Vol.65: e22210460, 2022
https://doi.org/10.1590/1678-4324-2022210460
ISSN 1678-4324 Online Edition

Article - Biological and Applied Sciences

Effects of Endurance Training with or without Rosehip Fruits (Rosa canina L) Extraction and D-galactose Solution on Plasmatic Liver Enzymes, Lipid Profiles, Selected Biochemical Variables in Male Rats

Abbass Ghanbari-Niaki[1]*
https://orcid.org/0000-0003-4972-3771

Ali-Akbar Kolbadinejad[1]
https://orcid.org/0000-0003-2881-894X

Saleh Rahmati-Ahmadabad[2]
https://orcid.org/0000-0001-8751-1759

Jamal Nikbakht[1]
https://orcid.org/0000-0001-9863-8288

David Robert Broom[3]
https://orcid.org/0000-0002-0305-937X

Martin Hofmeister[4]
https://orcid.org/0000-0002-0693-7887

[1]University of Mazandaran, Faculty of Sport Sciences, Exercise Biochemistry Division, Babolsar, Mazandaran, Iran; [2]Islamic Azad University, Department of Physical Education, Pardis Branch, Pardis, Iran; [3]Coventry University, Centre for Sport, Exercise and Life Sciences, Coventry, United Kingdom; [4]Consumer Centre of the German Federal State of Bavaria, Department of Food and Nutrition, Munich, Germany.

Editor-in-Chief: Paulo Vitor Farago
Associate Editor: Bruno Pedroso

Received: 14-Jul-2021; Accepted: 10-May-2022.

*Correspondence: ghanbara@umz.ac.ir; Tel.: +98 1135303565; Fax: +98 1135334253; Post Office Box: 4741613534. (A.G.N.).

HIGHLIGHTS

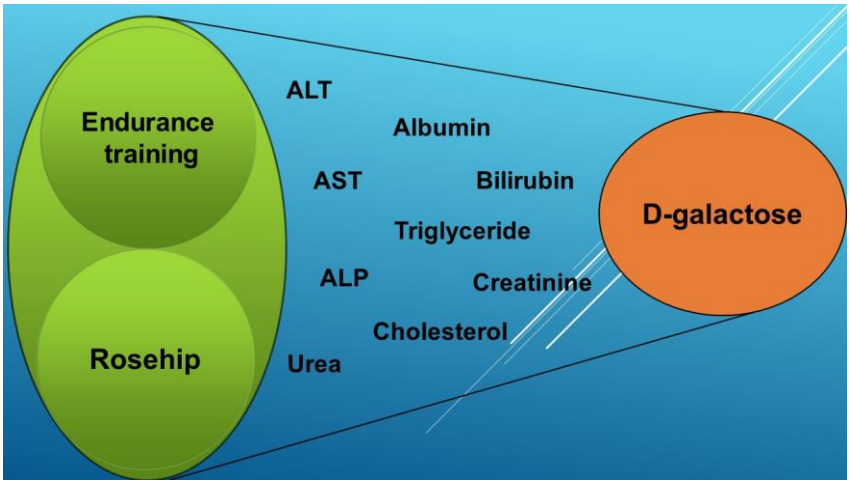
- Exercise increases plasma albumin, while reducing ALT and creatinine.
- Rosehip reduces AST, creatinine, urea, cholesterol, and triglyceride.
- D-galactose increases ALT, AST, ALP, creatinine, urea, cholesterol, and triglyceride.
- Rosehip adjusts the changes induced by D-galactose on some variables.

Abstract: The aims of the present study were to examine the effects of D-galactose (DG) supplementation on plasma aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), creatinine, albumin, urea, bilirubin, cholesterol, and triglyceride. We also investigated the effects of Rosehip (Rosa canina L) fruit extraction and endurance exercise training on DG-induced changes in the aforementioned variables in male rats. Eighty-six male rats were randomly assigned to 8 groups 1) Control Saline 2) Training Saline 3) Control D-galactose 4) Training D-galactose 5) Control Rosehip 6) Training Rosehip 7) Control combined group and 8) Training combined group. Animals received experiments on the base of groups' names (eight weeks and five times per week). Seventy-two hours after the last training or control session plasma was collected. The results showed that endurance training significantly increased plasma albumin while reducing ALT and creatinine. Rosehip significantly reduced plasma AST, creatinine, urea, cholesterol, and triglyceride, and increased bilirubin. A combination of training and Rosehip causes an additive effect

compared to each intervention alone on AST. The use of DG increased ALT, AST, ALP, creatinine, urea, bilirubin, cholesterol, and triglyceride, while decreasing albumin. The use of Rosehip in combination with DG was able to minimize DG-induced abnormal elevation on some variables. In conclusion, using a high dose of D-galactose solution or high galactose content foods could make a precondition background for the non-alcoholic fatty liver which could be attenuated by crud Rosehip extraction. Thus, it seems that the Rosehip can be considered a hepatoprotective herb.

Keywords: Albumin; aminotransferase (AST); bilirubin; cholesterol; creatinine; urea.

GRAPHICAL ABSTRACT



INTRODUCTION

D-galactose (DG) can be found in many food items such as nectarine, pepper (Capsicum pubescens), caraway, and common verbena [1]. Chronic D-galactose consumption (200 mg/kg, once a day for 8 weeks in mice) is harmful inducing oxidative stress, inflammation, and cell apoptosis [2]. DG consumption is associated with several disorders including heart, kidney, and liver disease [3, 4] as well as DNA damage in mice [5]. Generally, D-galactose hurts the body tissues and changes tissue and blood biochemical variables to abnormal levels [4-6].

Alanine aminotransferase (ALT) [7, 8], aspartate aminotransferase (AST) [9], alkaline phosphatase (ALP) [10], cholesterol, triglyceride, bilirubin, creatinine, albumin, and urea are blood markers that are commonly used in clinical tests as indicators of liver, kidney and cardiovascular disease [10, 11]. Generally, changes in these markers are related to ill health and can be mitigated by the use of antioxidant supplements, organic compounds, and exercise training [2, 12-15].

Antioxidants are compounds that protect against cell damage caused by molecules called reactive oxygen (ROS) and reactive nitrogen (RNS) species [16]. The body has a natural antioxidants defence system including vitamins C and E as well as enzymatic, and non-enzymatic antioxidants [17]. However, exogenous antioxidant consumption may enhance the endogenous antioxidant defence system and consequently decrease the damage to body organs [18, 19].

It has been suggested that the consumption of high galactose also resulted in early aging in rat models via increasing oxidative stress conditions and its markers which has been accompanied by a reduction in antioxidants components and its markers in rat plasma and tissues [20-22]. It has been shown that using the extract of some edible vegetables [23, 24] fruits [25, 26], medicinal plants, and herbs which are rich in antioxidants, Polyphones, vitamin C, and other effective components [27-31]. Rosa canina L. or dog rose is a wild rose species native to Europe, northwest Africa, and western Asia. The Rosa canina L. fruits (Rosehip) are rich in antioxidants (vitamin C, carotenoids, tocopherol, phenolic acid, bioflavonoids, tannin, pectin), amino acid, organic acids, essential oils, unsaturated fatty acids, and lycopene [32]. In a review study, it has been shown that Rosehip has antioxidant, anti-inflammatory, anti-obesity, anti-cancer, hepatoprotective, nephroprotective, cardioprotective, antiaging, anti H. pylori, neuroprotective and antinociceptive activities [33]. Histological evaluations indicate that Rosa canina L. fruits induced an improvement in the defective liver [34]. Another study showed that Rosa canina L. fruits induced an improvement in liver histological damage along with decreased ALT, AST, and urea [35].

The aim of the present study was to examine the effects of DG on well-known plasma markers used in diagnostic tests i.e. AST, ALT, ALP, creatinine, albumin, urea, bilirubin, cholesterol, and triglyceride and also to investigate the effects of Rosehip fruit extraction and endurance exercise on DG-Induced changes in mentioned variables in male rats. The effects of exercise training and Rosehip on present study variables in DG-induced rats are poorly understood. It has been shown that exercise had a significant effect on DG-elevated AST and ALT levels of DG-trained rats [36]. Exercise also lowered the degree of DG-exposed hepatic fibrosis, and restore the injured liver tissue back to the non-aging state in DG-exposed aging rats [37]. Exercise training restores Insulin-like growth factor-I receptor (IGFIR) survival signaling in DG-induced-aging rats to suppress cardiac apoptosis [38]. It has been shown that treatment with the leaf extract increased superoxide dismutase, catalase, and glutathione peroxidase activities and depressed lipid peroxidation in the serum, brain, and liver of DG-induced aging mice [39]. The protective role of green tea and ginkgo biloba extract against aging dysfunction induced by DG in rats was also shown by another study [40]. We hypothesized that DG supplementation would induce detrimental changes on the markers with and potentially long-term consequences. These detrimental effects would be mitigated by Rosehip supplementation and endurance training which in combination would have an accentuated effect rather than either intervention alone.

