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Research Article
Protective Effect of Morin, A Flavonoid Against Hypercholesterolemia-induced Hepatic and Renal Toxicities in Rats

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Abstract

Background and Objective: Morin is a natural yellow compound that is scientifically proven to have pharmacological activities including hypoglycemia, inflammation and anti-oxidative. The aim of the present study was to evaluate the anti-dyslipidemic, antioxidant and anti-inflammatory effects of morin in high cholesterol diet (HCD) fed rats. **Materials and Methods:** High cholesterol diet (HCD) in pellet form was prepared by adding 1% cholesterol+0.5% cholic acid in rat chow powder and fed male Wistar rats for 6 weeks. Morin with three different doses (25, 50 and 100 mg kg^{-1}, orally) were treated to HCD fed rats for 4 weeks further feeding HCD. In serum, lipid profile, liver enzymes, renal markers tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), Interleukin-1β (IL-1β), caspase-3, nitric oxide (NO) and nuclear factor kappa-B (NF-κB) levels were estimated. In renal and hepatic cells, thiobarbituric acid-reactive substance (TBARS), glutathione (GSH), Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (Gpx) and glutathione-S-transferase (GST) activities were measured. **Results:** Animals exposed to a HCD exhibited significant increases in serum lipid profile, liver enzymes, renal markers, interleukins, caspase-3, NO and NF-κB levels. Morin supplementation reversed these changes towards normal levels in a dose-dependent manner. The HCD feedings significantly altered the oxidative stress biomarkers TBARS, GSH, SOD, CAT, GST and GPx in hepatic and renal tissues. Four weeks of morin treatment with three different doses (25, 50 and 100 mg kg^{-1} day^{-1}) to hypercholesterolemic rats significantly reversed oxidative stress levels in liver and kidney tissues in a dose-dependent manner. **Conclusion:** Morin exhibited inhibitory effect against HCD-induced hepatic and renal damages by inhibiting oxidative and inflammatory progressions. Thus, it could be considered as a potential alternative therapeutic agent for management of hypercholesterolemia.

Key words: Morin, hypercholesterolemia, renal damages, inflammation, hepatotoxicity, nephrotoxicity, cholesterol diet

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Competing Interest: The author has declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Hypercholesterolemia can induce nonalcoholic fatty liver disease (NAFLD) by depositing lipids and triglycerides in hepatic cells resulting in cirrhosis or even hepatic cellular carcinoma[1]. Hypercholesterolemia is an important worldwide public health challenge. It can lead to severe complications and target organ damage[2]. Experimental and clinical studies demonstrated that oxidative stress associated with hypercholesterolemia has harmful effects on the heart, liver and kidneys among other organs[3]. Oxidative stress is also associated with the development of renal damage induced by hypercholesterolemia[4]. Moreover, reactive oxygen species (ROS) have been implicated in the pathophysiology of heart failure, ischemic heart disease, hepatic injury, chronic renal damage, renal failure and other diseases[5].

Earlier studies revealed that hypercholesterolemia potentiates circulating pro-inflammatory cytokines like IL-6, TNF-α and IL-1β in the blood and various organs[6]. Johnson *et al.*[7] considered both arterial and tubulointerstitial inflammation to be the hallmarks of essential hypertension. Elevated inflammatory cytokine levels induced membranous glomerulonephritis in rats[8]. It was demonstrated that inflammatory cytokines play an essential role in the pathogenesis of hypercholesterolemia-induced renal injury. They can cause glomerulosclerosis and tubulointerstitial fibrosis by promoting glomerular infiltration of monocytes and macrophages. Hyperlipidemic or hypercholesterolemic obesity causes organ expansion and a shift towards a pro-inflammatory environment. Immune cells are recruited and the levels of pro-inflammatory adipokines like TNF-α and IL-6 increase[9].

Flavonoids are the most abundant polyphenolic compounds in the human diet. They are abundant in fruits, vegetables and plant-derived beverages like tea and red wine. Morin has a wide range of biochemical and pharmacological properties. It has been reported as antioxidant, antiviral, anti-carcinogenic and anti-inflammatory[10]. Morin is a naturally occurring bioflavonoid originally isolated from plants in the Moraceae family and is reported to possess several pharmacological properties including antioxidant and anti-inflammatory[11-13]. However, the effects of morin on HCD-induced hepatic and renal toxicities are remain unknown. Thus the present study was designed to investigate the effects of morin on hepatic and renal oxidative and anti-oxidative markers as well as alterations in mitochondrial enzymes activities of feeding an HCD to rat and sought to elucidate the mechanisms of these processes.

MATERIALS AND METHODS

Time and place: This research was conducted between January and June, 2017 at the Department of Food Sciences and Nutrition, College of Food and Agriculture Sciences, King Saud University, Riyadh, Kingdom of Saudi Arabia.

Animals: Male albino Wistar rats weighing from 140-160 g were obtained from the Experimental Animal Care Center, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia. The animals were maintained under controlled conditions of temperature (22±1°C), humidity (50-55%) and light (12 h light/12 h dark cycles). Before the start of the experiment, the animals were acclimatized to laboratory conditions for 7 days. They had free access to Purina rat chow (Grain Silos and Flour Mills Organization, Riyadh, Saudi Arabia) and drinking water. All procedures, including euthanasia were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, National Institutes of Health (NIH Publications No. 80-23; 1996) and approved (647-EACC-2017 dated 02-01-2017) by the Ethical Committee of the Experimental Animal Care Center, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia.

