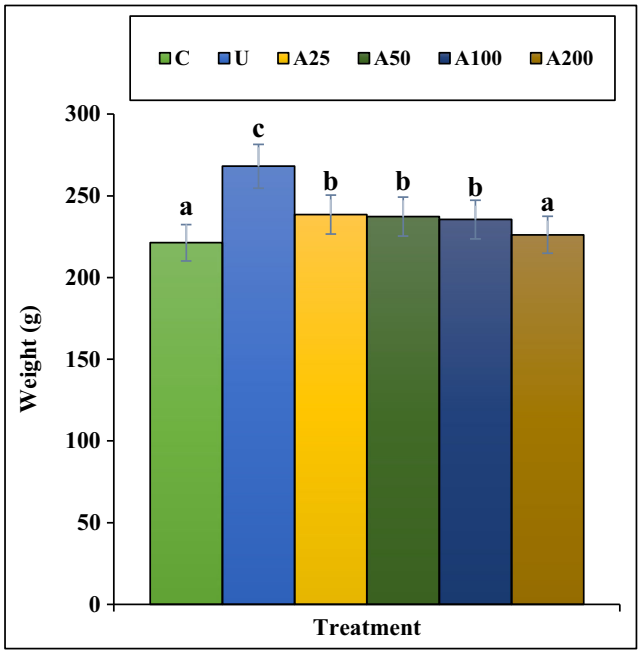

Fig. 1 The weight of the body in various groups. C, control; U, untreated; A, *Allium eriophyllum* Boiss. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

Effect of aqueous extract of *A. eriophyllum* on the concentrations of biochemical approaches

High-fat diet-induced fatty liver enhanced significantly ($p \leq 0.05$) the concentrations of ALP, AST, ALT, gamma-glutamyl transpeptidase (GGT), cholesterol, LDL, triglyceride, total and conjugated bilirubin, and glucose and decreased significantly ($p \leq 0.05$) the concentrations of HDL, total protein, and albumin as compared to the control group. Various doses of aqueous extract of *A. eriophyllum* could significantly ($p \leq 0.05$) improve the above parameters. There were not remarkable changes ($p \leq 0.05$) among all doses of *A. eriophyllum* and control group in concentrations of triglyceride and total and conjugated bilirubin. Also, administration of A100 and A200 could significantly ($p \leq 0.05$) ameliorate the concentrations of ALT, GGT, total protein, and albumin similar to the control group. No remarkable changes were found in concentration of HDL between A200 and control groups (Figs. 3, 4, 5, 6, and 7).

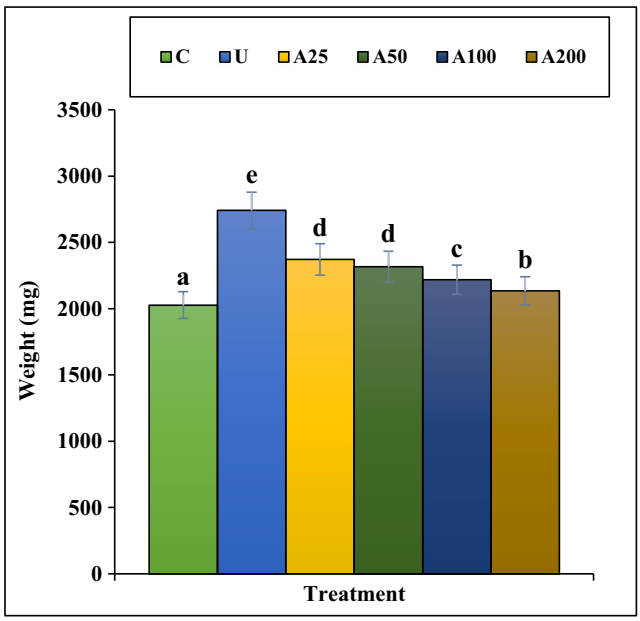

Fig. 2 The weight of the liver in various groups. C, control; U, untreated; A, *Allium eriophyllum* Boiss. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

