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ORIGINAL PAPER

Phytochemical composition, antioxidant, antihyperlipidemic, and hepatoprotective effects of phenolic components of Iraqi sumac (*Rhus coriaria*)

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ABSTRACT

Introduction and aim. Hyperlipidemia is a pathogenic disease associated with significant cardiovascular complications. *Rhus coriaria,* traditionally recognized as sumac, is abundant in numerous phenolic constituents that enhance its antioxidant, antibacterial, and anti-inflammatory characteristics. The aim was to investigate the phytochemical and pharmacological attributes of phenolic constituents of *R. coriaria*.

Material and methods. 32 male albino mice were assigned at random into 4 groups (n=8). Group 1 (control), group 2 (induced), group 3 (atorvastatin) and group 4 (phenolic). All groups received a diet that was rich in fat for a duration of 28 days, except the control group, which instead consumed a standard diet. Group 2 received no treatment, while group 3 and group 4 received atorvastatin 10 mg/kg and phenolic fractions of *R. coriaria* 500 mg/kg, respectively, for a further 28 days. Lipid profiles, oxidative indicators, biochemical parameters, and liver histopathological examination were estimated.

Results. Phenolic fractions substantially improved total cholesterol (167.5±2.4 vs. 280.4±17.6 mg/dL), triglycerides (181.1±12.5 vs. 238.6±11.05 mg/dL), low-density lipoprotein (109.0±1.6 vs. 209.2±16.8 mg/dL), and very low-density lipoprotein (36.2±2.5 vs. 47.7±2.21), while raising high-density lipoprotein levels (42.3±1.8 vs. 23.5±2.3 mg/dL) as opposed to the induced group ($p<0.05$). Furthermore, the phenolic constituents significantly reduced liver enzyme activities like alanine transaminase (27.4±1.8 vs. 45.2±2.8 U/L), aspartate aminotransferase (31.7±2.1 vs. 44.9±2.0 U/L), and alkaline phosphatase (28.0±2.1 vs. 50.9±1.9 U/L), and decreased total blood bilirubin (0.6±0.08 vs. 1.7±0.1 mg/dL) and albumin (4.7±0.7 vs. 6.6±0.3 g/dL) when compared to the induced nontreated group ($p<0.05$). Phenolic treatment also alleviated tissue malondialdehyde (221.09±3.2 vs. 475.98±44.02 nmol/mL) and increased reduced glutathione (35.48±1.86 vs. 11.65±0.78 µg/mL) as compared to the group without induced non-treated group ($p<0.05$) and restored liver histopathological changes.

Conclusion. Phenolic compounds have the potential to treat hyperlipidemia due to their anti-oxidative and anti-inflammatory properties.

Keywords. hyperlipidemia, phenolic constituents, *R. coriaria*

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Introduction

A medical condition known as hyperlipidemia is defined by an increase in the blood levels of lipoproteins and/or one or more components of the lipid profile, which encompass a variety of inherited and acquired illnesses.[1,2] Hyperlipidemia may also be specifically defined as triglycerides (TG), low-density lipoprotein (LDL) and overall cholesterol, or lipoprotein values that exceed 90% of the population average or fall below 10% of the average for high-density lipoprotein (HDL).[3,4] The term "primary prevention" refers to controlling risky variables, such hyperlipidemia, in order to minimize the likelihood of the development of atherosclerosis.[5,6] Additionally, hyperlipidemia is related to substantial generation of ROS, or reactive oxygen species, which play a critical part in the development and progression of cardiovascular diseases, including atherosclerosis.[7,8]

A pharmacological intervention must be selected based on the specific lipid abnormalities. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, resins, ezetimibe, hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase blockers (statins), and niacin are the most effective drugs to lower LDL cholesterol. Niacin, marine omega-3, and fibric acid derivatives are most effective in lowering TG levels with very-low-density lipoprotein (VLDL) while increasing HDL cholesterol level.[9,10] Nonetheless, the majority of these drugs are associated with various troubles, including myalgia, myopathy, rhabdomyolysis, altered liver function, gallstones, stomach irritation, and possible renal failure. Hence, the advancement of innovative lipid-lowering medicines as alternatives to allopathic medications is of vital importance.[11]