Diet: A high cholesterol diet (HCD) was prepared in pellet form (shed dried) by adding 1% cholesterol+0.5% cholic acid to rat chow powder. Animals receiving this diet had free access to it and water during the whole experimental period.

Chemicals: The chemicals used in present study are analytical grade and commercially available kits. Morin (Riedel-del Haen, Germany), cholesterol (Alpha Chemika, India) and cholic acid (Fluka, Switzerland) were purchased. The diagnostic kits of total cholesterol (TC), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), Alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine and urea (BUN) were purchased from Human Diagnostics, Wiesbaden, Germany. Tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), caspase-3, nitric oxide (NO) and nuclear factor kappa-B (NF-κB), Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (Gpx) and glutathione-S-transferase (GST) ELISA kits were purchased from R and D Systems, Minneapolis, MN, USA. Thiobarbituric acid-reactive substance (TBARS) and glutathione (GSH) ELISA kits were obtained from Cayman Chemical, Ann Arbor, MI, USA.

Experimental design: The animals were randomly divided into five groups of six rats in each as follows: Group 1, control; Group 2, HCD; Group 3, morin (25 mg kg^{-1} day^{-1})+HCD; Group 4: morin (50 mg kg^{-1} day^{-1})+HCD; Group 5: morin (100 mg kg^{-1} day^{-1})+HCD. Morin was suspended in 0.5% (w/v) carboxymethyl cellulose (CMC) and administered orally by gavage to HCD fed rats for four consecutive weeks. Body weights were measured weekly throughout the experimental period. Blood samples were collected by cardiac puncture under light ether anesthesia. Samples were centrifuged at 4,000 rpm for 10 min. Serum samples were suppurated and stored at -20°C until analysis. Animals were sacrificed by decapitation, immediately livers and kidneys were dissected and weighed. Small tissue samples were dipped in liquid nitrogen for 1 min and stored at -80°C until analysis. Cross sections of liver and kidney were preserved in 10% formaldehyde for histological evaluations.

Serum analysis: In serum, cholesterol, triglyceride, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, Alanine aminotransferase, aspartate aminotransferase, creatinine and urea levels were estimated using diagnostic kits by following the instructional manuals of the manufacturer. Inflammatory biomarkers in serum including tumor necrosis factor-alpha, interleukin-1 beta, interleukin-6, caspase-3, nitric oxide and nuclear factor Kappa-B activities were estimated using ELISA kits for rats using diagnostic kits by following the instructional manuals of the manufacturer.

Tissue analysis: Liver and kidney tissues were homogenized in phosphate buffer 1:10 (w/v). Thiobarbituric acid-reactive substance and glutathione levels were measured using ELISA kits by following the instructional manuals of the manufacturer. Post-mitochondrial supernatant (PMS) was extracted centrifuging the homogenate on 12,000 rpm for 10 min at 4°C. Enzymatic activities of superoxide dismutase, catalase, glutathione peroxidase and glutathione-S-transferase in hepatic and renal cells were measured using ELISA kits by following the instructional manuals of the manufacturer.

Histological study: Cross sections of the livers and kidneys from each treatment group were preserved in 10% buffered formalin and embedded in paraffin blocks. Sections 5 µm thick were sliced with an American optical rotary microtome (Leica Camera AG, Wetzlar, Germany). The sections were stained with hematoxylin and eosin and examined under a microscope to observe any histological changes.

Statistical analysis: Data were expressed as mean±standard error of the mean (SEM) and analyzed using one-way analysis of variance (ANOVA) followed by the Student-Newman-Keuls multiple comparisons test (n = 6). Differences between groups were considered statistically significant when $p \leq 0.05$. All statistics tests were conducted using Graph Pad Prism (v. 5) software.

RESULTS

Effect of morin on organ and body weights of hypercholesteremic rats: Mean body weights were not significantly altered when they compared between the groups: Control vs. HCD group, HCD vs. Morin (25) or HCD vs. Morin (50) or HCD vs. Morin (100). Liver ($p<0.05$) weight (g/100 g body weight) increased in HCD-fed rats relative to those for control animals. Morin administration (100 mg kg^{-1} day^{-1}) to HCD-fed rats significantly ($p<0.05$) decreased liver weight relative to untreated HCD-fed rats (Table 1).

Effect of morin on lipid profile: Serum lipid profiles are shown in Table 2. The total cholesterol levels 41.15±3.42 mg dL^{-1} in control group increased 92.54±4.51 mg dL^{-1} in HCD group were found statistically ($p<0.001$) significant. The TG and LDL levels were also significantly ($p<0.001$) increased in HCD-fed rats compared to the controls. Morin administration to HCD-fed rats significantly ($p<0.05$, $p<0.01$ and $p<0.001$) reduced the TG levels in a dose-dependent manner. The TC and LDL-C levels were significantly lower ($p<0.05$ and $p<0.01$) in the morin-treated

