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ORIGINAL ARTICLE

Effect of aqueous extract of *Allium saralicum* R.M. Fritsch on fatty liver induced by high-fat diet in Wistar rats

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Abstract

The fatty liver as a metabolic disorder has involved human beings globally and is usually followed by extreme obesity, increased blood lipid, and diabetes type II. Appropriate strategies for treating this disease are prioritized by each country. The aim of the recent research was to survey the remedial potential of aqueous extract of *Allium saralicum* R.M. Fritsch on the high-fat diet-induced fatty liver disease in Wistar male rats. In this study, 60 rats were used. 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. 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. saralicum* at 20, 40, 80, and 160 mg/kg concentrations. After 2 months, the rats were sacrificed and blood and liver samples of them were collected to analyze the biochemical and histopathological parameters. The data were analyzed by SPSS-21 software. All doses of *A. saralicum* (especially A160) could significantly ($p \leq 0.05$) decrease the raised levels of ALP, AST, ALT, GGT, cholesterol, LDL, triglyceride, total and conjugated bilirubin, glucose, and GR and increased HDL, total protein, albumin, SOD, CAT, and GPx as compared to the untreated group. Also, aqueous extract of *A. saralicum* (especially A160) decreased the degree of hepatic steatosis as compared to the untreated group. In conclusion, the acquired results showed the hepatoprotective potential of aqueous extract of *A. saralicum*, so that it can use for the treatment of fatty liver disease.

Keywords *Allium saralicum* R.M. Fritsch · Aqueous extract · Fatty liver disease · High-fat diet

Introduction

The fatty liver disease is one of the most usual metabolic diseases among people around the world. In this disease, triglycerides accumulated in liver cells due to stratification of glycerol and free fatty acids (Fan and Farrell 2009; Ganz et al. 2014; Jacobs et al. 2002; Day 2006, 2011). Fat accumulation in the liver can occur due to the raised synthesis of fat and decreased disposal or oxidation of lipid (Ganz et al. 2014; Jacobs et al. 2002; Day 2011). The fatty liver disease is amalgamated by a series of histopathologic changes varying from steatosis to cirrhosis (Haga et al. 2015; Flora et al. 1998; Tamayo and Diamond 2007; Shaker et al. 2010).

The possible pharmacologic treatments include antioxidants, insulin sensitizers, hepatic protectors, or lipid reducing factors (Comar and Sterling 2005). Since there are numerous pharmaceutical plants with antioxidant and anti-inflammatory potentials, their administrations can be impressive in the treatment of fatty liver disease.

In traditional medicine, plant medicines have been the basis of prevention, control, and treatment of several diseases (Ghashghaii et al. 2017; Hagh-Nazari et al. 2017; Farzaei et al. 2018; Zhaleh et al. 2018; Hamelian et al. 2018). One of the most important herbal medicines which are widely used is *Allium saralicum* R.M. Fritsch. The plant is widely distributed in Iraq, Iran, and Turkey. *A. saralicum* is a good source of low-cost food and is a perfect part of Iranian diet (Sherkatolabbasieh et al. 2017; Zangeneh et al. 2018). It applied as a medicinal plant has been used for its antibacterial, antifungal, anti-inflammatory, immunostimulatory,

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nephroprotective, and hepatoprotective properties (Sherkatolabbasieh et al. 2017; Zangeneh et al. 2018; Goodarzi et al. 2017; Goodarzi et al. 2018).

In this research, we attempted to survey the remedial potential of aqueous extract of *A. saralicum* on the high-fat diet-induced fatty liver disease in rats.

Materials and methods

Plant collection and extraction

A. saralicum was collected from Kermanshah city in the west of Iran. The leaves of the plant were dried in shadow, and after grinding, each time 100 g of the obtained powder was dissolved in 1000 cc of distilled water and put in 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.

Experimental design

This experimental study was conducted on 60 Wistar male rats with the weight of 200 ± 5 g that were kept in individual cages for 10 days to adapt to the environment. During the experiments, the temperature of the animal house was adjusted at 22 ± 3 °C under a 12-h dark/light cycle. 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 20 mg/kg of *A. saralicum*, III. Fatty diet plus 40 mg/kg of *A. saralicum*, IV. Fatty diet plus 80 mg/kg of *A. saralicum*, and V. Fatty diet and 160 mg/kg of *A. saralicum*. All 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. Blood samples were taken from the rats' heart to analyze biochemical parameters. The capacity of antioxidant enzymes was evaluated by determining the activity of superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), and glutathione peroxidase (GPx) in livers of each group ($n = 5$). Also, the rats' liver ($n = 5$) was subjected to microscopic analysis. The histopathological changes were rated based on fat accumulation in the 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).