Table 1 The degrees of hepatic steatosis in various groups

Groups	The degrees of hepatic steatosis					*P*
	0	1	2	3	4	
C	10	0	0	0	0	–[b]
U	0	3	3	2	2	–[a]
A25	2	4	2	2	0	–[a,b]
A50	2	6	2	0	0	–[a,b]
A100	4	5	1	0	0	–[a,b]
A200	7	2	1	0	0	–[b]

C control, *U* untreated, *A Allium eriophyllum* Boiss

[a] Reveal a remarkable change between the control group and other groups

[b] Reveal a remarkable change between untreated group and other groups

Effect of aqueous extract of *A. eriophyllum* on the concentrations of antioxidant enzymes

As revealed in Figs. 8 and 9, the concentrations of SOD, CAT, and GPx enzymes were significantly ($p \leq 0.05$) reduced and the concentration of GR was significantly ($p \leq 0.05$) enhanced in the untreated group. The treatment with aqueous extract of *A. eriophyllum* significantly ($p \leq 0.05$) ameliorated them. There were no remarkable changes ($p \leq 0.05$) in the concentration of GPx enzyme among several groups of *A. eriophyllum* and control group. Also, consumption of A100 and A200 could significantly ($p \leq 0.05$) increase the concentration of SOD similar to the control group. No remarkable changes were found between A25 and A50 groups.

Discussion

The remedial potentials of the traditional medicine have been determined for centuries by clinical practice and experience (Farzaei et al. 2018; Sayyedrostami et al. 2018). They have the strong potential on the prevention, control, and treatment of every disease such as fatty liver (Hemmati et al. 2015; Lee et al. 2010; Nazni et al. 2006; Sabzghabaee et al. 2013; Yao et al. 2016; Sherkatolabbasieh et al. 2017). In Iranian

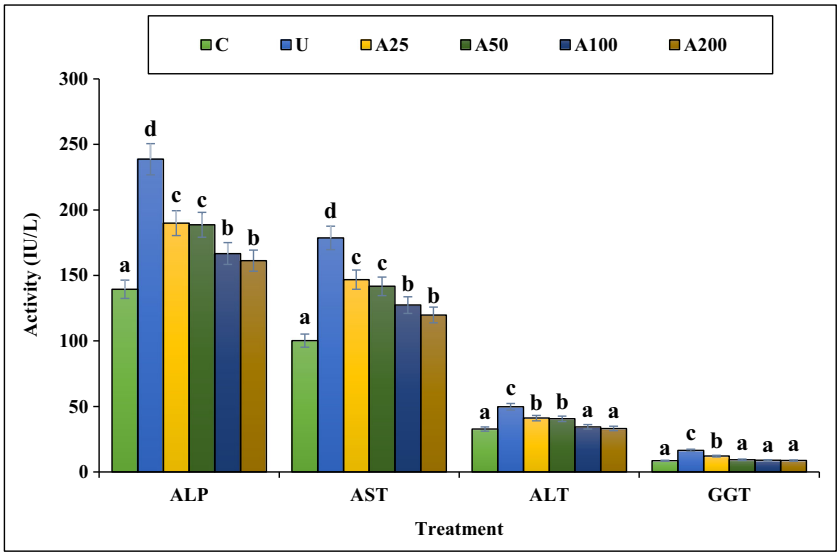

Fig. 3 The level of ALP, AST, ALT, and GGT in various groups. C, control; U, Untreated; A, *Allium eriophyllum* Boiss; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

traditional medicine, people used *A. eriophyllum* to treat fatty liver disease.