Natural ingredients and their bioactive constituents are widely explored as potential effective remedies for various types of ailments.[12-16] *Rhus coriaria (R. coriaria)*, the Mediterranean herb named sumac, is an element of the Anacardiaceae clan. Historically, it has been used as spices and in the cosmetic, veterinary, and pharmaceutical industries.[17,18] The primary phenolic molecules isolated from sumac include gallic acid, ellagic acid, tannins, quercetin, rutin, catechins and anthocyanins.[19,20] The combination of these phenolic substances imparts *R. coriaria* its distinctive medicinal characteristics, making it useful in traditional medicine for multiple diseases.[21] These phytochemicals have been proven to be effective in avoiding cardiovascular diseases and tumors, diabetes, wounds, also skin aging.[22-26] Phenolics function principally by detoxifying ROS and strengthening endogenous antioxidant defenses.[27-29] Furthermore, they exert remarkable anti-inflammatory benefits by regulating cell activity and modulating cytokine secretion.[30-34] These constituents are currently used to provide hepatoprotection in a variety of settings, including acute liver damage and prevention of chronic liver pathology.[35,36]

Aim

This research was planned to explore the phytochemical composition of the phenolic fractions obtained from *R. coriaria* and to examine their antioxidant, antihyperlipidemic, and hepatoprotective activities in a mouse model of hyperlipidemia evoked by the high-fat diet (HFD).

Material and methods

Plant materials

In April 2020, the fruitful plant *R. coriaria* was acquired from Rawendos, which is located in northern Iraq. After being cleaned, it was ground using mechanized grinding equipment, allowed to dry at ambient temperatures in a shaded area, and then weighed.

Separation and fractionation of distinct active ingredients

400 g of coarsely ground, shade-dried powder of R. coriaria plant was stripped of fat with hexane for 24 hours and subsequently dried at room temperature (25°C) in order to extract and fractionate the active ingredients. Two liters of ethanol with a concentration of 85% were used in the Soxhlet apparatus to extract the plant components until they were completely gone. A deep greenish residual that represents the original portion was produced when the ethanolic extracts were dried at lower pressures and temperatures no greater than 40°C[37] and acidified to a pH of 2 using 300 milliliters of 5% HCl and then split three occasions using the same amount of ethyl acetate to create two distinct phases (ethyl acetate and watery acidic).[38,39]

Qualitative preliminary analyses of phytochemicals

Chemical investigations were carried out using the plant's ethanolic extract; we used recognized techniques to identify the active components.[40]

Test for flavonoids

NaOH test: liquid solutions of sodium hydroxide and hydrogen chloride were added to roughly two milliliters of extraction and portions, and the formation of an orange-yellow color was monitored.[25] Flavonoids typically absorb UV light, particularly in the range of 300-400 nm.

Separation of phenolic elements via high-performance liquid chromatography

The phenolic fraction is identified using high performance liquid chromatography. After the combination has been isolated using the principles of column-based chromatography, it is identified and quantified employing spectroscopy.[41] At the end of the column is a meter that counts the quantity of the split constituents.

The result of this detection is known as a liquid chromatogram.

HPLC condition model SYKAMN (Germany)

The C18-OSD column (25 cm, 4.6 mm) was used at 30°C with eluent A (methanol) and B (1% formic acid in water (v / v)) in particular circumstances: first 0 4 min at 40% B; 4–10 min at 50% B; at a flow velocity of 0.7 mL / min. The spectra were acquired at 280 n.

Preparation of drugs

A dose of 10 mg/kg of the usual medication, atorvastatin, was administered after 0.3 mg of 0.3 mg of the solution had been disintegrated in a 2% ethanolic mixture and adjusted to the appropriate proportion.[42] The phenolic fraction was prepared in distilled water by dissolving 17.5 mg in 300 units and administered at a concentration of 500 mg/kg. This dose is selected based on latest literature indicating the advantages of phenolic fractions as anti-inflammatory properties and antioxidants in the treatment of hyperlipidemia.[43-45]

Induction of hyperlipidemia

The typical nutrition (vegetables, cereals, fruits like apples and grapes, seeds like sunflower and groundnut, and vitamins A, E and D3) was supplemented with HFD (2% cholesterol and 1% peanut butter) to create elevated lipid levels for a period of 28 days. Every week, the body weight was determined.

Extract administrant

An intragastric tube was used to give a phenolic component of R. coriari for a period of 28 days.[45]