MATERIAL AND METHODS

Ethics, Animals and Groups

This study was conducted under the National Institutes of Health guidelines (NIH publications [41] with ethical permission granted by the Mazandaran University of Medical Science.

Eighty-six Wistar male rats (six weeks old, 170±20 g body weight) were used in this study. Animals were obtained from Pasteur's Institute (Tehran, Iran) and maintained in the Central Animal House, Faculty of Sciences, University of Mazandaran. The animals were housed 4-5 per cage (volume 46 L). The light was controlled on a 12:12 h light-dark cycle. The temperature was 22± 1.4 C^{o} and humidity was 55.6±4.0%. Animals were fed a pellet rodent diet ad libitum and had free access to water. Strewment was changed every 3 days, and the same person handled the rats throughout the study. Following one week of habituation, rats were randomly divided into two main weight match control (n = 43) and training (n = 43) groups. Animals were further divided into Control Saline (n = 8), Training Saline (n = 9), Control D-galactose (n = 11), Training D-galactose (n = 12), Control Rosehip (n = 12), Training Rosehip (n = 12), Control combined group (n = 12), and Training combined group (n = 10).

Exercise Training Protocol

All training groups ran on a motorized rodent treadmill (Iranian Model, designed by Prof. Abbass Ghanbari-Niaki, Faculty of Sports, University of Mazandaran, Mazandaran, Iran) for 8 weeks. The treadmill had twelve lines for running and was on a level gradient. The exercise training protocol was performed for 90 min/session, 25 m/min (moderate-intensity exercise training [42]), five days/week for eight weeks (Table 1) [43]. The rats completed 6 minutes warm-up and 6 minutes cool-down before and after each session respectively. For each exercise intervention session, the Control groups walked on the treadmill (5 min, 6 m/min) to ensure stress synchronization between the control and exercise groups.

Table 1. Endurance training protocol of the present study. Rats trained on the motorized rodent treadmill with 0 degrees of slope.

Days	Saturday	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Time (min)
Familiarization	-	-	10 (m/min)	10 (m/min)	10 (m/min)	-	-	10
1st week	15 (m/min)	15 (m/min)	15 (m/min)	15 (m/min)	15 (m/min)	-	-	20-30
2nd week	20 (m/min)	20 (m/min)	20 (m/min)	20 (m/min)	20 (m/min)	-	-	30-60
3rd week	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	-	-	60-90
4th week	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	-	-	60-90
5th week	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	-	-	60-90
6th week	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	-	-	60-90
7th week	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	-	-	60-90
8th week	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	25 (m/min)	-	-	60-90

Supplements Preparation and Consumption Protocol

The Rosehip fruits (Rosa canina L. cups) were collected from the countryside of Nosar highland of the Baijan region in close proximity to Amol city, Mazandaran province – Iran. The fruits were pilled and seeds were removed then all collected shells, were dried at normal room temperature away from sunlight in darkness. 25 g of the dried Rosehip shells were then finely powdered by a home blender and mixed with 200 mL hot distilled water then cooked in the oven at 40 ºC for 24 for hours. It noted that content of vitamin C was measured in whole dried ripe rosehip fruit and flash by titration procedure. The extraction procedure was followed based on methods reported previously [44] and DG solution was prepared based on methods by Haider and coauthors, 2015 [45, 46]. DG was purchased from an importing company (made in Switzerland). All supplementary groups consumed the supplement orally (by intragastric gavage) received a daily extract of Rosehip extract and DG solution (35%) and a combined solution (DG + Rosehip extract/175mg+175mg) at a dose of 350 mg (1.75 mL) per 100 g of body weight immediately after the end of each session. The saline groups were treated the same as other supplementary groups.

Plasma Collection

Rats were sacrificed 72 hours after the last session and anaesthetized with a ketamine and xylazine mixture (30–50 mg/kg and 3–5 mg/kg of body weight, respectively). Blood samples obtained from the abdominal cavity were collected into EDTA content tubes. Plasma was separated by centrifugation (15 minutes at 1000 g) then divided into two parts and frozen in liquid nitrogen and stored at -80 Cº for future analysis.

Blood marker analysis

Plasma enzymes ALT, AST, and ALP were measured by using the quantitative kits which have been obtained from Bionic Company (intra-assay coefficient of variation: 1.9% and sensitivity range was at least: 1 U/L). Plasma albumin and urea were also determined by the same method and kits from Bionic company (intra-assay coefficient of variation: 1.9% and sensitivity range was at least: 1 U/L). Plasma levels of bilirubin were measured using photometry with a special kit with variation 0.1-30 mg/dl from Pars Azmoon (Tehran, Iran). Plasma triglyceride (TG) was determined by using an enzymatic colorimetric method (glycerol-3-phosphate oxidase by a kit obtained from Pars Azmoon (Tehran, Iran) (intra-assay coefficient of variation: 2.2% and sensitivity of this method: 1 mg/dL). Plasma total cholesterol (TC) was also determined using an enzymatic colorimetric method (cholesterol oxidase-amino antipyrine) (Pars Azmoon, Tehran, Iran) (intra-assay coefficient of variation: 1.9% and sensitivity of this method: 0.08 mmol/L).

Statistical Analysis

Normality of data was checked using the Kolmogorov–Smirnov test, then analyzed by using a two-way (training x solution) analysis variance (ANOVA). The present study was performed with 2 (training–control (rest) groups) and with 4 solutions (saline/S, D-galactose/DG, D-galactose Rosa/DG, and Rosa/R). In this regard, any significant changes between training status or treatment groups were followed by using a suitable post hoc Bonferroni test. A one-way ANOVA was also employed to clarify within and between groups' effect and the same post hoc Bonferroni test was used. SPSS (IBM software) version 24 was used to perform the

statistical analysis and data are expressed as mean ± standard deviation (SD). The significance level was set at $P<0.05$. Partial eta squared ($\eta 2$) was also reported to emphasize the size of the difference in which 0.01, 0.03, and >0.05 were considered the cut offs for small, medium, and large effects respectively.

RESULTS

Plasma enzymes

Plasma ALT concentrations were significantly higher in DG-treated control and training groups when compared to SC, ST, RC, and RT groups. But the concentration of plasma ALT was significantly lower in DGT and DGR-treated groups after endurance training. This reduction was much higher in DGR-treated groups than DG-treated groups. Rosehip extraction accentuated the endurance training effect to reduce DG-elevated plasma ALT. The magnitude of changes observed was~542% and ~111% for DGC and DGRC groups respectively (Figure 1A, Table 2).

The plasma AST response was somewhat similar to the ALT. As the figure shows the concentrations of plasma AST were higher in DG (~246% change) and DGR-treated (~22% change) groups compared to control. But, the magnitude changes of AST were lower in DGR when compared to the DG-treated groups (Figure 1B Table 2). However, changes in AST concentration were not significant in S and R–treated groups. The result indicates that rosehip extraction alone did not affect AST, but rosehip extraction in combination with DG was able to restore the somewhat DG-induced elevation of plasma AST (Figure 2B).

Plasma ALP concentration was not significantly different in the trained animals versus the non-trained animals, as well as in the Rosehip animals in comparison to the saline groups (Table 2 and Figure 1C). Interaction of the training and the Rosehip on the ALP showed no significant change compared to independent effects ($P >0.05$). DG (~149% change) and DGR (~60% change) increased the ALP concentration compared to the saline. ALP concentration was significantly lower in the DGR consumed animals compared to the DG consumed animals ($P=0.04$) (Figure 1C). Trained DGR animals had no significant change in the ALP compared to the DGR consumed animals ($P=0.33$) (Figure 1C).