Table 1: Effects of morin on body and organ weight changes in HCD-fed rats

			Organ weights (g/100 g body weight)	
Treatments	Initial body weight (g)	Final body weight (g)	Liver	Kidney
Control	156.24±4.15	289.64±6.85	4.62±0.28	1.26±0.26
HCD	155.67±5.27	295.45±9.65	5.94±0.27[a]*	1.62±0.21
Morin (25)	159.23±6.78	305.89±7.56	5.36±0.39	1.60±0.29
Morin (50)	154.29±4.54	297.27±6.96	5.34±0.24	1.51±0.25
Morin (100)	157.26±6.26	287.33±5.28	4.86±0.17[b]*	1.42±0.29

Data were expressed as Mean±SE (n = 6) and analyzed using one-way ANOVA followed by Student Newman-Keuls as *post hoc* test. [a]Control vs. HCD group, [b]HCD vs. Morin (25) or HCD vs. Morin (50) or HCD vs. Morin (100). p-values consider significant when *p<0.05, **p<0.01 and ***p<0.001

Table 2: Effect of morin on hypercholesterolemia-induced changes in serum TC, TG, HDL-C, LDL-C, ALT, AST, creatinine and urea levels

Parameters	Control	HCD	Morin (25)+HCD	Morin (50)+HCD	Morin (100)+HCD
TC (mg dL^{-1})	41.15±3.42	92.54±4.51^{a***}	87.25±5.45	74.56±4.26^{b*}	62.16±3.19^{b***}
TG (mg dL^{-1})	34.15±2.75	69.87±4.21^{a***}	58.26±2.87^{b*}	50.27±5.14^{b**}	41.36±2.18^{b***}
LDL-C (mg dL^{-1})	34.45±3.15	78.56±4.65^{a***}	72.65±6.12	62.54±3.24^{b*}	56.26±4.16^{b**}
HDL-C (mg dL^{-1})	34.20±2.76	31.98±2.45	31.78±1.56	32.14±1.45	34.21±1.78
AST (U L^{-1})	32.51±4.26	63.67±5.45^{a***}	58.16±4.67	49.24±3.68^{b*}	40.68±2.89^{b**}
ALT (U L^{-1})	19.56±3.27	41.26±4.16^{a***}	35.87±3.68	28.46±2.87^{b*}	21.33±2.54^{b**}
Creatinine (mg dL^{-1})	38.42±3.27	52.45±2.46^{a**}	48.32±3.19	44.05±1.98	40.19±2.17^{b*}
Urea (mg dL^{-1})	45.63±4.16	67.15±5.68^{a**}	60.78±3.21	52.46±3.57^{b*}	47.26±2.84^{b**}

Data were expressed as Mean±SE (n = 6) and analyzed using one-way ANOVA followed by Student Newman-Keuls as *post hoc* test. [a]Control vs. HCD group, [b]HCD vs. Morin (25) or HCD vs. Morin (50) or HCD vs. Morin (100). p-values consider significant when *p<0.05, **p<0.01 and ***p<0.001

groups (50 and 100 mg kg^{-1} day^{-1}) than in the HCD group. However, HDL-C levels in the morin-treated groups did not significantly differ from those in the HCD group or the controls.

Effect of morin on hepatic and renal biomarkers: Liver AST (32.51±4.26 vs. 63.67±5.45 U L^{-1}) and ALT (19.56±3.27 vs. 41.26±4.16 U L^{-1}) levels were found significant (p<0.001) increase in the HCD group compared to the control groups. Morin administration (50 and 100 mg kg^{-1} day^{-1}) significantly decreased AST and ALT relative to those of the other groups (p<0.05 and p<0.01, respectively). Creatinine values (38.42±3.27 mg dL^{-1}) in control group significantly (p<0.01) increased in HCD fed rats (52.45±2.45 mg dL^{-1}). The serum urea levels in control animals (45.63±67.15 mg dL^{-1}) increased significantly (p<0.01) compared to the HCD fed rats (67.15±5.68 mg dL^{-1}) (Table 2).

Effect of morin on serum inflammatory biomarkers: Serum TNF-α, IL-6, IL-1β, NF-κB, caspase-3 and NO were significantly higher (p<0.001) in the HCD-fed rats than in the control rats. Morin administration to HCD-fed rats for 4 weeks significantly reduced these biomarkers in a dose-dependent manner relative to untreated HCD-fed rats (Fig. 1).

Effect of morin on oxidative stress biomarkers in hepatic cells: In liver homogenate, TBARS and GSH levels were significantly (p<0.001) increased and decreased in HCD group when compared to controls, respectively. Morin treatment with higher two doses (50 and 100 mg kg^{-1} day^{-1}) showed significant inhibition p<0.05 and p<0.01 in TBARS levels compared to HCD group, respectively. Only high dose of morin markedly (p<0.05) enhanced the GSH levels in hepatic cells compared to HCD group. Enzymatic activities of SOD, CAT, GPx and GST in PMS of hepatic cells of hypercholesteremic rats significantly (p<0.001) inhibited compared to control group of rats. The enzymatic activities of SOD, CAT and GPx in morin treated with 50 and 100 mg kg^{-1} day^{-1} groups markedly p<0.05 and p<0.01 enhanced compared to HCD group, respectively. However, hepatic GST activity was increased in morin treated groups in dose dependent manner (Fig. 2).