Experimental design

This work was implanted in the Faculty of Medicine's Department of Pharmacology at AL Nahrain University from the second of September 2022, until July 1, 2023. The Ethics Review Board of Al-Nahrain University School of Medicine (approved number 168) ensured that all procedures adhered to moral principles. From AL Nahrain University, 32 male albino mice, weighing between twenty and thirty grams, were acquired at the age of two to three months. A week before the start of the trial, the animals were acclimated to normal settings. The mice were randomly assigned to 4 groups, 8 mice in each group. In preclinical studies, a group size of 8 animals may be statistically acceptable due to several factors. First, power analysis typically demonstrates that, for large effect sizes, this number could indicate significant differences with sufficient statistical power. Furthermore, the use of homogeneous mouse strains and standardized conditions reduces variability, thus improving the accuracy of findings. Ethical guidelines prioritize minimizing animal use, and a sample size of 8 per group achieves a balance between statistical reliability and ethical considerations. Repeated measures can further diminish the need for larger sample sizes. In general, 8 animals are often a suitable number when justified by the size of the effect and experimental design. Animal grouping using a randomization approach reduces stress and ensures appropriate control of the environment. Reducing variability and variations in behavior can be achieved by keeping mice in distinct cages that are the right size and that use the same bedding, enhancement and food for every group. Proper experimental procedures for handling and treatment might also reduce external influences that may provide contradictory findings. After randomization, we compared the baseline characteristics to ensure that the groups were balanced. The age and weight of animals that underwent histopathology or treatment administration were comparable in all studied animal groups. The study groups were separated as follows: group 1 (normal) was fed a typical diet. The second group (induced) received HFD for a duration of 28 days. After 28-every-day HFD, Group 3 (atorvastatin) received 10 mg/kg of atorvastatin for an additional 28 days.[43] After 28 days of HFD.[43] Group 4 (phenolic fraction) received 500 mg / kg of phenolic fraction of R. coriaria for an additional 28 days.

Blood collections

Mice were fasted for 24 hours before having their hearts punctured to draw blood. Centrifugation at ambient temperature for fifteen minutes at three thousand revolutions per minute followed. Lipid profile indices and liver function enzymes were biochemically analyzed using acquired serum.[46-48]

Tissue homogenization

At the end of the trial, the animals were anesthetized and sacrificed, and the liver organ was separated into two halves to create tissue homogenate for histology and biomarker evaluation. Malondialdehyde (also known as MDA) and reduced glutathione (GSH) samples were extracted by homogenizing the initial portion of liver tissue, which was then centrifuged at 5000 rpm for 15 minutes.[49-51]

Biochemical analysis

Measurement of liver enzymes and indicators of lipid profile

The covenantal detecting kits were employed for the estimation of serum concentrations of total cholesterol and TG (Catalog No.: 303113050, ELITech Group, France, assay method: enzymatic calorimetric, intra-assay CV: ≤3%, inter-assay CV: not specified,), LDL, VLDL, and HDL (Catalog No.: 0599, Stanbio Laboratory, USA, assay method: enzymatic calorimetric, intra-assay CV: ≤3%, inter-assay CV: not specified) absorbance reader: AutoAnalyzer, SEAL Analytical GmbH, Germany.

The alanine transaminase (ALT), aspartate amino-

transferase (AST), alkaline phosphatase (ALP), and total circulating bilirubin (TSB) values were measured in serum using standard test kits and an automated analyzer (ARCHITECT c4000 chemistry analyzer, Abbott Diagnostics, USA) and a pertinent kit (ALP2 REF: 04S87R, ALT2 REF: 04S88R, AST2 REF: B4S900, and Total Bilirubin Kit REF: 04V510) donated by Abbott Diagnostics and designed for use with the ARCHITECT analyzer as directed in the manufacturer's guide.

The bubbles of air divide the continuous passage of the substance into distinct sections where chemical reactions take place. After that, the reagents and specimens are combined and transported through mixture coils and pipes. The samples are transferred by tubing between various devices, each of which performs a different set of operations, including the distillation process, dialysis, extraction procedure, ion exchange, heating, incubation, and output monitoring.[52-55] ISE, flame photometry, ICAP, fluorometry, and other techniques have been developed, but a continuous flow analyzer is based on color responses utilizing a flow by photometer.[56,57] Three repetitions of biochemical analysis experiments were performed, and the results did not reveal any significant differences.

Measurement of oxidative stress parameters

The oxidative stress parameters were measured in three separate experiments and no major variations were noticed in the findings were observed. The standard competitive enzyme-linked immunosorbent assay (ELISA) was adopted for the determination of tissue MDA and GSH levels (MDA Invitrogen: Catalogue No.: EEL160; Sensitivity (LOD): 18.75 pg/ml; GSH Invitrogen: Catalogue No.: EEL155; Sensitivity (LOD): 0.94 µg/ml). The microtiter plate was precoated with antibodies selective for MDA or GSH. Standards or specimens are introduced into designated plate wells with biotin-conjugated antibodies. After the washing procedure, Horseradish peroxidase (HRP) coupled with avidin was added to the holes.[58,59] The color development resulting from the addition of substrate solution was inversely corresponding to the concentration of MDA or GSH in the sample. At 450 nm, the generated color strength was determined.[60,61]