Plasma creatinine, albumin, urea and bilirubin

Plasma creatinine concentration was significantly lower in the trained animals versus the non-trained animals (~16% change), as well as in the Rosehip animals in comparison to the saline (~18% change) (Table 2 and Figure 2A). Interaction of the training and the Rosehip on plasma creatinine concentration showed no significant changes compared to independent effects ($P\leq0.05$). DG (~50% change) and DGR (~49% change) increase the creatinine compared to the saline (Table 2). The creatinine was no significant change in the DGR consumed animals compared to the DG consumed animals ($P=0.99$) (Figure 2A). Trained DGR animals had no significant change in the creatinine compared to the DGR consumed animals ($P=0.11$) (Figure 2A). Plasma albumin concentration was found to have a significant increase in the trained animals versus the non-trained animals (~15% change), not in the Rosehip animals in comparison to the saline (Table 2 and Figure 2B). Interaction of the training and the Rosehip on the plasma albumin concentration showed significant changes compared to the saline training group ($P=0.001$) not the control Rosehip ($P=0.37$). DG (~22% change) and DGR (~14% change) decrease the albumin compared to the saline (Table 2). The albumin was significantly higher in the DGR consumed animals compared to the DG consumed animals ($P=0.001$) (Figure 2B). Trained DGR animals were significantly higher in the albumin compared to the DGR consumed animals ($P=0.001$) (Figure 2B).

Plasma urea concentration was not significantly different in the trained animals versus the non-trained animals (Table 2 and Figure 2C). The Rosehip animals had significantly lower plasma urea concentration in comparison to the saline (Table 2). Interaction of the training and Rosehip on plasma urea concentration showed no significant change compared to independent groups ($P>0.05$). DG (~78% change) and DGR (~67% change) increase the urea compared to the saline (Table 2). The urea was no significant change in DGR consumed animals compared to the DG consumed animals ($P=0.43$) (Figure 2C). Trained DGR animals showed no significant changes in the urea compared to the DGR consumed animals ($P=0.97$) (Figure 2C).

Plasma total bilirubin concentration was found to have no significant change in the trained animals versus the non-trained animals (Table 2 and Figure 2D). The Rosehip animals had significantly higher plasma total bilirubin concentration in comparison to the saline (~57% change) (Table 2). Interaction of the training and the Rosehip on the bilirubin showed no significant changes compared to independent effects ($P>0.05$). DG (~196% change) and DGR (~209% change) increase the total bilirubin compared to the saline (Table 2). The total bilirubin showed a significant decrease in the DGR consumed animals compared to the DG consumed animals ($P=0.001$) (Figure 2D). Trained DGR animals showed no significant change in the total bilirubin

compared to the DGR consumed animals (P=0.06) (Figure 2D). Plasma total bilirubin was higher in DG and DGR-treated rats. Interestingly there is no similar responses between DG-trained and DGR-trained rats. Although Rosehip extraction somehow reduced DG-induced elevation in plasma total bilirubin, it was not able to reinforce endurance-induced reduction in plasma total bilirubin in DGR-trained group (Figure 2D).

Plasma total cholesterol (TC) and triglycerides (TG)

The results of plasma TC revealed a significant (P=0.001) elevation about 4.3 times (~ 430%) higher in Control-DG treated rats when compared to control-S treated rats (Figure 3A, Table. 2), Although, the levels of plasma TC was significantly (P=0.001) decreased in DG-trained rats, it still near about 3.6 times (360%) higher when compared to S-trained rats. As results show, the concentration of plasma TC was 2.33-2.22 times low in control and trained DGR-treated groups when compared to control and trained DG-groups, respectively. The concentration of plasma TC were unchanged in S and R groups (Figure 3A, Table 2). It seems rosehip extraction in combination with DG solution was able to minimize a DG-induced elevation in plasma TC in DG-treated rats.

There was no significant difference in plasma triglycerides between the control and training groups (Table 2, Figure 3B) A lower and significant plasma triglyceride concentration (25%) was also observed in R-treated rats when compared to saline-treated rats. However, we did not find any interaction between endurance training and rosehip extraction treatment (P>0.05). The considerable increases in plasma triglyceride were observed in DG (~174% change) and DGR (~114% change) treated groups when compared to the saline-treated rats (Table 2). The triglyceride concentration showed no significant change in the DGR-treated rats when also compared to the DG alone (P=0.74) (Figure 3B). Data analysis for plasma triglycerides showed a significant difference between treatment groups (P=0.001) and a significant difference has no found between training and control groups (P=0.09). A highest and significant plasma TG was observed in DG groups when compared with DGR, R and S groups (Figure 3B, Table 2). Further analysis by using a one-way ANOVA revealed a lowest and significant plasma TG in RT when compared to S, DG, and DGR –trained groups. However, in this regard, we observed a lower and significant plasma TG in DGR (DG+Rosa) trained rats when compared to DG-trained rats, but the level of plasma TG in DGR-trained rats was significantly (P<0.003) higher when compared to S-trained rats. It means endurance training reinforced TG lowering effect of rosehip extraction which induced by DG consumption.

Table 2. The effects of the present study interventions on plasma variables in different groups. Data were analyses using the two-way ANOVA. *: significant effect.

Variables	Endurance training vs. Control			Rosehip vs. Saline			D-galactose vs. Saline			Rosehip + D-galactose vs. Saline		
	F	***P***	η^2	***F***	***P***	η^2	***F***	***P***	η^2	***F***	***P***	η^2
ALT(U/L)	4.51	0.03*	0.05	0.02	0.88	0.001	98.45	0.001*	0.70	12.91	0.001*	0.25
AST(U/L)	1.72	0.19	0.02	150.35	0.001*	0.79	182.88	0.001*	0.81	4.01	0.05*	0.09
ALP(U/L)	0.13	0.71	0.002	0.50	0.48	0.01	38.00	0.001*	0.47	9.45	0.004*	0.20
Creatinine(mg/dL)	6.31	0.01*	0.07	8.00	0.007*	0.17	11.52	0.001*	0.21	27.88	0.001*	0.43
Albumin(mg/dL)	17.50	0.001*	0.17	1.12	0.29	0.02	13.58	0.001*	0.24	6.54	0.01*	0.15
Urea(mg/dL)	0.43	0.51	0.005	37.23	0.001*	0.48	21.23	0.001*	0.33	94.73	0.001*	0.71
Total bilirubin(mg/dL)	0.30	0.58	0.004	33.42	0.001*	0.46	29.31	0.001*	0.41	132.49	0.001*	0.78
Cholesterol(mg/dL)	0.70	0.40	0.08	13.41	0.001*	0.25	295.82	0.001*	0.87	70.68	0.001*	0.65
Triglyceride(mg/dL)	1.00	0.32	0.01	100.58	0.001*	0.72	33.44	0.001*	0.44	48.10	0.001*	0.56