The obtained results from biochemical parameters revealed that high-fat diet increased significantly ($p \leq 0.05$) the concentrations of ALP, AST, ALT, GGT, total and conjugated bilirubin, and glucose and decreased significantly ($p \leq 0.05$) the concentration of total protein and albumin as compared to the control group. Therefore, this diet caused severe hepatic toxicity. In spite of hepatotoxicity potential of the high-fat diet, the treatment with aqueous extract of *A. eriophyllum* could significantly ($p \leq 0.05$) improve the concentration of the above parameters. In a study reported that extract of *Allium saralicum* (as a species of *Allium* genus) reduced the raised concentration of ALP, AST, and ALT and also the volume of the liver, hepatocytes, and sinusoids as compared to the CCl_4-treated group (Goodarzi et al. 2017). In another study, Goodarzi et al. (2018) indicated that extract of *A. saralicum* decreased the concentrations of ALP, AST, and ALT and also the volumes of the liver, hepatic artery, portal vein, and central vein in diabetic mice. Also in the study of Ogunlade et al. (2002), aqueous extract of *Allium cepa* (as a species of *Allium* genus) lowered the increased concentration of ALP, AST, AST, and GGT as compared to the alcohol-received group.

The analysis of antioxidant enzymes of the recent study showed that the high-fat diet significantly ($p \leq 0.05$) decreased the concentrations of SOD, CAT, and GPx and increased the concentration of GR. But, the treatment with all doses of aqueous extract of *A. eriophyllum* could significantly ($p \leq 0.05$) improve the concentrations of them. A study demonstrated that the aqueous extract of *A. cepa*, with increasing the degradation of free radicals, increased the concentrations of SOD, CAT, GPx, malondialdehyde (MDA), and reduced glutathione (GSH) in rabbits with alcohol-induced

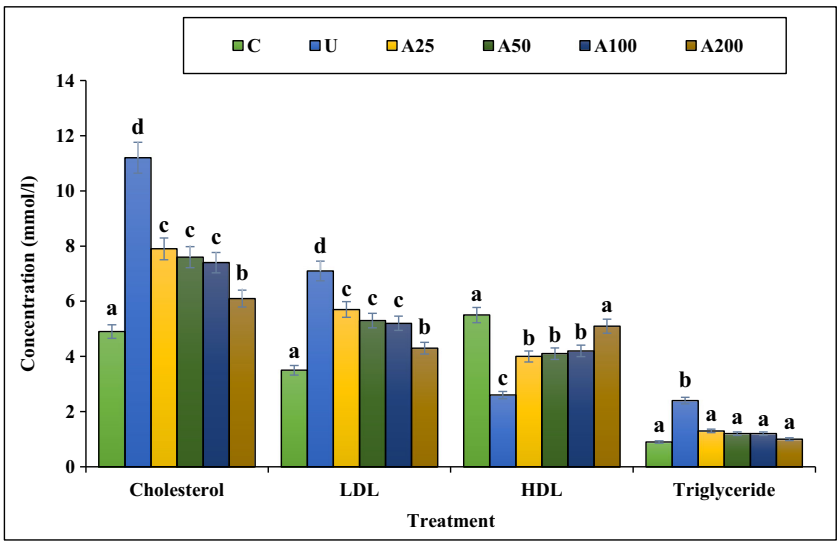

Fig. 4 The level of cholesterol, LDL, HDL, and triglyceride in various groups. C, control; U, untreated; A, *Allium eriophyllum* Boiss; LDL, low-density lipoprotein; HDL, high-density lipoprotein. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

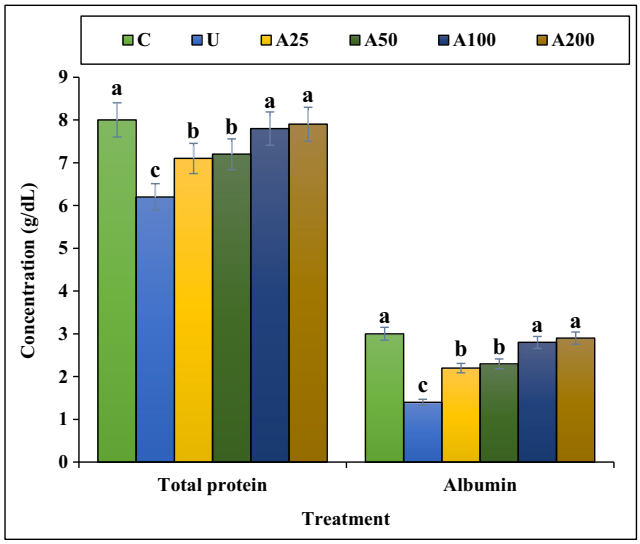

Fig. 5 The level of total protein and albumin in various groups. C, control; U, untreated; A, *Allium eriophyllum* Boiss. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