Histopathological examination

The isolated liver was immediately preserved, encased in paraffin after being fixed in a 10% formalin solution. Subsequently, after fixation, the samples were dehydrated by passing through ascending grades of ethanol concentrations: 70%, 80%, 95% and 100%. The samples were treated with xylol to remove the dehydrating agent (alcohol).[62-64] Next, the tissue samples were embedded by pouring out paraffin that had melted in metallic templates. A rotating microtome set to 5 µm thickness was used to cut liver slices.[65-67] Hematoxylin and eosin (H&E) were used to stain tissue biopsies. Background and excess stain were removed with 1% acid alcohol (1% HCl in 70% alcohol). Afterwards, DPX, or di-n-butyl phthalate in xylene, was applied as droplets. Covering sheets were placed on the slides, and they were maintained at room temperature overnight to dry.[68-70]

Statistical analysis

Microsoft Excel 2010 and SPSS version 26 (IBM, Armonk, NY, USA) were used for data entry and analysis. The mean SD was used to express continuous variables. A nonparametric test (Mann-Whitney) was used in place of parametric examinations (independent t test and one-way ANOVA) when the Shapiro-Wilk test of Normality showed that the data did not have typical distributions. When 0.05 was the p-value, the significance level was taken into account.[71,72]

Results

Qualitative and quantitative estimation of phenolic compounds by HPLC

A homogenized plant sample (3 g) was treated with a water and ethanol (70/30) to extract the phenolic components. An ambient temperature ultrasound bath was used for the extraction procedure. A rotating evaporator operating under vacuum extracted the solvent, which was subsequently dried to a constant mass at 40°C. Several bands representing distinct phenolic components of R. coriaria are shown in the chromatogram. As indicated in Table 1, Figure 1, and Figure 2, HPLC was used to identify quercetin, vanillic acid, p-coumaric acid, gallic acid, ferulic acid, and caffeineic acid.

Table 1. Retention times (Rt) in the fraction of minutes of phenolics in *R. coriaria*

Constituent	Rt of *R. coriaria* fraction	Rt of Standard
Caffeic acid	9.20	9.25
Gallic acid	3.22	3.25
Ferulic acid	7.85	7.85
p-coumaric acid	2.18	2.15
Quercetin	5.95	5.92
Vanillic acid	4.00	4.08

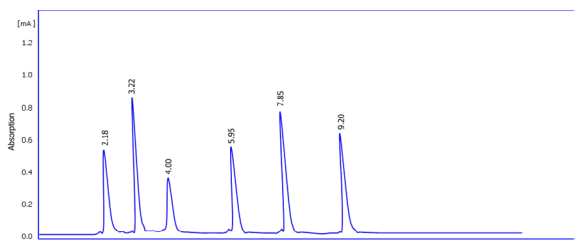

Fig. 1. HPLC chromatogram presenting the peaks of different constituents of the phenolic fraction of *R. coriaria*