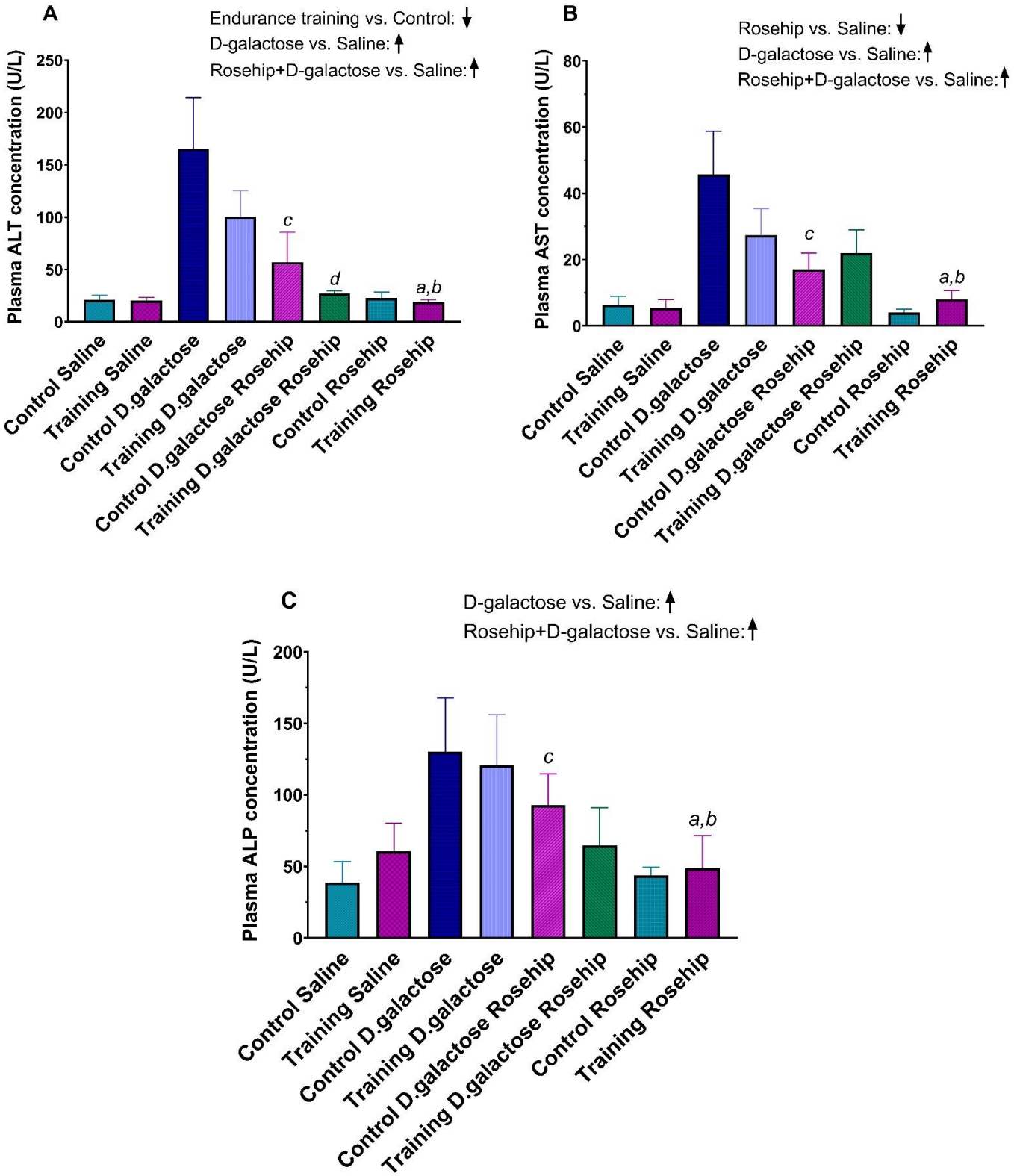


Figure 1. Plasma ALT (U/L) (A), AST (U/L) (B), and ALP (U/L) (C) concentrations in different groups of the present study. Data were expressed mean±SD, P-value set at ≤ 0.05. a: significant change vs Training Saline, b: significant change vs Control Rosehip, c: significant change vs Control D-galactose, d: significant change vs Control D-galactose+Rosehip.

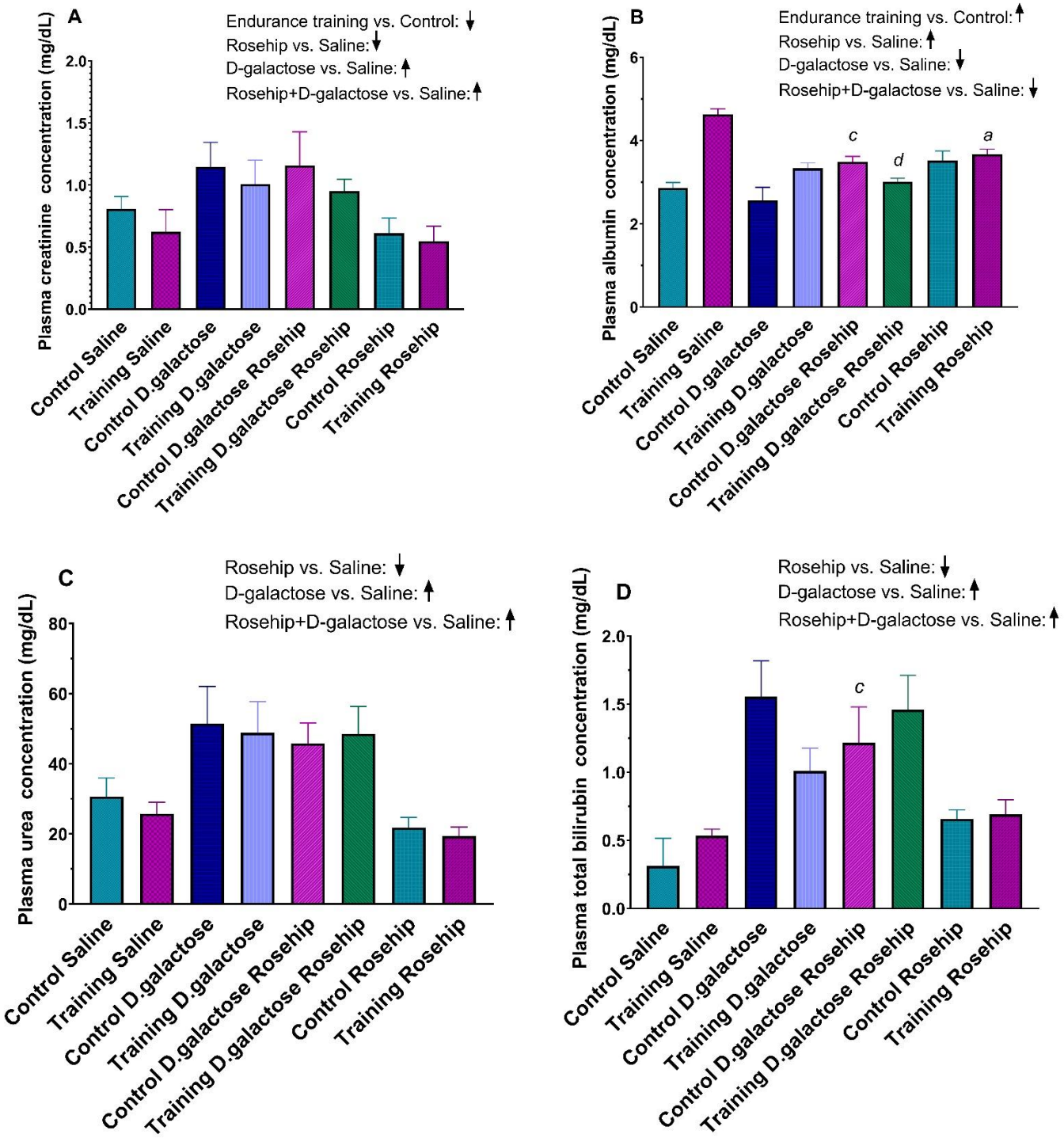


Figure 2. Plasma creatinine (mg/dL) (A), albumin (mg/dL) (B), urea (mg/dL) (C), and bilirubin (mg/dL) concentrations in different groups of the present study. Data were expressed mean±SD, P-value set at ≤ 0.05. a: significant change vs Training Saline, c: significant change vs Control D-galactose, d: significant change vs Control D-galactose+Rosehip.

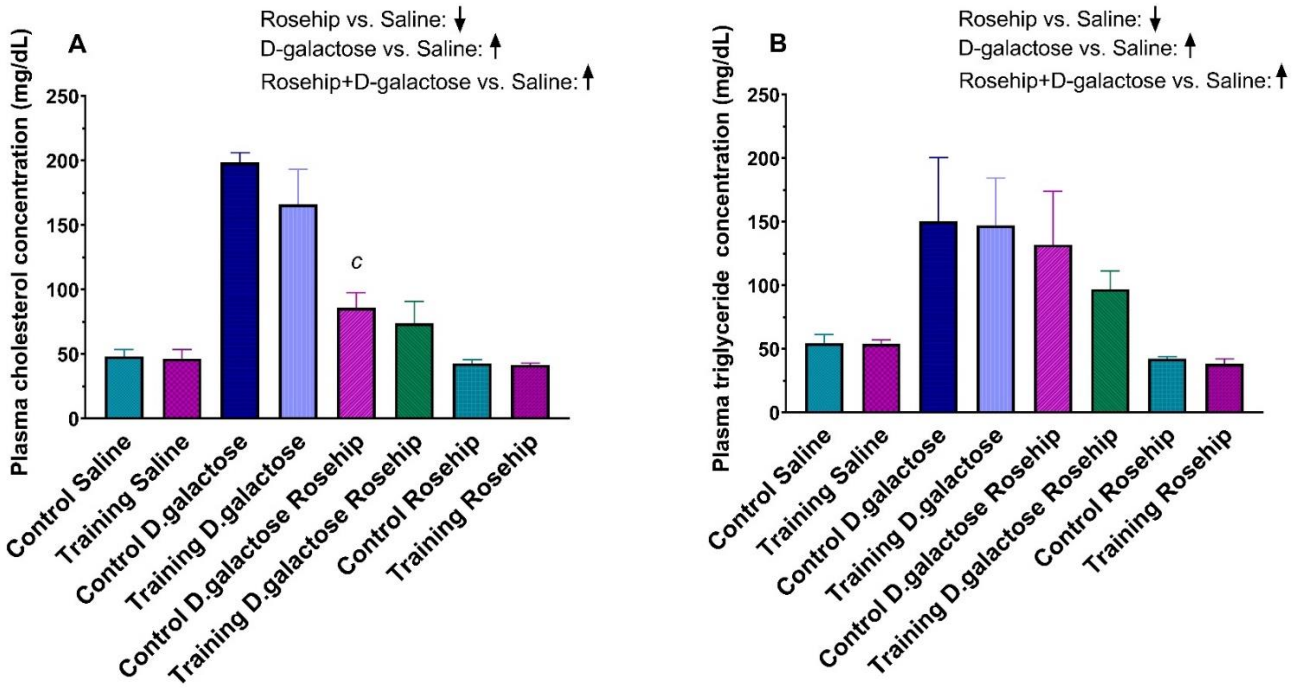


Figure 3. Plasma cholesterol(mg/dL) (A) and triglyceride (mg/dL) (B) concentrations in different groups of the present study. Data were expressed mean±SD, P-value set at ≤ 0.05. c: significant change vs Control D-galactose.