Effect of morin on oxidative stress biomarkers in renal cells: In kidney homogenate, TBARS and GSH levels were significantly (p<0.001) increased and decreased HCD group when compared to controls, respectively. Treatment with different dose of morin to hypercholesteremic rats inhibited the renal tissue TBARS levels in dose dependent manner compared to HCD group. While, morin treatment (50 and 100 mg kg^{-1} day^{-1}) showed significant increase p<0.05 and p<0.01 in GSH levels compared to HCD group, respectively. The SOD increased in morin treated group compared to HCD fed rats in dose dependent manner. The enzymatic activities of CAT, GPx and GST were markedly enhanced p<0.05 and p<0.01 in morin (50 and 100 mg kg^{-1} day^{-1}) treated groups compared to untreated hypercholesteremic rats, respectively (Fig. 3).

Histopathological evaluation of liver and renal tissues: Histological changes in the liver are shown in Fig. 4. In the control group, the hepatocytes appeared normal. However, in the HCD-fed group, the foci were scattered, the hepatocytes were swollen, inflammatory cells were present and there was a moderate degree of hepatotoxicity. Liver sections from the 50 and 100 mg kg^{-1}/day morin treatment groups showed significantly milder hepatotoxicity than those from the HCD-fed group.

The renal cortices of HCD-fed rats presented with enlarged urinary spaces, thickened glomerular basement membranes, vacuumation and mononuclear cell infiltration. The renal cortices of HCD-fed rats treated with 50 and 100 mg kg^{-1} day^{-1} morin showed distinct morphological improvement in their glomeruli and renal tubules (Fig. 5).

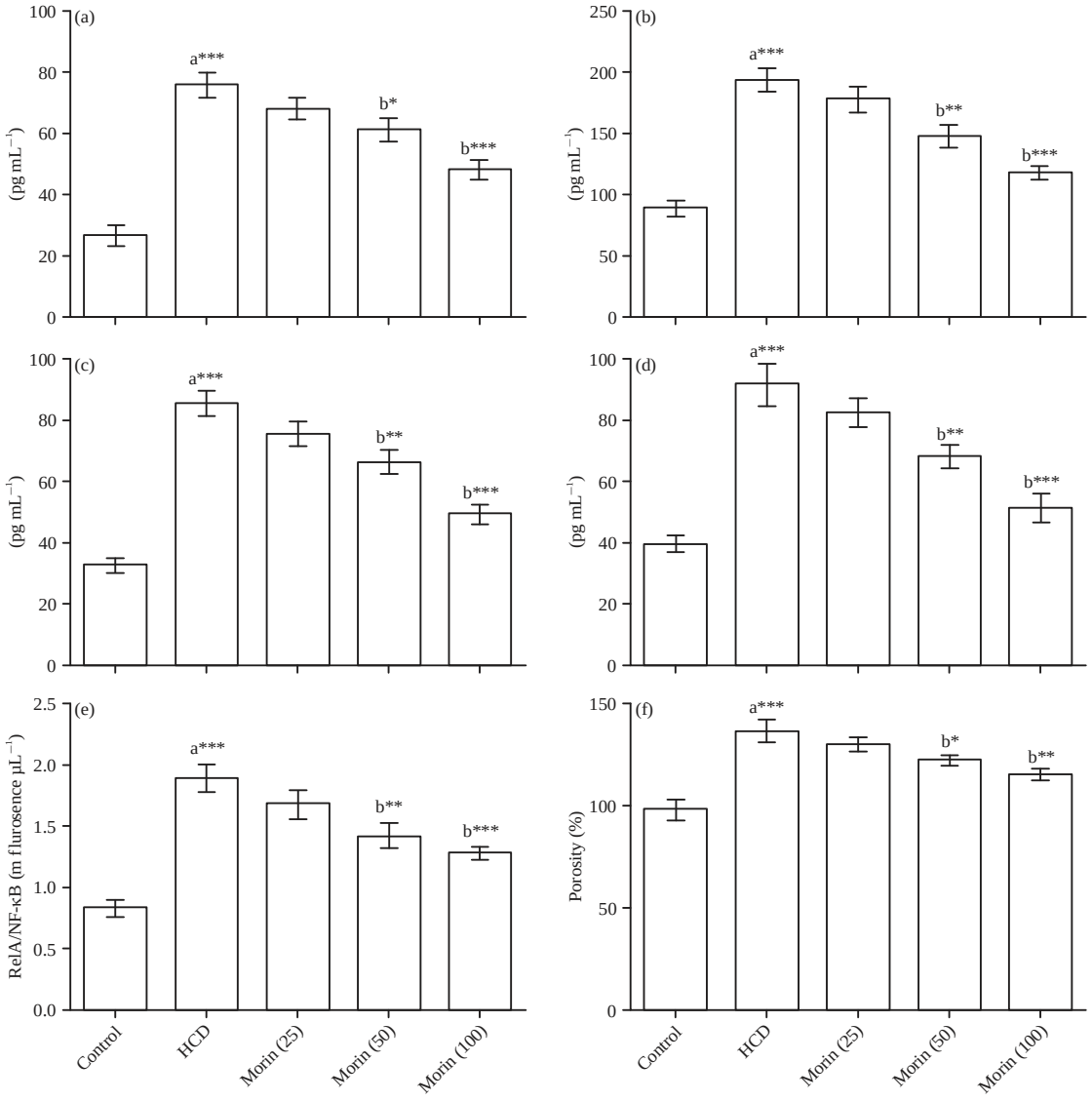

Fig. 1(a-f): Effect of morin on hypercholesterolemia-induced changes in serum pro-inflammatory biomarkers including (a) Tumor necrosis factor-alpha (TNF-α), (b) Interleukin-6 (IL-6), (c) Interleukin-1beta (IL-1β), (d) Nitric oxide (NO), (e) Nuclear factor kappa-B (NF-κB) and (f) caspase-3 levels