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 a 100 °C oven for 30 min and was given to the rats as a pellet. The fatty diet was prepared weekly and stored in the refrigerator (Mohammadifar et al. 2018).

Statistical analysis

The quantitative data were analyzed by SPSS-21 software using one-way ANOVA followed by Duncan's 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. saralicum* on the body and liver weights

The body and liver weights enhanced significantly ($p \leq 0.05$) in untreated rats as compared to the control ones (Figs. 1 and 2). Consumption of aqueous extract of *A. saralicum* at all doses could significantly ($p \leq 0.05$) reduce above weights in comparison with the untreated group. There were no significant differences ($p \leq 0.05$) among A80, A160, and control groups in the weight of the liver. Also, administration of

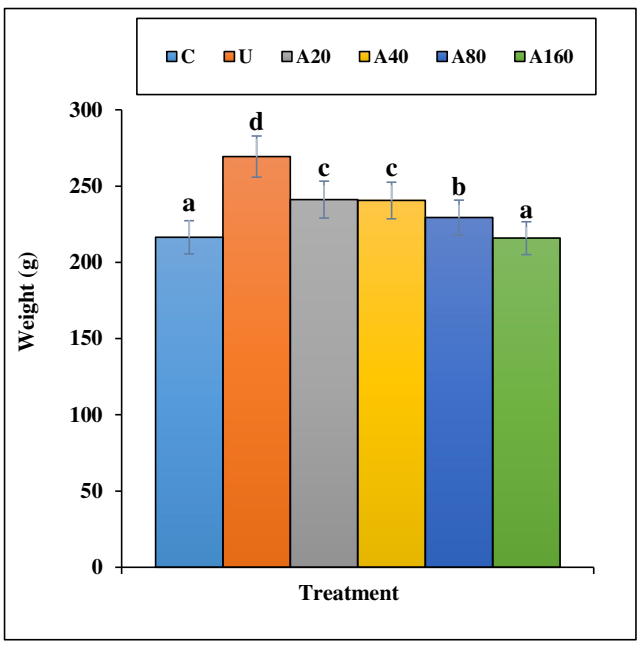

Fig. 1 The weight of the body in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

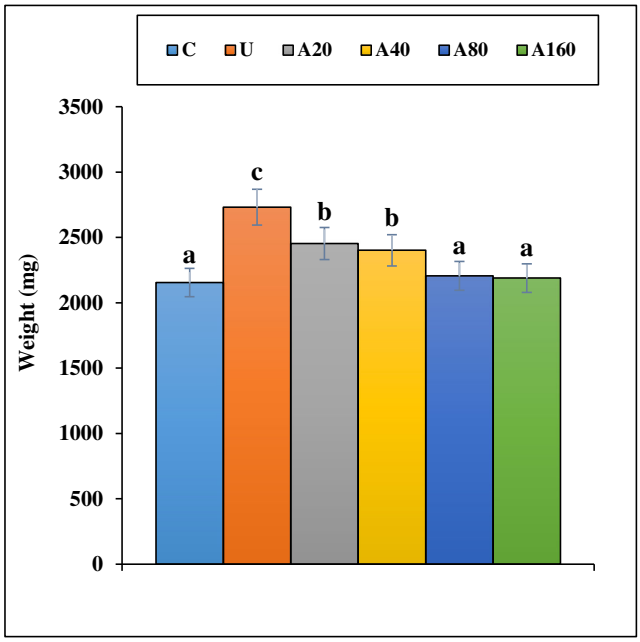

Fig. 2 The weight of the liver in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

A160 could significantly ($p \leq 0.05$) reduce the body weight similar to the control group. No significant differences ($p \leq 0.05$) were found between A20 and A40.

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

As indicated in Table 1, the degree of hepatic steatosis increased in untreated rats compared to the control ones. All groups of aqueous extract of *A. saralicum* could decrease it. There were no significant differences in the degree of hepatic steatosis between A160 and control groups. No significant differences were found between A20 and A40.