DISCUSSION

The key findings of the present study are 1) Endurance training significantly increases plasma albumin, while reduces ALT and creatinine. 2) Rosehip extract reduced plasma AST, creatinine, urea, cholesterol, and triglyceride, while increasing bilirubin. 3) The combination of endurance training and Rosehip extract led to an additive effect compared to each intervention alone on AST. 4) The use of DG increased the ALT, AST, ALP, creatinine, urea, bilirubin, cholesterol, and triglyceride concentration, while decreasing albumin concentration. 5) The use of Rosehip extract along with DG mitigates the harmful effects of DG on ALT, AST, ALP, bilirubin, and cholesterol concentration.

Taghizadeh and coauthors (2018) [47] examined the effects of Rosehip fruit hydroalcoholic extraction at doses 250 and 500 mg/kg of rat body weight on hepatic markers in diabetic rats for 42 days, the results indicate that a diabetes-induced elevation in fasting blood glucose AST, ALT, and reduction in total antioxidant capacity were restored by both given doses of Rosehip fruit extraction. They also mentioned that the lower dose was more effective than a higher dose of Rosa canina fruit extraction. Karimmojahed and coauthors (2020) showed that Rosa canina distilled water improved liver enzyme and renal function indices which disturbed due to tamoxifen treatment [48]. Sadeghi and coauthors (2016) showed the hepatoprotective effects of the extract of Rosa canina on CCl_4-induced hepatic damage in rats [49]. They suggested that these effects may be produced through reducing oxidative stress [49]. Changizi and coauthors (2013) showed the protective effects of Rosa canina fruit extract on renal disturbances induced by reperfusion injury in rats [50]. In another study prior to this Taghaizadeh and coauthors (2016) [51] who studied the anti-lipidemic effects of Rosa canina fruit extract in diabetic rats; reported that the supplementation of Rosa extraction at doses 250 and 500 mg/kg rat body weight significantly reduced a diabetes-induced elevation in plasma TG, but the effect of 250 mg/kg of body weight was more effective. They also mentioned that Rosa extraction has no effect on plasma TC concentration. Regarding the DG-induced increase in plasma TC our results are not in agreement with Taghaizadeh et al. (2016) [51], but are similar for Rosehip extraction. In one study using the same doses of Rosehip fruit extraction in diabetic rats glucose, creatinine and urea were decreased but the supplementation did not change plasma albumin concentration [52].

Several published articles have studied the effects of different kinds of medicinal herbs in combination with exercise training on plasma liver enzymes [53-56]. Although the mechanism(s) by which the aqueous Rosehip fruit extraction can exert its anti-glycemic, anti-lipidemic antioxidant effect on the plasmatic liver-related enzymes, total bilirubin, creatinine, TG, TC and other biochemical variables is not fully understood we postulate that vitamin C and its related family are acting as an antioxidant in the Rosa species. Georgieva and coauthors (2014) [57] who measured the content of vitamin C in different fractions of rosehip extracts.

Also reported that the content of vitamin C was 1.1 mg/g in whole fruit of the dried ripe fruits 2.3 mg/g in skin, 0.4 mg/g in seeds, and 0.2 mg/g in pappi. Demir and coauthors (2014) determined the content of ascorbic acid content in 5 Rosa varieties and reported that the levels of ascorbic acid content ranged from 65.75 mg/100 g in Rosa dumalis to 160.30 mg/100g in Rosa canina dry weight [58]. In another study by Ercisli (2007) [59] who reported the ascorbic acid contents were ranged from 727 mg/100 mL in Rosa villosa to 943 mg/100 mL in Rosa dumalis. In the present study, the content of vitamin C was measured in whole dried ripe Rosehip fruit and flash. The content was ranged from 135 to 149 mg/100 g dry weight.

Adaramoye and coauthors (2008) who reported that vitamin C supplementation (800 mg/kg of rat body weight) significantly reduced gamma radiation-induced increase in rat liver ALT and AST activities which accompanied with a significant increase in reduced GSH whose recognized as the main part of an endogenous non-enzyme antioxidant defence system [60]. As we showed plasma total bilirubin was significantly higher in Control-DG treated rats, the elevated total bilirubin was significantly decreased after endurance training. Therefore, total bilirubin elevation was prevented somewhat in the control-DGR group, while at the end of endurance training significantly increased. These findings are in agreement with Swift and coauthors (2012) [61], Hinds and coauthors (2020) [62], and Witek and coauthors (2016) [63]. One of the possible mechanisms for the change in total bilirubin might be attributed to hepatic biliverdin reductase-A (BVRA) expression and suppression of UGT1A1 as noted by Hinds and coauthors (2020) [62], which will be measured in future studies.

Using GC-MS analysis method has shown that the fresh and dried Rosehip extractions and its seeds oil contain bio-compounds including unsaturated fatty acids (Oleic acids, linoleic acid, alpha-linolenic acid) and methlhydroxyfurfural (HFM) which have anti-inflammatory, antidiabetic, antioxidant, and hepatoprotective effects [64-66]. Rosehip fruits are also rich in other antioxidants (carotenoids, tocopherol, phenolic acid, bioflavonoids, tannin, pectin), amino acid, organic acids, essential oils, and lycopene [32]. The antioxidants in the Rosehip appear to prevent oxidative stress and prevent the release of aminotransferase enzymes from liver cells to help treat hepatotoxicity [67]. Studies show that D-galactose may alter the function of liver enzymes and impair liver function by disrupting the antioxidant balance. Induction of D-galactose has been shown to reduce the natural ability to convert galactose to glucose, increasing galactitol and activating aldose reductase, which in turn reduces the NADPH and leads to the accumulation of hydrogen peroxide and other free radicals [68]. Thus, Rosehip due to antioxidants may prevent the harmful effects of D-galactose. Antioxidants, essential oils, and unsaturated fatty acids also showed to have beneficial effects on creatinine, albumin, urea, bilirubin, and plasma lipids [69-71].

The effects of regular exercise training on the present study variables have been confirmed by several studies [72, 73]. The influences of regular exercise training on body antioxidant defence also are reported [74]. There is a paucity of data on rosehip supplementation and exercise training with only one published article by Ali Asghari Gelodar and coauthors (2020) [75] who studied on the effects of aqueous Rosehip fruit extraction (350 mg/ 100 g of rat body weight in 1.7 mL solution) plus endurance exercise training (25 m/min, 90 minutes/session, 5 days/week and for 8 weeks) on liver enzymes. They reported that a lower and significant liver AST concentration in Rosehip groups when compared to saline groups with the consideration that endurance exercise training reduced liver AST concentration in both saline and Rosehip-trained groups. The reduction was more pronounced in Rosehip-trained rats so our results are aligned for liver ALT, GGT, and ALP concentration. In the present study, it seems that the inclusion of Rosehip has an additive beneficial effect on the study variables.