Effects of tested agents on serum lipid profiles

Table 2 illustrates that HFD-treated mice developed hy-

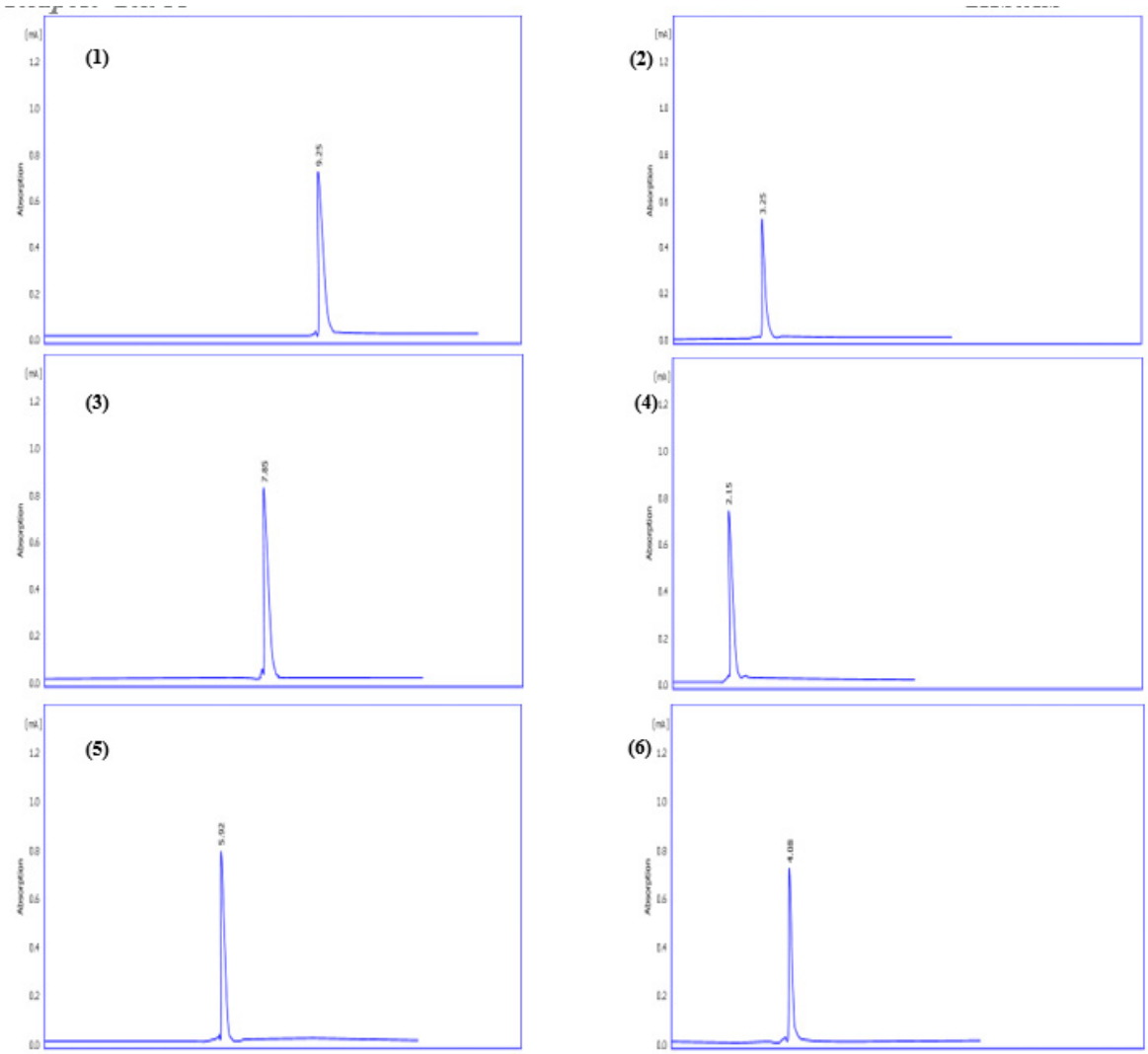

Fig. 2. HPLC chromatograms of each peak of standards for the constituents of the phenolic fraction.
(1) Caffeic acid reference, (2) gallic acid reference, (3) ferulic acid reference, (4) p-coumaric acid reference (5) quercetin acid reference, and (6) vanillic acid reference

perlipidemia, as seen by marked increases in TG, LDL, and VLDL levels and a marked decrease in good cholesterol in the induced nontreated group matched to the control group. Additionally, compared to the induced untreated group, the groups obtaining atorvastatin (10 mg/kg) and the phenolic component (500 mg / kg) found a noteworthy reduction in serum amounts of overall cholesterol, TG, LDL, and VLDL, with a notable increase in the amount of HDL ($p<0.05$). LDL values were markedly lower in the atorvastatin group compared to the phenolic group ($p<0.05$). However, in contrast to the atorvastatin group, the phenolic group showed nearly identical outcomes in terms of overall cholesterol, TG, and VLDL levels ($p>0.05$), with a notable increase in HDL relative to the atorvastatin group ($p<0.05$).

Effects of tested agents on liver function parameters

The result in Table 3 shows a remarkable up-regulation of serum ALP, ALT, AST, albumin, and TSB amounts within the induced untreated group compared to the seemingly healthy controls ($p<0.05$). Additionally, the groups given atorvastatin and the phenolic portion showed notable decreases in the serum levels of ALP, ALT, AST, albumin, and TSB in opposition to the induced untreated group ($p<0.05$). It is noteworthy that the phenolic fraction group revealed a significant difference in ALT, AST and TSB levels juxtaposed to the atorvastatin group ($p<0.05$).

Effects of tested agents on oxidative stress parameters

The concentration of MDA and a considerable decline ($p<0.05$) in GSH activity compared to the healthy control group. Compared to the induced untreated group, the groups receiving atorvastatin and phenolic components exhibited a considerable increase in GSH and a substantial reduction in MDA ($p<0.05$). Table 4 shows a considerable increase in GSH and a substantial reduction in MDA in the phenolic group compared to the

atorvastatin group (p<0.05).