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	**
U	0	3	3	2	2	*
A20	2	4	3	1	0	*, **
A40	2	6	2	0	0	*, **
A80	4	4	2	0	0	*, **
A160	7	2	1	0	0	**

C control, *U* untreated, *A Allium saralicum* R.M. Fritsch

*Reveals a significant difference between control group and other groups

**Reveals a significant difference between untreated group and other groups

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

The concentrations of SOD, CAT, and GPx enzymes were significantly ($p \leq 0.05$) reduced and the concentration of GR was significantly ($p \leq 0.05$) increased in the untreated group. The treatment with aqueous extract of *A. saralicum* significantly ($p \leq 0.05$) improved them. There were no significant differences ($p \leq 0.05$) in the level of GPx among several doses of *A. saralicum* and control group. The concentration of GR was significantly ($p \leq 0.05$) increased in A80 and A160 and was similar to the control group. No significant differences ($p \leq 0.05$) were found between A20 and A40 in the concentrations of antioxidant enzymes (Figs. 3 and 4).

Effect of aqueous extract of *A. saralicum* on the concentrations of biochemical parameters

High-fat diet-induced fatty liver disease, decreased significantly ($p \leq 0.05$) the concentrations of HDL, total protein, and albumin and enhanced significantly ($p \leq 0.05$) the concentrations of ALP, AST, ALT, GGT, cholesterol, LDL, triglyceride, total and conjugated bilirubin, and glucose, as compared to the control group. All doses of aqueous extract of *A. saralicum* could significantly ($p \leq 0.05$) improve the above parameters. There were no significant differences ($p \leq 0.05$) among all doses of *A. saralicum* and control group in concentrations of ALT, GGT, triglyceride, total protein, albumin, and total and conjugated bilirubin. Also, administration of A80 and A160 could significantly ($p \leq 0.05$) decrease the concentration of AST similar to the control group (Figs. 5, 6, 7, 8, and 9).

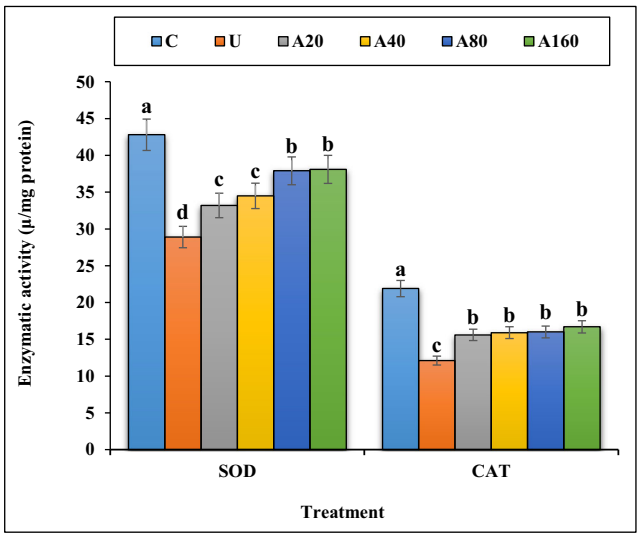

Fig. 3 The level of liver SOD and CAT in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch, SOD superoxide dismutase, CAT catalase. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

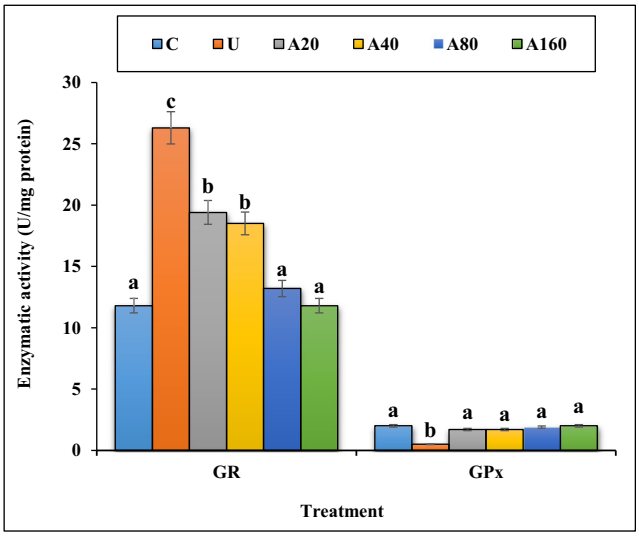

Fig. 4 The level of liver GR and GPx in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch, GR glutathione reductase, GPx glutathione peroxidase. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