The effects of exercise training plus other herb extracts has been studied by Akbari-Fakhrabadi and coauthors (2019) [76] who examined a progressive endurance training (10 m to 20 m/min, 5 days/week and for 8 weeks at 60% VO_2 max) plus ethanolic extraction of saffron (Crocus Sativus) at a dose of 40 mg/kg of body weight in rats. They reported a significant lowering of TG and AST but no significant change in ALT in the exercise plus saffron group when compared to control rats. Huang et al. (2013) [77] studied hepatoprotective effects of Ganoderma tsugae (GT) a well-known medicinal mushroom at 0, low (0.1875 g), moderate (0.9375 g), and high (1.875 g/kg/day) doses on exhaustive exercise-induced liver damage. They reported that GT supplemented rats had considerably lower but nonsignificant AST and ALT levels all treated –GT rats when compared with a control group. Yada and coauthors (2020) [78] who showed that acacia polyphenol (AP) supplementation significantly increased plasma ALT and AST levels and exhaustive exercise reinforced elevation in AST levels. A reduction in liver GSH and GSH reductase after exercise with AP supplementation. Huang and coauthors (2013) [36] who studied the effect of 12 weeks swimming exercise (5 times/week for 60 min/time) on D-galactose-induced ageing model in rats (intraperitoneal d-galactose injections by 150 mg/kg/day for 12 weeks). They suggested that a significant DG-elevated AST, ALT levels were reduced by swimming training in DG-trained rats. They also reported that plasma GGT activities was also reduced in trained groups. Wasityastuti and coauthors (2019) investigated the effects of low and

moderate treadmill exercise on liver of d-galactose-exposed aging rats [37]. They showed that low intensity exercise lowered the degree of DG-exposed hepatic fibrosis, and moderate intensity exercise restore the injured liver tissue back to the non-aging state. DG causes inflammation marked by the elevated number of M1 and M2 macrophages. Moderate exercise drove M1/M2 ratio back to the control condition [37].

Limitations and Strengths

The limitations of this study are 1) lack of Rosehip gas chromatography-mass-spectrometry (GC-MS) analyses. However, previous studies have reported significant findings with Rosehip GC-MS and content of vitamin C was measured in present study 2). We have limited our analyses to plasma, and tissue samples so need to examine other mechanistic variables in research. Despite some limitations, this study has notable strengths including: 1) Novelty of research regarding the combined effects of endurance training and Rosehip supplementation on numerous study variables which has not been published previously to the authors' knowledge 2) Measurements of both enzymatic and non-enzymatic variables, as well as common clinical variables.

Future research

Our findings for novel study variables need confirming so we encourage other researchers to explore this topic. Future lines of enquiry will explore potential differences between fresh and dried Rosa canina fruits extraction on liver antioxidant enzymes including varying the dose, Gene expression as well as the related mechanism(s) warrants further study. Likewise, different doses of exercise by manipulating the frequency, intensity and duration should be explored as well as changing the mode.

Practical application

Rosa canina fruits can be considered a functional food which has positive effects on numerous disease markers.

CONCLUSION

Chronic D-galactose consumption is detrimental to numerous health markers but Rosehip supplementation mitigated some of these effects in male rats. Endurance training and Rosehip have an additive and positive effect on plasmatic liver markers so should be used as an intervention to improve health.

Funding: The authors have no funding to report.
Acknowledgments: The authors appreciate the Prof. Rozita Fathi for helpful comments.
Conflicts of Interest: The authors declare that they have no conflict of interest.

REFERENCES

1. PubChem [Internet]. Bethesda (MD): National Library of Medicine (US), National Center for Biotechnology Information; 2004-. PubChem Compound Summary for CID 6036, D-Galactose; [cited 2020 Dec. 14]. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/D-Galactose.
2. Xu LQ, Xie YL, Gui SH, Zhang X, Mo ZZ, Sun CY, et al. Polydatin attenuates d-galactose-induced liver and brain damage through its anti-oxidative, anti-inflammatory and anti-apoptotic effects in mice. Food Funct. 2016; 7 (11): 4545-55. doi: 10.1039/c6fo01057a.
3. Berry GT, Segal S and Gitzelmann R. Disorders of Galactose Metabolism. In: Fernandes J, Saudubray J-M, van den Berghe G, Walter JH, editors. Inborn Metabolic Diseases: Diagnosis and Treatment. Berlin, Heidelberg: Springer Berlin Heidelberg; 2006. p. 121-30.
4. Bo-Htay C, Palee S, Apaijai N, Chattipakorn SC, Chattipakorn N. Effects of d-galactose-induced ageing on the heart and its potential interventions. J Cell Mol Med. 2018;22(3):1392-410. doi: 10.1111/jcmm.13472.
5. Xiao M-H, Xia J-Y, Wang Z-L, Hu W-X, Fan Y-L, Jia D-Y, et al. Ginsenoside Rg1 attenuates liver injury induced by D-galactose in mice. Exp Ther Med. 2018;16(5):4100-6. doi: 10.3892/etm.2018.6727.
6. Chen P, Chen F, Zhou B. Antioxidative, anti-inflammatory and anti-apoptotic effects of ellagic acid in liver and brain of rats treated by D-galactose. Sci Rep. 2018;8(1):1465. doi: 10.1038/s41598-018-19732-0.
7. Kallai L, Hahn A, Roeder V, Zupanic V. Correlation between Histological Findings and Serum Transaminase Values in Chronic Diseases of the Liver. Acta Med Scand. 1964;175:49-56. doi: 10.1111/j.0954-6820.1964.tb00549.x.
8. Sheth SG, Gordon FD, Chopra S. Nonalcoholic steatohepatitis. Ann Intern Med. 1997;126(2):137-45. doi: 10.7326/0003-4819-126-2-199701150-00008.
9. Thapa BR and Walia A. Liver function tests and their interpretation. Indian J Pediatr. 2007;74(7):663-71. doi: 10.1007/s12098-007-0118-7.