Table 2. Impact of agents tested on serum lipid profiles[a]

Groups	Serum lipid levels (mg/dL)				
	Total cholesterol	TG	LDL	VLDL	HDL
Control (apparently healthy)	128.7±17.1	173.3±19.3	56.1±17.8	34.6±3.8	38±1.2
Induced (non-treated)	280.4±17.6*	238.6±11.05*	209.2±16.8*	47.7±2.21*	23.5±2.3*
Atorvastatin (10 mg/kg/day)	171.6±3.5**	189.9±14.9**	99.7±6.2**ϕ	38.35±3.3**	29.82±2.3**
Phenolic (500 mg/kg/day)	167.5±2.4**	181.1±12.5**	109.0±1.6**	36.2±2.5**	42.3±1.8**#

[a] The results are indicated as Mean±SD, n=8, *– marked change (p<0.05) vs. control group, ** marked change (p<0.05) opposed to induced group (nontreated), # marked change (p<0.05) opposed to atorvastatin group, marked change (p<0.05) opposed to phenolic fraction group. TG triglycerides, VLDL – very low-density lipoprotein, LDL low-density lipoprotein, HDL high-density lipoprotein, SD standard deviation

Table 3. Impact of agents tested on liver function parameters[a]

Groups	Liver marker levels				
	ALT (U/L)	AST (U/L)	ALP (U/L)	Albumin (g/L)	TSB (mg/dL)
Control (apparently healthy)	37.6±2.2	38.0±1.2	21.5±3.0	5.4±0.2	0.7±0.0
Induced (non-treated)	45.2±2.8*	44.9±2.0*	50.9±1.9*	6.6±0.3*	1.7±0.1*
Atorvastatin (10 mg/kg/day)	37.0±2.0**	38.2±1.7**	31.3±5.2**	5.5±0.2**	0.8±0.07**
Phenolic (500 mg/kg/day)	27.4±1.8**#	31.7±2.1**#	28.0±2.1**	4.7±0.7**	0.6±0.08**#

[a] results are indicated as Mean±SD, n=8, *– marked change (p<0.05) opposed to control group, ** marked change (p<0.05) opposed to induced group (nontreated), # marked change (p<0.05) opposed to atorvastatin group, AST aspartate aminotransferase, ALT alanine transaminase, TSB – total serum bilirubin, ALP alkaline phosphatase, SD – standard deviation

Impact of the drugs examined on changes in liver histopathology

Analysis of histological sections of the mouse liver in the seemingly healthy control group demonstrated a normal hepatic architecture without any histopathological alterations. The induced untreated group had notable alterations in the liver region, including significant steatosis and inflammation, compared to the normal controls. Furthermore, liver tissue of mice administered atorvastatin (10 mg/kg/day) exhibited mild lipid steatosis and inflammation compared to the induced untreated group. Histopathological evaluation of the mouse liver treated with the phenolic portion (500 mg/kg/day) revealed almost normal liver tissue, devoid of steatosis and inflammation, in contrast to the induced non-treated control group. The marked indicators (arrows) represent changes in specific areas within the histological section as depicted in Figure 3.

Table 4. Effects of tested agents on oxidative stress parameters[a]

Groups	Levels of oxidative indicators	
	MDA (nmol/mL)	GSH (µg/mL)
Control (apparently healthy)	229.95±9.61	48.62±5.11
Induced (non-treated)	475.98±44.02*	11.65±0.78*
Atorvastatin (10 mg/kg/day)	334.41±11.15**	26.51±2.85**
Phenolic (500 mg/kg/day)	221.09±3.2**#	35.48±1.86**#

[a] Results are indicated as Mean±SD, n=8, *– marked change (p<0.05) opposed to the control group, ** marked change (p<0.05) opposed to the induced (nontreated) group, #– marked change (p<0.05) opposed to the atorvastatin group, GSH reduced glutathione peroxidase, MDA malondialdehyde, SD – standard deviation

Discussion

Hyperlipidemia is a notable contributing cause of heart problems and often occurs in people with coronary artery disease.[73] Existing therapies to manage hyperlipidemia have a history of recurring adverse effects, particularly a higher likelihood of gallstone development, myopathy, and rhabdomyolysis. Therefore, there is a dire need to discover new and successful anti-hyperlipidemic medicines with minimal complications.[74,75] Recently, herbal remedies have become a popular way of treating dyslipidemia due to their better pharmacologic profile and fewer undesirable reactions.[76] In this study, the changes observed in lipid profiles in the non-treated induced group may be attributed to hyperlipidemia caused by a HFD, which disrupts lipid metabolism primarily via diminishing β-oxidation and improving cholesterol biosynthesis and oxidative injury by down-regulating the expression of free radical scavenging enzymes.[77] Cholesterol uptake increases in tandem with the rate of bile acid re-absorption, which in turn enhances the liver's ability to utilize cholesterol. Furthermore, higher blood concentrations of overall cholesterol, TG, and LDL, together with decreased lipoprotein lipase function, are associated with a compromised anti-oxidative defensive mechanism.[78]

However, alterations in serum lipid profiles were reversed by treatments with atorvastatin and phenolic fractions, suggesting a hypolipidemic impact. Atorvastatin is the main HMG-CoA blocker prescribed for the treatment of dyslipidemia. It substantially lowers blood lipid concentrations and may diminish hepatic fat deformity.[43] While various statins exhibit lipid-lowering results,