Discussion

Medicinal plants are used in traditional medicine to prevent, control, and treat various diseases including anorexia, nasopharyngitis, diabetes, hypertension, nephrotoxicity, hepatotoxicity, hemorrhoid, anemia, rheumatism, atherosclerosis, Alzheimer, cancer, gastroduodenal ulcers, fatty liver disease, etc. (Sharafzadeh and Alizadeh 2012; Sayyedrostami et al. 2018; Ebrahimi-Mameghani et al. 2014). In this regard, a list of medicinal plants used for their remedial potentials on fatty liver disease includes *Cinnamomum zeylanicum* (Askari et al. 2014; Nikkhajoei et al. 2016), *Berberis vulgaris* L. (Kashkooli et al. 2015), *Cuminum cyminum* L. (Shavakhi et al. 2015), *Silybum marianum* (Hashemi et al. 2009), *Phyllanthus urinaria* (Wong et al. 2013), *Camelia sinensis* (Sakata et al. 2013), and *Chlorella vulgaris* (Ebrahimi-Mameghani et al. 2014; Panahi et al. 2012). One of the herbs consumed in Iranian traditional medicine to treat fatty liver disease is *A. saralicum*.

The results of antioxidant enzymes of our study indicated that the high-fat diet significantly ($p \leq 0.05$) reduced the concentrations of SOD, CAT, and GPx and enhanced the concentration of GR. But, the treatment with several doses of aqueous extract of *A. saralicum* could significantly ($p \leq 0.05$) improve the concentrations of them. In the study of Ogunlade et al. (2012), it was reported that the aqueous extract of *Allium cepa* (as a species of *Allium* genus), with enhancing the degradation of free radicals, enhanced the concentrations of SOD, CAT, GPx, and malondialdehyde (MDA) and reduced glutathione (GSH) in rabbits with alcohol-induced hepatotoxicity. In another study, it was revealed that the extract of *Allium cepa* had good antioxidant activity, because it increased the concentration of antioxidant enzymes including SOD, CAT, and GPx as compared to the tartrazine-received group (untreated group) (Hoseinpouran et al. 2015). Also, in the study of Saravanan and Ponmurugan (2013), it indicated the very strong antioxidant property of *Allium sativum* Linn (as a species of *Allium* genus) with improving the levels of SOD, CAT, and GPx in diabetic rats.

The analysis of biochemical approach of the recent study revealed that a high-fat diet increased significantly ($p \leq 0.05$) the concentrations of ALP, AST, ALT, GGT, total and conjugated bilirubin, and glucose and reduced significantly ($p \leq 0.05$) the concentrations of total protein and albumin as compared to the control group. Therefore, this high-fat diet caused severe hepatic toxicity. In spite of hepatotoxicity

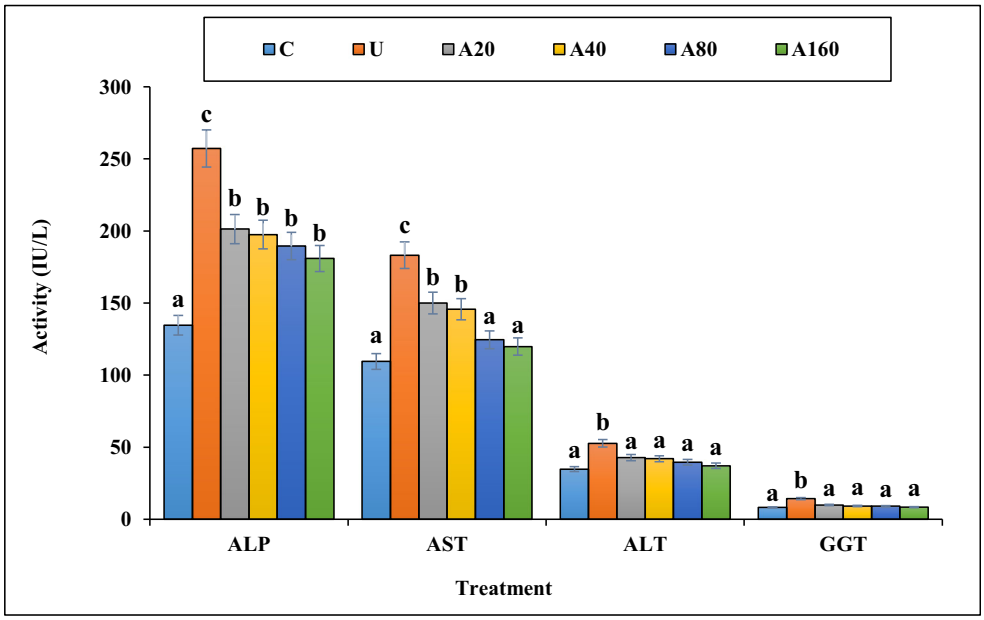

Fig. 5 The level of ALP, AST, ALT, and GGT in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch, ALP alkaline phosphatase, AST aspartate aminotransferase, ALT alanine aminotransferase, GGT gamma-glutamyl transferase. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