hepatotoxicity (Ogunlade et al. 2002). In the study of Hoseinpouran et al. (2015), the extract of *A. cepa* having good antioxidant potential has been reported, because it raised the concentration of antioxidant enzymes including SOD, CAT, and GPx as compared to the tartrazine-treated group. Also, another study revealed the very strong antioxidant potential of *Allium sativum* Linn (as a species of *Allium* genus) with ameliorating concentrations of SOD, CAT, and GPx in diabetic rats (Saravanan and Ponmurugan 2013).

In our study, aqueous extract of *A. eriophyllum* decreased the concentrations of cholesterol, LDL, triglyceride, and the degree of hepatic steatosis and increased the concentration of the HDL as compared to the untreated group. Lee et al. (2017) reported the hepatoprotective potential of *Allium hookeri* (as a

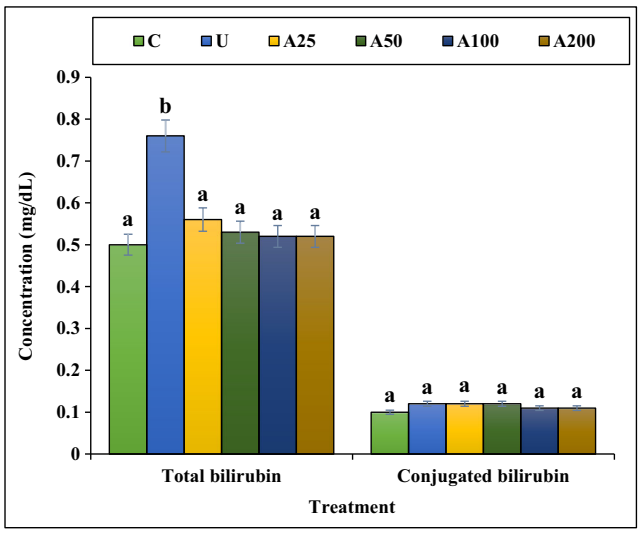

Fig. 6 The level of total and conjugated bilirubin in various groups. C, control; U, untreated; A, *Allium eriophyllum* Boiss. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

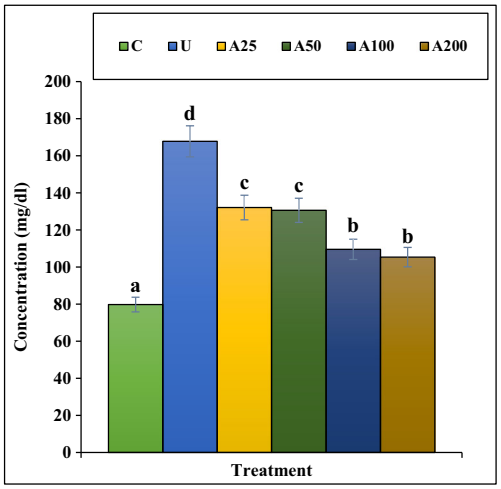

Fig. 7 The level of glucose in various groups. C, control; U, untreated; A, *Allium eriophyllum* Boiss. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

species of *Allium* genus) against high-fat diet-induced fatty liver disease in the guinea pig. In the previous research, *A. hookeri* lowered the concentrations of cholesterol, triglyceride, and LDL. Also, there was a similar study which reported that *A. hookeri* decreased the serum LDL and cholesterol (Won et al. 2013). In another study, *A. sativum* Linn treated the fatty liver disease in rats with decreasing the concentrations of triglyceride and cholesterol (Augusti et al. 2001).