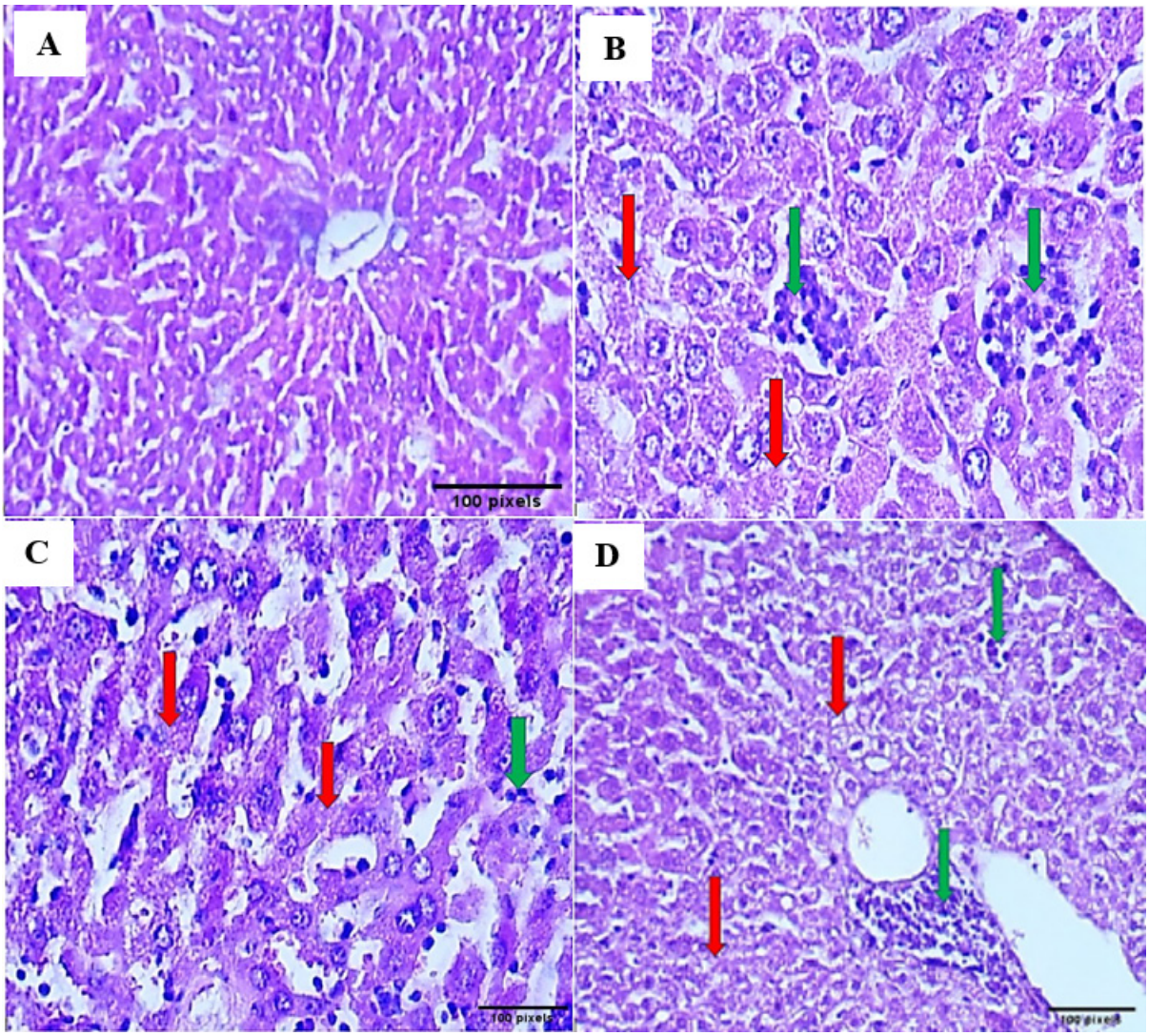

Fig. 3. Effect of the agents tested on histological examination of mouse liver, red arrow: steatosis level, green arrow indicates the degree of inflammation. A: standard control group (scale bars = 100 mm; H&E 20×), B: caused (group not treated, scale bars = 100 mm, H&E 20×), C: group treated with atorvastatin (H&E 20×, scale bars=100 mm), D: group received with phenolic component (H&E 20×, scale bars=100 mm)

atorvastatin displays superior declines in serum LDL and TG than other statins, likely attributable to its prolonged action, which probably reflects a prolonged retention of atorvastatin and its main metabolites in the liver.[79]