10. Gowda S, Desai PB, Hull VV, Math AA, Vernekar SN, Kulkarni SS. A review on laboratory liver function tests. Pan Afr Med J. 2009;3:17.
11. Washington IM, Van Hoosier G. Clinical Biochemistry and Hematology. The Laboratory Rabbit, Guinea Pig, Hamster, and Other Rodents. 2012; 57-116. doi: 10.1016/B978-0-12-380920-9.00003-1.
12. Purkins L, Love ER, Eve MD, Wooldridge CL, Cowan C, Smart TS, et al. The influence of diet upon liver function tests and serum lipids in healthy male volunteers resident in a Phase I unit. Br J Clin Pharmacol. 2004;57(2):199-208. doi: 10.1046/j.1365-2125.2003.01969.x.
13. Selvakumar K, Bavithra S, Suganya S, Ahmad Bhat F, Krishnamoorthy G, Arunakaran J. Effect of Quercetin on Haematobiochemical and Histological Changes in the Liver of Polychlorined Biphenyls-Induced Adult Male Wistar Rats. J Biomark. 2013;2013 960125. doi: 10.1155/2013/960125.
14. Mann S, Beedie C, Jimenez A. Differential effects of aerobic exercise, resistance training and combined exercise modalities on cholesterol and the lipid profile: review, synthesis and recommendations. Sport Med (Auckland, NZ). 2014;44(2):211-21. doi: 10.1007/s40279-013-0110-5.
15. Shamsoddini A, Sobhani V, Ghamar Chehreh ME, Alavian SM, Zaree A. Effect of Aerobic and Resistance Exercise Training on Liver Enzymes and Hepatic Fat in Iranian Men With Nonalcoholic Fatty Liver Disease. Hepat Mon. 2015;15(10) e31434-e.doi: 10.5812/hepatmon.31434.
16. Pham-Huy LA, He H and Pham-Huy C. Free radicals, antioxidants in disease and health. IJBS. 2008;4(2):89-96.
17. Lobo V, Patil A, Phatak A and Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev. 2010;4(8):118-26. doi: 10.4103/0973-7847.70902.
18. Kurutas EB. The importance of antioxidants which play the role in cellular response against oxidative/nitrosative stress: current state. Nutr J. 2016;15(1):71. doi: 10.1186/s12937-016-0186-5.
19. Bouayed J and Bohn T. Exogenous antioxidants--Double-edged swords in cellular redox state: Health beneficial effects at physiologic doses versus deleterious effects at high doses. Oxid Med Cell Longev. 2010;3(4):228-37. doi: 10.4161/oxim.3.4.12858.
20. Bo-Htay C, Shwe T, Higgins L, Palee S, Shinlapawittayatorn K, Chattipakorn SC, et al. Aging induced by D-galactose aggravates cardiac dysfunction via exacerbating mitochondrial dysfunction in obese insulin-resistant rats. GeroScience. 2020;42(1):233-49. doi: 10.1007/s11357-019-00132-9.
21. Bo-Htay C, Palee S, Apaijai N, Chattipakorn SC, Chattipakorn N. Effects of d-galactose-induced ageing on the heart and its potential interventions. J Cell Mol Med. 2018;22(3):1392-410. doi: 10.1111/jcmm.13472.
22. Umbayev B, Askarova S, Almabayeva A, Saliev T, Masoud AR, Bulanin D. Galactose-Induced Skin Aging: The Role of Oxidative Stress. Oxid Med Cell Longev. 2020; 2020 7145656. doi: 10.1155/2020/7145656.
23. Ahangarpour A, Oroojan AA, Khorsandi L, Lamoochi Z. Effect of Hydroalcoholic Extract of Purslane (Portulaca Oleracea L.) on Diabetic Variables in D-Galactose Induced Aging Mouse Model. Acta Endocrinol (Buchar). 2018; 14 (1): 24-9. doi: 10.4183/aeb.2018.24.
24. Shan Q, Lu J, Zheng Y, Li J, Zhou Z, Hu B, et al. Purple sweet potato color ameliorates cognition deficits and attenuates oxidative damage and inflammation in aging mouse brain induced by d-galactose. J Biomed Biotechnol. 2009; 2009. ID 564737. doi: 10.1155/2009/564737.
25. Zhuang Y, Ma Q, Guo Y, Sun L. Protective effects of rambutan (Nephelium lappaceum) peel phenolics on H2O2-induced oxidative damages in HepG2 cells and d-galactose-induced aging mice. Food Chem Toxicol. 2017;108(Pt B): 54-62. doi: 10.1016/j.fct.2017.01.022.
26. Ma Y, Ma B, Shang Y, Yin Q, Wang D, Xu S, et al. Flavonoid-Rich Ethanol Extract from the Leaves of Diospyros kaki Attenuates D-Galactose-Induced Oxidative Stress and Neuroinflammation-Mediated Brain Aging in Mice. Oxid Med Cell Longev. 2018; 2018 8938207. doi: 10.1155/2018/8938207.
27. Mohammadi E, Mehri S, Badie Bostan H, Hosseinzadeh H. Protective effect of crocin against d-galactose-induced aging in mice. Avicenna J Phytomed. 2018; 8 (1): 14-23.
28. Shahroudi MJ, Mehri S, Hosseinzadeh H. Anti-Aging Effect of Nigella Sativa Fixed Oil on D-Galactose-Induced Aging in Mice. J Pharmacopuncture. 2017;20(1):29-35. doi: 10.3831/KPI.2017.20.006.
29. Lee J, Kim YS, Kim E, Kim Y, Kim Y. Curcumin and hesperetin attenuate D-galactose-induced brain senescence in vitro and in vivo. Nutr Res Pract. 2020;14(5):438-52. doi: 10.4162/nrp.2020.14.5.438.
30. Zhu SY, Dong Y, Tu J, Zhou Y, Zhou XH, Xu B. Silybum marianum oil attenuates oxidative stress and ameliorates mitochondrial dysfunction in mice treated with D-galactose. Pharmacogn Mag. 2014;10(Suppl 1):S92-9. doi: 10.4103/0973-1296.127353.
31. Nam SM, Seo M, Seo JS, Rhim H, Nahm SS, Cho IH, et al. Ascorbic Acid Mitigates D-galactose-Induced Brain Aging by Increasing Hippocampal Neurogenesis and Improving Memory Function. Nutrients. 2019; 11 (1): doi: 10.3390/nu11010176.
32. Koczka N, Stefanovits-Bányai É and Ombódi A. Total Polyphenol Content and Antioxidant Capacity of Rosehips of Some Rosa Species. Medicines (Basel, Switzerland). 2018;5(3):84. doi: 10.3390/medicines5030084.
33. Ayati Z, Amiri MS, Ramezani M, Delshad E, Sahebkar A, Emami SA. Phytochemistry, Traditional Uses and Pharmacological Profile of Rose Hip: A Review. Curr Pharm Des. 2018; 24 (35): 4101-24. doi: 10.2174/1381612824666181010151849.
34. Taghizadeh M, Rashidi AA, Taherian AA, Vakili Z and Mehran M. The Protective Effect of Hydroalcoholic Extract of Rosa canina (Dog Rose) Fruit on Liver Function and Structure in Streptozotocin-Induced Diabetes in Rats. J Diet Suppl. 2018; 15 (5): 624-35. doi: 10.1080/19390211.2017.1369205.

35. Gholampour F, Owji SM. Liver Ameliorative Effects of the Hydroalcohol Extract of Rosa canina L. Fruit against Ischemic Acute Renal Failure-induced Hepatic Damage in Wistar Rats. Int J Zool Res. 2013;9 58-65. doi: 10.3923/ijzr.2013.58.65
36. Huang C-C, Chiang W-D, Huang W-C, Huang C-Y, Hsu M-C, Lin W-T. Hepatoprotective Effects of Swimming Exercise against D-Galactose-Induced Senescence Rat Model. eCAM. 2013; 2013 275431. doi: 10.1155/2013/275431.
37. Wasityastuti W, Habib NA, Sari DCR, Arfian N. Effects of low and moderate treadmill exercise on liver of d-galactose-exposed aging rat model. Physiol Rep. 2019;7(21) e14279-e. doi: 10.14814/phy2.14279.
38. Lay I-S, Kuo W-W, Shibu MA, Ho T-J, Cheng S-M, Day CH, et al. Exercise training restores IGFIR survival signaling in d-galactose induced-aging rats to suppress cardiac apoptosis. J Adv Res. 2020;28:35-41. doi: 10.1016/j.jare.2020.06.015.
39. Turgut NH, Mert DG, Kara H, Egilmez HR, Arslanbas E, Tepe B, et al. Effect of black mulberry (Morus nigra) extract treatment on cognitive impairment and oxidative stress status of D-galactose-induced aging mice. Pharm Biol. 2016;54(6):1052-64. doi: 10.3109/13880209.2015.1101476.
40. Sofy S, Kakey E, Alshamaa S. The Protective Role of Green Tae and Ginkgo biloba Extract against Aging Dysfunction Induced by D-Galactose in Rats. Glob J Biol Agric Health Sci. 2014; 3(3):97-101.
41. National Research Council (US) Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Guide for the Care and Use of Laboratory Animals. 8th edition. Washington (DC): National Academies Press (US); 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK54050/ doi: 10.17226/12910.
42. Rahmati-Ahmadabad S, Broom DR, Ghanbari-Niaki A, Shirvani H. Effects of exercise on reverse cholesterol transport: A systemized narrative review of animal studies. Life Sci. 2019;224:139-48. doi: 10.1016/j.lfs.2019.03.058.
43. Khabazian BM, Ghanbari-Niaki A, Safarzadeh-Golpordesari A, Ebrahimi M, Rahbarizadeh F, Abednazari H. Endurance training enhances ABCA1 expression in rat small intestine. Eur J Appl Physiol. 2009;107(3):351-8. doi: 10.1007/s00421-009-1133-3.
44. Deliorman Orhan D, Hartevioğlu A, Küpeli E, Yesilada E. In vivo anti-inflammatory and antinociceptive activity of the crude extract and fractions from Rosa canina L. fruits. J Ethnopharmacol. 2007;112(2):394-400. doi: 10.1016/j.jep.2007.03.029.
45. Haider S, Liaquat L, Shahzad S, Sadir S, Madiha S, Batool Z, et al. A high dose of short term exogenous D-galactose administration in young male rats produces symptoms simulating the natural aging process. Life Sci. 2015;124:110-9. doi: 10.1016/j.lfs.2015.01.016.
46. Ho S-C, Liu J-H, Wu R-Y. Establishment of the mimetic aging effect in mice caused by D-galactose. Biogerontology. 2003;4(1):15-8. doi: 10.1023/A:1022417102206.
47. Taghizadeh M, Rashidi AA, Taherian AA, Vakili Z, Mehran M. The Protective Effect of Hydroalcoholic Extract of Rosa canina (Dog Rose) Fruit on Liver Function and Structure in Streptozotocin-Induced Diabetes in Rats. J Diet Suppl. 2018;15(5):624-35. doi: 10.1080/19390211.2017.1369205.
48. Karimimojahed F, Hosseini RH, Ziamajidi N, Abbasalipourkabir R, Nourian A. Effect of Rosa canina Distilled Water on Tamoxifen-treated Male Wistar Rats. Pak J Biol Sci. 2020;23(2):173-80. doi: 10.3923/pjbs.2020.173.180.
49. Sadeghi H, Hosseinzadeh S, Akbartabar Touri M, Ghavamzadeh M, Jafari Barmak M, Sayahi M, et al. Hepatoprotective effect of Rosa canina fruit extract against carbon tetrachloride induced hepatotoxicity in rat. Avicenna J Phytomed. 2016;6(2):181-8. doi: 10.22038/ajp.2016.5481
50. Changizi Ashtiyani S, Najafi H, Jalalvandi S, Hosseinei F. Protective effects of Rosa canina L fruit extracts on renal disturbances induced by reperfusion injury in rats. Iran J Kidney Dis. 2013;7(4):290-8.
51. Taghizadeh M, Rashidi AA, Taherian AA, Vakili Z, Sajad Sajadian M, Ghardashi M. Antidiabetic and Antihyperlipidemic Effects of Ethanol Extract of Rosa canina L. fruit on Diabetic Rats: An Experimental Study With Histopathological Evaluations. J Evid Based Complementary Altern Med. 2016;21(4):Np25-30. doi: 10.1177/2156587215612626.
52. Khojasteh S, Ansari Ozi S, Sheikhzadeh F, Dehghan G, Mohammad Nezhad D, Farsad Akhtar N. Effect of ethanolic extract of Rosa canina on some serum biochemical parameters of diabetic male rats. Anim Res Int. 2014;11(3).
53. Ghalandari K, Shabani M, Khajehlandi A, Mohammadi A. Effect of aerobic training with silymarin consumption on glycemic indices and liver enzymes in men with type 2 diabetes. Arch Physiol Biochem. 2020;1-6. doi: 10.1080/13813455.2020.1797104.
54. Moradi Kelardeh B, Rahmati-Ahmadabad S, Farzanegi P, Helalizadeh M, Azarbayjani MA. Effects of non-linear resistance training and curcumin supplementation on the liver biochemical markers levels and structure in older women with non-alcoholic fatty liver disease. J Bodyw Mov Ther. 2020;24(3):154-60. doi: 10.1016/j.jbmt.2020.02.021.
55. Cavalera M, Axling U, Berger K, Holm C. Rose hip supplementation increases energy expenditure and induces browning of white adipose tissue. Nutr Metab (Lond). 2016;13 91. doi: 10.1186/s12986-016-0151-5.
56. Naghavi-Azad E, Rahmati-Ahmadabad S, Amini H, Azizbeigi K, Helalizadeh M, Iraji R, et al. Effects of simultaneous intake of chamomile and ibuprofen on delayed-onset muscle soreness markers and some liver