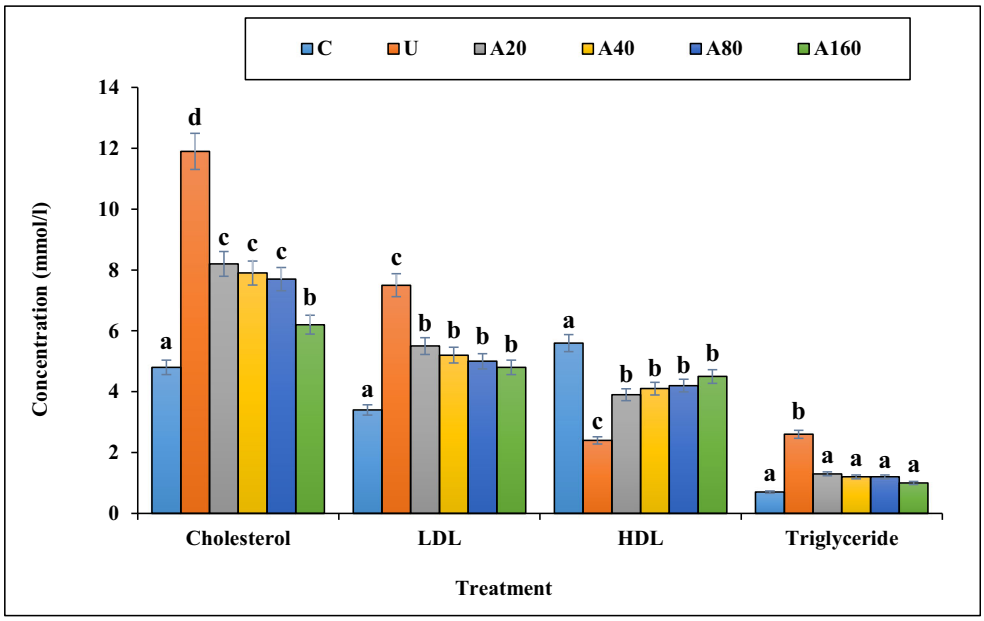

Fig. 6 The level of cholesterol, LDL, HDL, and triglyceride in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch, LDL low-density lipoprotein, HDL high-density lipoprotein. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

potential of the diet, the treatment with aqueous extract of *A. saralicum* could significantly ($p \leq 0.05$) ameliorate the concentrations of the above parameters. In the study of Goodarzi et al. (2017), it was revealed that extract of *A. saralicum* decreased the raised levels of hepatic biochemical parameters (ALP, AST, and ALT) and also the volume of the liver, hepatocytes, and sinusoids as compared to the CCl_4-treated group. In another study, it was reported that extract of *A. saralicum* reduced the concentrations of ALP, AST, and ALT and also the volumes of the liver, central vein, hepatic artery, and portal vein in diabetic mice (Goodarzi et al. 2018). Also in the study of Ogunlade et al. (2012), aqueous extract of *Allium cepa* decreased the raised concentration of ALP, AST, AST, and gamma-glutamyl transpeptidase (GGT) as compared to the alcohol-treated group.

In the study, aqueous extract of *A. saralicum* reduced 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. In the similar study, the hepatoprotective effect of *Allium hookeri* (as a species of *Allium* genus) against high-fat diet-induced fatty liver disease in the guinea pig was demonstrated. In the previous experiment, *Allium hookeri* reduced the concentrations of cholesterol, triglyceride, and LDL (Lee et al. 2017). Also, there was a similar study reported that *Allium hookeri* lowered the serum cholesterol and LDL (Won et al. 2013). In another study,