Data were expressed as Mean±SE (n = 6) and analyzed using one-way ANOVA followed by Student Newman-Keuls as *post hoc* test. [a]Control vs. HCD group, [b]HCD vs. Morin (25) or HCD vs. Morin (50) or HCD vs. Morin (100). p-values consider significant when *p<0.05, **p<0.01 and ***p<0.001

DISCUSSION

In present study, morin showed restoration of hepatic and renal antioxidant capacity and also anti-inflammatory and anti-necrosis properties in hypercholesterolemic rats. The morin associated improvement of hypercholesterolemia-caused significant alterations in the histological architecture of hepatic and renal tissues confirmed its protective value. Present results also revealed that hypercholesterolemia significantly elevated the TC, TG and LDL-cholesterol levels in serum. Morin treatment lowered these levels in a dose-dependent manner, which further confirm as anti-lipedemic agent. Similar morin effects were reported in earlier studies[14,15]. The results of current study corroborate those of earlier reports which attributed elevated ALT and AST levels[16]. A recent report indicated that morin administration attenuates acute lipopolysaccharide/D-galactosamine-induced liver injury by altering liver enzymes levels[17]. Serum urea, creatinine and histological changes in the kidneys of HCD-fed rats were restored to near-normal conditions in

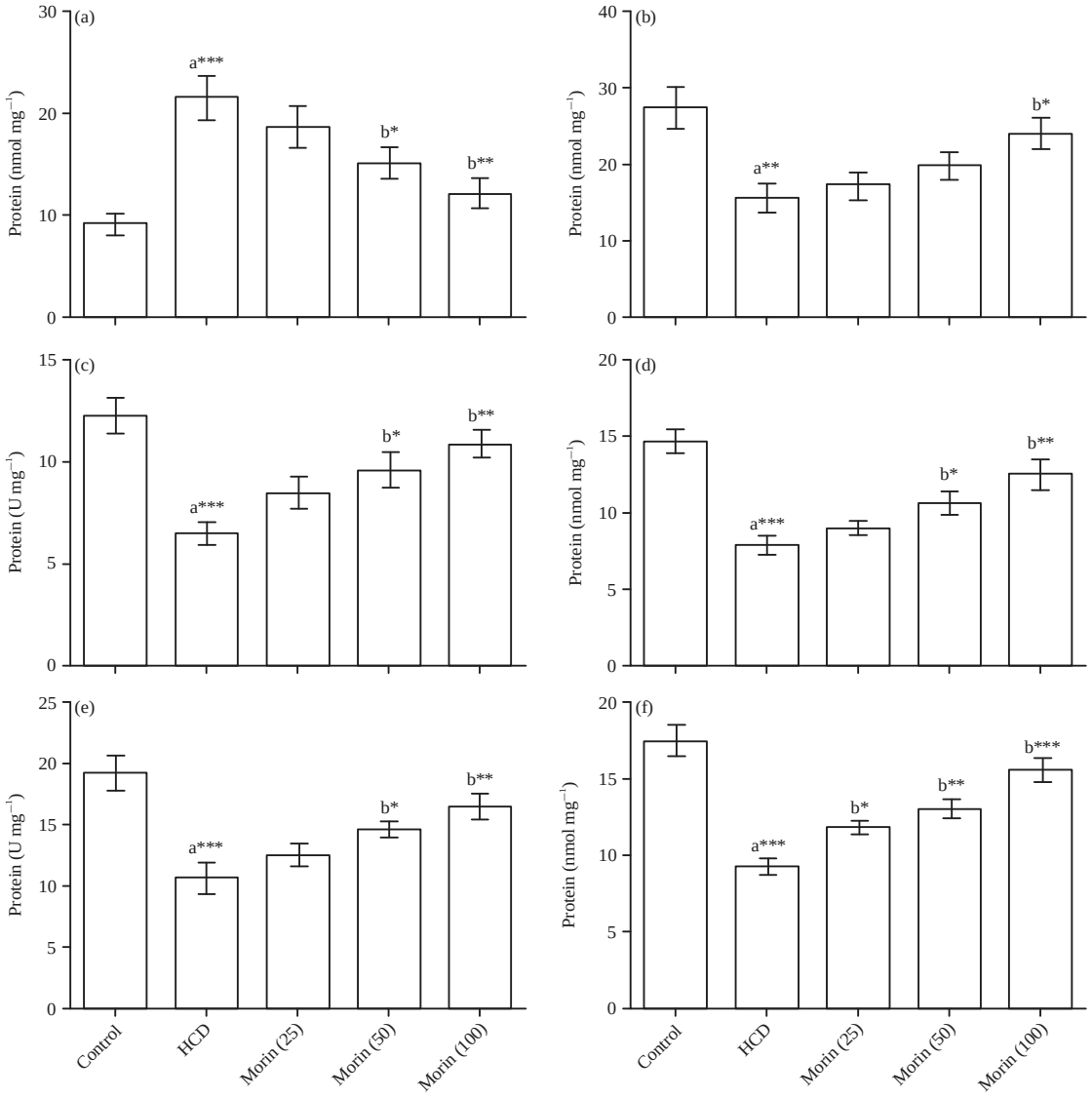

Fig. 2(a-f): Effect of morin on hypercholesterolemia-induced, (a) Thiobarbituric reactive substances (TBARS), (b) Glutathione (GSH) levels, (c) Enzymatic activities of superoxide dismutase (SOD), (d) Catalase, (e) Glutathione oxidase (GPx) and (f) Glutathione-S-transferase (GST) in hepatic cells

Data were expressed as Mean±SE (n = 6) and analyzed using one-way ANOVA followed by Student Newman-Keuls as *post hoc* test. [a]Control vs. HCD group, [b] HCD vs. Morin (25) or HCD vs. Morin (50) or HCD vs. Morin (100). p-values consider significant when *p<0.05, **p<0.01 and ***p<0.001

hypercholesterolemic rats receiving 4 weeks of morin treatment. It has been demonstrated that chronic hypercholesterolemia is a major risk factor in the progression of various renal diseases[18]. Creatinine is synthesized in the liver, enters circulation and is absorbed almost exclusively by the skeletal muscles. Creatinine retention in the blood is a marker of kidney impairment[19].

Proinflammatory cytokines like TNF-α, IL-6 and IL-1β regulate several biological processes and participate in inflammation, host defense against organ disorders and others[20]. In present study, HCD supplementation significantly increased proinflammatory cytokine levels. In an experimental study, HCD-fed rats presented with significant increases in cardiac TNF-α and IL-6 levels relative to the control[21]. HCD-induced caspase-3 activation was observed in the present study. Current results align with those in a recent report which showed that HCDs upregulate caspase-3 expression in hepatic cells. Morin administration to HCD-fed