Oxidative stress stems from ROS overproduction and / or diminished antioxidant defenses.[80-82] MDA is a product of lipid peroxidation, while glutathione serves as the primary intrinsic antioxidative molecule against oxidative harm.[83-88] Phenolic compounds can reduce lipid levels and modulate redox pathways through several interconnected mechanisms. They act as potent antioxidants by donating hydrogen atoms or electrons to neutralize ROS, thus reducing oxidative stress, which is a major contributor to lipid peroxidation and atherosclerosis.[89,90] Phenolics can also up-regulate natural detoxifying enzymes such as catalase, superoxide dismutase, and glutathione peroxidase through activation of Nrf2 signaling.[91,92] In lipid metabolism, they inhibit enzymes such as HMG-CoA reductase, hindering cholesterol synthesis, and promote LDL receptor transcription, enhancing lipid clearance. Furthermore, they can suppress inflammation by downregulating NF-κB signaling, which indirectly affects lipid metabolism and oxidative balance.[93] Phenolics can also modulate gut microbiota, influencing bile acid metabolism and lipid absorption.[94] Their interaction with peroxisome proliferator activated receptors (PPARs) helps regulate fatty acid oxidation and storage.[95] Through these combined actions, phenolic fractions exert lipid-lowering and antioxidant effects.

Liver diagnostic enzymes, including AST, ALT, and ALP, assess the internal stability and deterioration.[96] The present investigation revealed that the administration of HFD gave rise to elevated amounts of ALP, ALT, AST, albumin, and TSB amounts. The breakdown of cellular integrity contributed to the leakage of liver enzymes into the bloodstream. Circulatory ALT level is

liver-specific and serves as a crucial indication of liver dysfunction or potential injury. Furthermore, increased serum amounts of AST and ALP may suggest enhanced biliary congestion.[97] In general, significant elevation in AST, ALT, and ALP amounts in the induced nontreated group implies hepatic injury and steatosis perhaps resulting from deposits of lipid intermediates [98] The use of atorvastatin and phenolic fraction reduced the levels of liver enzymes, TSB, and albumin amounts, perhaps related to their hypolipidemic activities. The hepatic histological analysis verifies the mitigative impact of the examined agents.[99,100]

Furthermore, a double-blinded randomized study involving 41 type 2 diabetics found that daily intake of 3 g of sumac extract optimized paraoxonase activities and lessened insulin resistance, MDA and C-reactive protein.[101,102] Supplementing sumac to patents with fatty liver ailment resulted in profound decrement in liver fibrosis, hepatic enzymes, and insulin resistance after 12 weeks of consumption.[103] The impacts of R. coriaria can depend on a multitude of bioactive polyphenols like gallic acid and flavonoids such as kaempferol, quercetin, myricetin and rutin, as they are established for their antioxidant, anti-inflammatory, and liver-protective properties.[104-106]

Study limitations

To the greatest extent of our ability, this is a novel investigation to analyze the phytochemical compositions of phenolic elements derived from *R. coriaria*, together with their antioxidant defense, hyperlipidemia prevention, and hepatoprotection. Even so, it is important to emphasize the shortcomings of the work. Initially, more information from clinical protocols is essential to estimate the established pharmacological benefits of phenolic compounds extracted from *R. coriaria*. Furthermore, measurement of inflammatory mediators is recommended because hyperlipidemia sufferers are associated with exceptionally high amounts of inflammatory cytokines, namely interleukin-1β (IL-1β), IL-6, and tumor necrosis factor-α (TNF-α).

Conclusion

*R. coriaria*is an *R. coriaria* is enriched in a variety of phenolic constituents, namely gallic acid, ferulic acid, quercetin, p-coumaric acid, and vanillic acid. These phenolic fractions confer a beneficial impact on hyperlipidemia provoked via a fatty diet, completely normalizing lipid profiles, biochemical indicators, and oxidative markers while dramatically preventing the majority of liver histopathological alterations. The findings suggest that the phenolic ingredients appear to be equivalent to or even more effective than the standard drug, atorvastatin.

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Declarations

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Author contributions

Conceptualization, S.F.H., A.R.A.R. and E.J.K.; Methodology, S.F.H. and E.J.K.; Software, H.R.S.; Validation, S.F.H., A.R.A.R. and E.J.K.; Formal Analysis, A.H.A.; Investigation, S.F.H. and A.H.A.; Resources, A.H.A.; Data Curation, S.F.H.; Writing – Original Draft Preparation, H.R.S.; Writing – Review & Editing, H.R.S. and A.H.A.; Visualization, A.R.A.R..; Supervision, A.R.A.R. and E.J.K.; Project Administration, H.R.S.; Funding Acquisition, S.F.H.

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval

The study adhered rigorously to the Declaration of Helsinki's ethical norms. The Ethics Review Committee of the College of Medicine (approval no. 168) ensured that all treatments followed ethical standards on 22 March 2024.

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