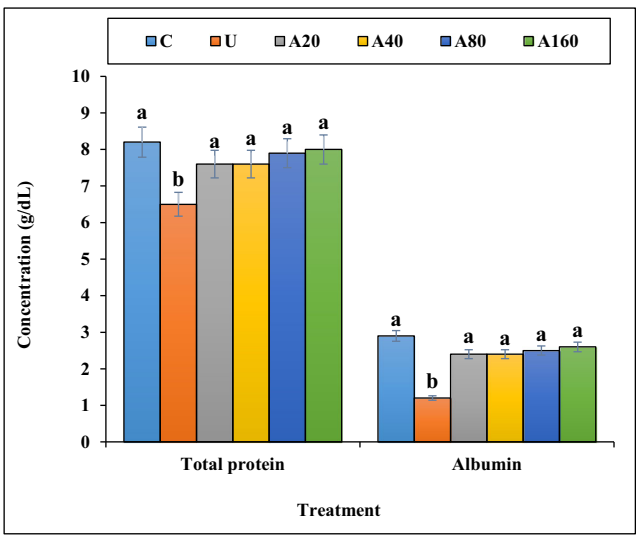

Fig. 7 The level of total protein and albumin in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

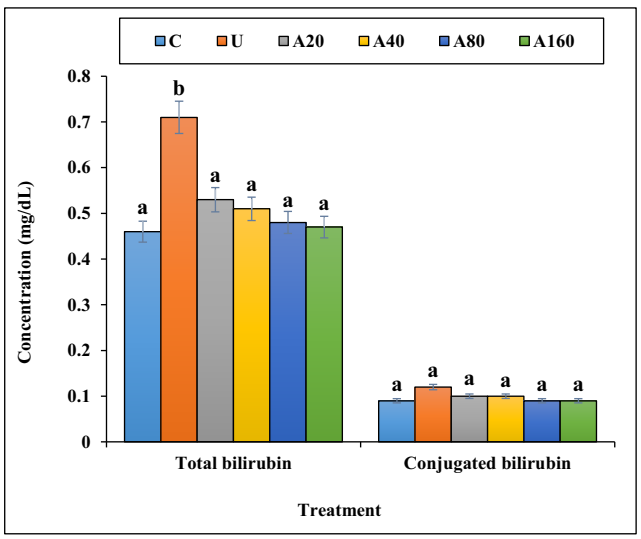

Fig. 8 The level of total and conjugated bilirubin in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

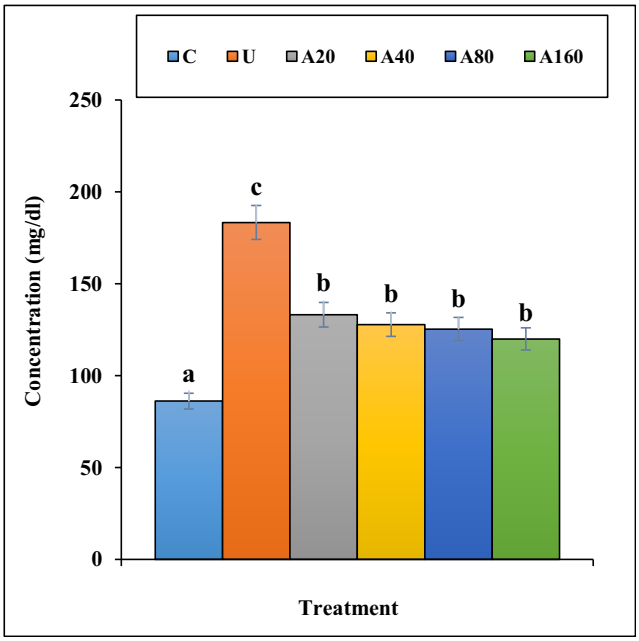

Fig. 9 The level of glucose in various groups. C control, U untreated, A *Allium saralicum* R.M. Fritsch. Non-like letters show a significant difference between the various groups ($p \leq 0.05$)

Augusti et al. (2001) indicated that *Allium sativum* Linn treated the fatty liver disease in rats with decreasing the concentrations of triglyceride and cholesterol.

It is revealed that antioxidant compounds played a very necessary and important role in the treatment of fatty liver disease (Ferramosca et al. 2017). In Goodarzi et al. (2018) study, they reported that *A. saralicum* collected in Kermanshah city was rich in antioxidant compounds including linolenic acid-methyl ester, phytol, neophytadiene 2-phenyl-5-methylindole, hexadecanoic acid, vitamin E, ethanol, 2-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. So, it was normal in our study that *A. saralicum* treated fatty liver disease in rats.

Conclusion

In accordance with the study, it concludes that aqueous extract of *A. saralicum* at all doses (especially A160) indicated meaningful hepatoprotective potentials. This extract also revealed amelioration in histopathological and biochemical approaches and so might be of value in the treatment of fatty liver disease.

Compliance with ethical standards

Conflict of interest The authors declare 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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