enzymes following eccentric exercise. Ger J Exerc Sport Res. 2020;50(3):395-405. doi: 10.1007/s12662-020-00662-x.
57. Georgieva S, Angelov G, Boyadzhieva S, Bonchev G, editors. Concentration of vitamin C and antioxidant activity of rosehip extracts. 2014.
58. Demir N, Yildiz O, Alpaslan M, Hayaloglu AA. Evaluation of volatiles, phenolic compounds and antioxidant activities of rose hip (Rosa L.) fruits in Turkey. LWT. 2014;57(1):126-33. doi: 10.1016/j.lwt.2013.12.038.
59. Ercisli S. Chemical composition of fruits in some rose (Rosa spp.) species. Food Chem. 2007;104(4):1379-84. doi:10.1016/j.foodchem.2007.01.053.
60. Adaramoye O, Ogungbenro B, Anyaegbu O, Fafunso M. Protective effects of extracts of Vernonia amygdalina, Hibiscus sabdariffa and vitamin C against radiation-induced liver damage in rats. J Radiat Res. 2008;49(2):123-31. doi: 10.1269/jrr.07062.
61. Swift DL, Johannsen NM, Earnest CP, Blair SN, Church TS. Effect of different doses of aerobic exercise training on total bilirubin levels. Med Sci Sports Exerc. 2012;44(4):569-74. doi: 10.1249/MSS.0b013e3182357dd4.
62. Hinds TD, Jr. Creeden JF, Gordon DM, Spegele AC, Britton SL, Koch LG, et al. Rats Genetically Selected for High Aerobic Exercise Capacity Have Elevated Plasma Bilirubin by Upregulation of Hepatic Biliverdin Reductase-A (BVRA) and Suppression of UGT1A1. Antioxidants (Basel, Switzerland). 2020;9(9). doi: 10.3390/antiox9090889.
63. Witek K, Scislowska J, Turowski D, Lerczak K, Lewandowska-Pachecka S, Pokrywka A. Total bilirubin in athletes, determination of reference range. Biol Sport. 2017;34(1):45-8. doi: 10.5114/biolsport.2017.63732.
64. Dragana P, Ana K, Tanja P, Tijana U, Dušica D, Viktor N, et al. Assessment of Chemical and Antioxidant Properties of Fresh and Dried Rosehip (Rosa canina L.). Not Bot Horti Agrobot. 2018;47(1). doi: 10.15835/nbha47111221.
65. Wenzig EM, Widowitz U, Kunert O, Chrubasik S, Bucar F, Knauder E, et al. Phytochemical composition and in vitro pharmacological activity of two rose hip (Rosa canina L.) preparations. Phytomedicine. 2008;15(10):826-35. doi: 10.1016/j.phymed.2008.06.012.
66. Ozyurt D, Demirata B, Apak R, Hamilton JF, Lewis AC, Ozel MZ. GC×GC-TOF/MS chromatographic analysis, antioxidant capacity and phenolic content of Rosa Canina L. at different maturities. Rec Nat Prod. 2016;10(4):407-25.
67. Muriel P, Moreno MG. Effects of Silymarin and Vitamins E and C on Liver Damage Induced by Prolonged Biliary Obstruction in the Rat. Basic Clin Pharmacol Toxicol. 2004;94(2):99-104. doi: 10.1111/j.1742-7843.2004.pto940207.x.
68. Budni J, Pacheco R, da Silva S, Garcez ML, Mina F, Bellettini-Santos T, et al. Oral administration of d-galactose induces cognitive impairments and oxidative damage in rats. Behav Brain Res. 2016;302:35-43. doi: 10.1016/j.bbr.2015.12.041.
69. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. CMAJ. 2006;174(6):801-9. doi: 10.1503/cmaj.051351.
70. Xiao Y, Liu Y, Yu K, Zhou L, Bi J, Cheng J, et al. The Effect of Chinese Herbal Medicine on Albuminuria Levels in Patients with Diabetic Nephropathy: A Systematic Review and Meta-Analysis. Evidence-Based Complementary and Alternative Medicine. 2013; 2013 937549. doi: 10.1155/2013/937549.
71. Choi EM, Hwang JK. Effect of some medicinal plants on plasma antioxidant system and lipid levels in rats. Phytother Res. 2005;19(5):382-6. doi: 10.1002/ptr.1464.
72. Foran SE, Lewandrowski KB, Kratz A. Effects Of Exercise On Laboratory Test Results. Lab Med. 2003;34(10):736-42. doi: 10.1309/3PDQ4AH662ATB6HM.
73. Fragala MS, Bi C, Chaump M, Kaufman HW, Kroll MH. Associations of aerobic and strength exercise with clinical laboratory test values. PLoS One. 2017;12(10) e0180840-e. doi: 10.1371/journal.pone.0180840.
74. Teixeira de Lemos E, Oliveira J, Páscoa Pinheiro J, Reis F. Regular Physical Exercise as a Strategy to Improve Antioxidant and Anti-Inflammatory Status: Benefits in Type 2 Diabetes Mellitus. Oxid Med Cell Longev. 2012;2012 741545. doi: 10.1155/2012/741545.
75. Ali Asghari Gelodar S, Ghanbari-Niaki A and Nasiri K. Effect of Moderate Endurance Training and Consumption of Rosa Canina L. Extract on Liver Enzyme Profile in Male Rats. J Maz Univ Med Sci. 2020;30(190):11-23.
76. Akbari-Fakhrabadi M, Najafi M, Mortazavian S, Rasouli M, Memari AH, Shidfar F. Effect of saffron (Crocus sativus L.) and endurance training on mitochondrial biogenesis, endurance capacity, inflammation, antioxidant, and metabolic biomarkers in Wistar rats. J Food Biochem. 2019;43(8) e12946. doi: 10.1111/jfbc.12946.
77. Huang C-C, Huang W-C, Yang S-C, Chan C-C, Lin W-T. Ganoderma tsugae hepatoprotection against exhaustive exercise-induced liver injury in rats. Molecules (Basel, Switzerland). 2013;18(2):1741-54. doi: 10.3390/molecules18021741.
78. Yada K, Roberts LA, Oginome N, Suzuki K. Effect of Acacia Polyphenol Supplementation on Exercise-Induced Oxidative Stress in Mice Liver and Skeletal Muscle. Antioxidants (Basel). 2019;9(1). doi: 10.3390/antiox9010029.