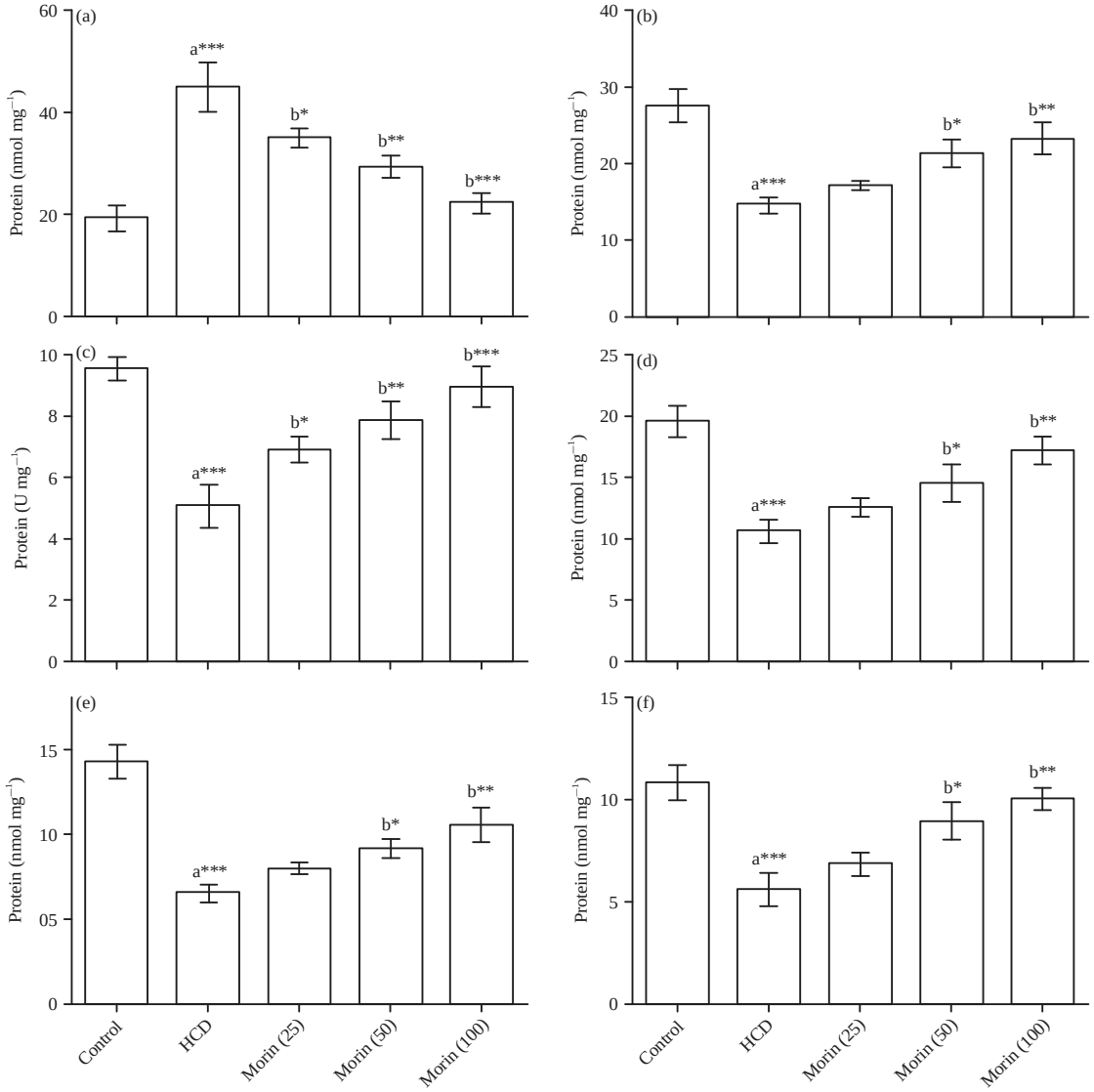

Fig. 3(a-f): Effect of morin on hypercholesterolemia-induced, (a) Thiobarbituric reactive substances (TBARS), (b) Glutathione (GSH) levels, (c) Enzymatic activities of superoxide dismutase (SOD), (d) Catalase, (e) Glutathione oxidase (GPx) and (f) Glutathione-S-transferase (GST) in kidneys

Data were expressed as Mean±SE (n = 6) and analyzed using one-way ANOVA followed by Student Newman-Keuls as *post hoc* test. [a]Control vs. HCD group, [b]HCD vs. Morin (25) or HCD vs. Morin (50) or HCD vs. Morin (100). p-values consider significant when *p<0.05, **p<0.01 and ***p<0.001

rats significantly decreased pro-inflammatory biomarkers, similar results that morin has inti-inflammatory properties were reported earlier by Al Sharari *et al.*[11]. It was also reported that morin reduced liver inflammation in rats fed a high-fructose diet by down regulating SphK1 activity, blocking NF-κB nuclear translocation and inhibiting IL-1β, IL-6 and TNF-α secretion by hepatocytes[22]. Furthermore, Lee *et al.