It is revealed that antioxidant compounds played a very necessary role in the treatment of fatty liver disease (Ferramosca et al. 2017). The studies reporting that *Allium* genus was rich in antioxidant compound includes linolenic acid-methyl ester, phytol, neophytadiene 2-phenyl-5-methylindole, hexadecanoic acid, vitamin E, ethanol, 2-

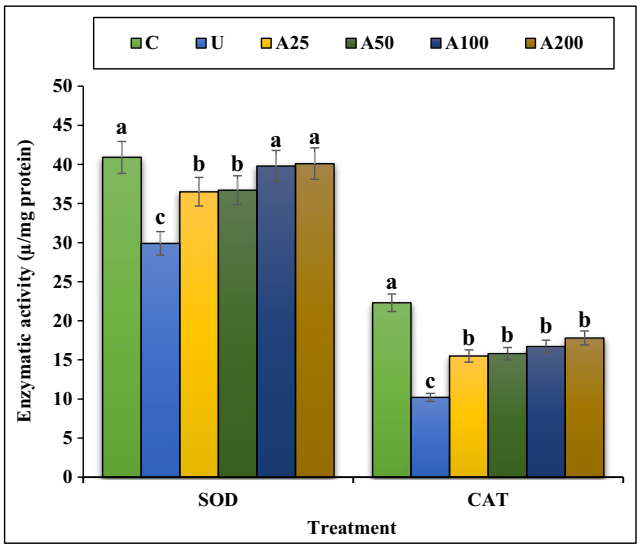

Fig. 8 The level of liver SOD and CAT in various groups. C, control; U, Untreated; A, *Allium eriophyllum* Boiss; SOD, superoxide dismutase; CAT, catalase. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

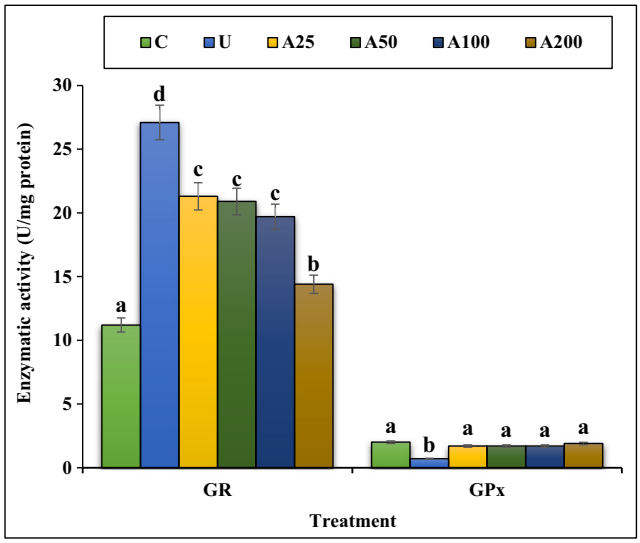

Fig. 9 The level of liver GR and GPx in various groups. C, control; U, untreated; A, *Allium eriophyllum* Boiss; GR, glutathione reductase; GPx, glutathione peroxidase. Unlike letters show a remarkable change between the various groups ($p \leq 0.05$)

tetradecyloxy, *n*-tetracosane, hexatriacontane, γ-tocopherol, eicosane, *n*-ethyl-1,3-dithioisoindoline, 2-hexadecene, 3,7,11,15-tetramethyl, hexanedioic acid, and 1,4,8,11-tetraazacyclotetradecane (Goodarzi et al. 2018; Zangeneh et al. 2018a). So, it was normal in our study that *A. eriophyllum* treated fatty liver disease in rats.

Conclusion

Based on the obtained results, it can be concluded that aqueous extract of *A. eriophyllum* at all doses (especially A200) exhibits remarkable hepatoprotective potentials against high-fat diet-induced fatty liver disease. This extract also indicated amelioration in histopathological and biochemical parameters. It is suggested that clinical trials be done to gain this remedial potential in human.

Compliance with ethical standards

Conflict of interest The authors claim that there is no conflict of interest.

Ethic approval All institutional and national guidelines for the care and use of laboratory animals were followed.

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