*[23] demonstrated that morin pre-treatment protected mice from hepatic damage by reducing NF-kB activation and the expression levels of TNF-α, IL-1, IL-6 and iNOS.

In the present study, HCD supplementation significantly enhanced the levels of oxidative stress biomarkers. Similar alterations in the levels of lipid peroxidation products were observed in various organs of animals fed HCD[24]. Enzymatic activities of SOD, CAT and GPx in response to hypercholesterolemia inhibited in hepatic and renal cells. These findings were reported in a previous study by Cai *et al.*[25]. Earlier studies suggested that hypercholesterolemia-induced organ damage is probably associated with ROS accumulation[4,26].

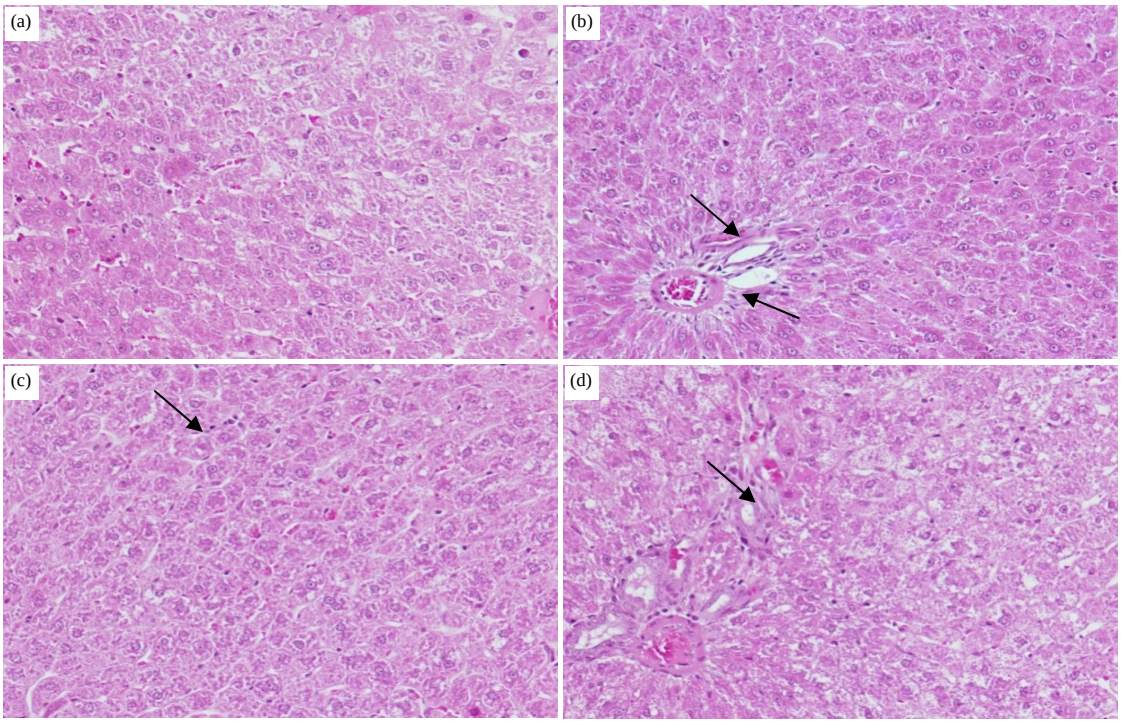

Fig. 4(a-d): Effect of morin on high cholesterol diet (HCD)-induced changes in hepatic tissue where (a) Control, (b) HCD, (c) Morin (50 mg kg^{-1} day^{-1}) treated to HCD fed rats and (d) Morin (100 mg kg^{-1} day^{-1}) treated to HCD fed rats

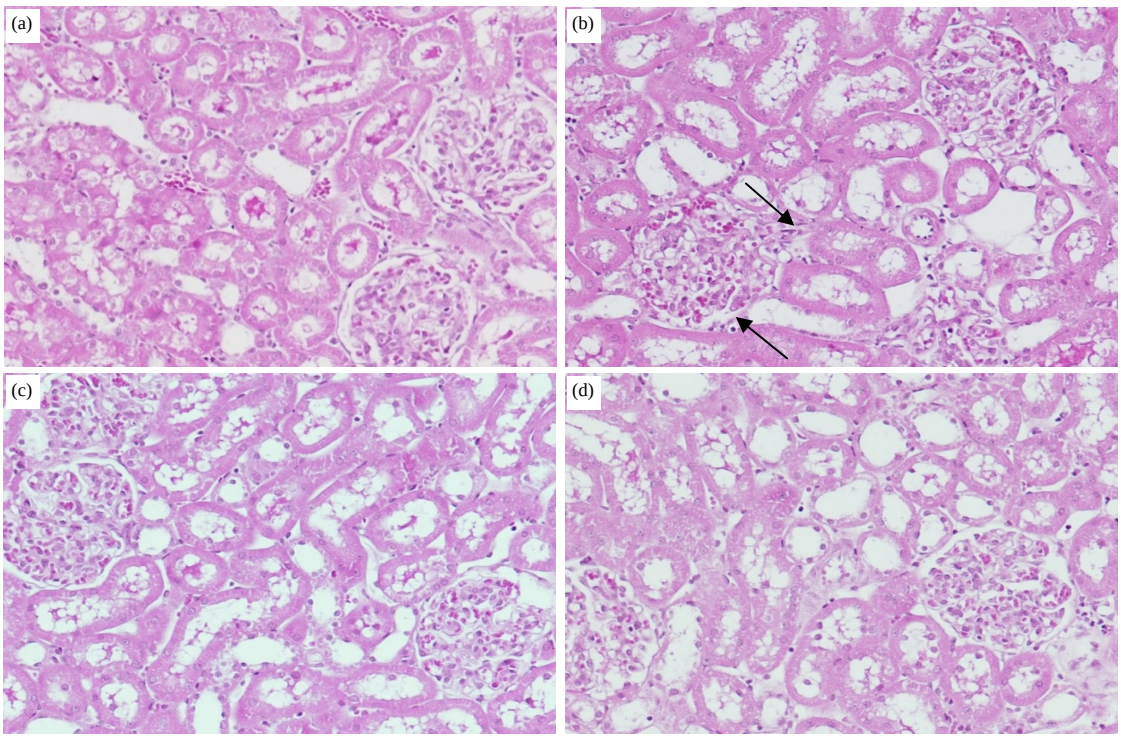

Fig. 5(a-d): Effect of morin on high cholesterol diet (HCD)-induced changes in renal tissue where (a) Control, (b) HCD, (c) Morin (50 mg kg^{-1} day^{-1}) treated to HCD fed rats and (d) Morin (100 mg kg^{-1} day^{-1}) treated to HCD fed rats

Polyphenols are natural antioxidants. They can serve as the first line of cellular defense against ROS[27]. Aleisa *et al.*[28] stated that morin protected against gentamicin-induced nephrotoxicity because of its antioxidant and anti-inflammatory properties. Morin also inhibits inflammation and cell death by preventing the depletion of intracellular reducing agents and by inhibiting malondialdehyde (MDA) production. Kapoor *et al.*[29] revealed that morin decreased ROS levels in primary rat hepatocytes exposed to high glucose concentrations (40 mM). Morin preserves intracellular glutathione, ascorbic acid and α-tocopherol levels[30]. Morin maintained mitochondrial integrity, inhibits the release of pro-apoptotic proteins, prevents DNA damageand also induces genes encoding antioxidant proteins like superoxide dismutase, catalase, heme oxygenase-1, glutathione peroxidase and glutathione reductase both *in vitro* and in animal models.

CONCLUSION

The present findings suggest the therapeutic value of morin co-administration in HCD animals. The protective efficacy of morin was considerable in ameliorating hepatic and renal oxidative injury via restoration of tissues regular histological features and antioxidant status. Regulation of pro-inflammatory and tissue apoptosis cellular mechanisms could contribute to morin protective mechanism against hypercholesterolemia and promotes its ability to attenuate ROS formation and antioxidant enzymes dysfunction.

SIGNIFICANCE STATEMENT

In the present study, the hypolipidemic, antioxidant and anti-inflammatory effects of morin were investigated in rats with hypercholesterolemia induced by HCD. The results showed that HCD feeding significantly enhanced lipid profile, liver and kidney markers, increased inflammatory biomarkers and induced oxidative stress in hepatic and renal cells. Morin treatment at 25, 50 and 100 mg kg^{-1} day^{-1} significantly mitigated hepatotoxicity and nephrotoxicity in a dose-dependent manner. Present study discovered that, morin could be considered as a potential alternative therapeutic agent for management of hypercholesterolemia.

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