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RESEARCH ARTICLE

Quinoa Seed Extract Attenuates Acute Kidney Injury in Hyperuricemic Rats Via Upregulation of Antioxidant Defense Genes, Metabolic Physiological Parameters, and Immunological Properties

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ABSTRACT

The present study aimed to characterize the *in vitro* antioxidant/antimicrobial activities of quinoa seed extract (QE) and to evaluate its protective effects on renal, hematological, and metabolic parameters in hyperuricemic rats, including modulation of renal defense genes and immune responses. QE showed antioxidant activity with DPPH IC_{50}=42.3µg/mL, and total phenolics were 55.6±2.7mg GAE/g. QE demonstrated antibacterial activity against both uropathogens and key oral pathogens in a dose-dependent manner. With inhibition zones of 16 and 15.8 mm against *Porphyromonas gingivalis* and *Streptococcus mutans.* For *in-vivo* experiments, male Wistar rats were divided into five groups (n=6): control, hyperuricemic AKI (potassium oxonate + uric acid, 7 days), QE alone (200mg/kg), and hyperuricemic+QE (200 mg/kg). Renal function (creatinine, BUN), oxidative stress markers (MDA, SOD, CAT, GPx), inflammatory cytokines (IL-1β, TNF-α, IL-10) and mRNA expression of Nrf2, HO-1, SOD1, and catalase were measured. QE alone caused no adverse effects. Hyperuricemic rats showed elevated serum uric acid (8.4 mg/dL), creatinine (1.5 mg/dL) and BUN (45 mg/dL), increased renal MDA, decreased antioxidant enzyme activities, reduced expression of Nrf2 (0.4 fold), HO 1 (0.3 fold), and SOD1 (0.5 fold), and a pro inflammatory state with high IL 1β and TNF α and low IL 10. Treatment with QE (200mg/kg) significantly restored renal physiology: uric acid reduced to 3.1mg/dL, creatinine to 0.6 mg/dL, BUN to 18 mg/dL ($P<0.01$); MDA lowered by 65%; SOD, CAT and GPx activities normalized; and Nrf2, HO-1, and SOD1 mRNA upregulated (3.5, 4.2 and 2.8-fold, respectively). QE (200mg/kg) exhibited potent immunological properties, reducing renal IL-1β by 58% and TNF-α by 62% while increasing anti-inflammatory IL-10 by 3.1-fold, indicating a shift toward an immunoregulatory phenotype. These immunological properties were confirmed by histology, which showed reduced tubular necrosis and attenuated immune cell infiltration. Finally, the combination of antioxidant and immunomodulatory activities together with antimicrobial effects suggests that QE is a promising nutraceutical for the management of hyperuricemia-induced AKI.

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INTRODUCTION

Acute kidney injury is a sudden decline in kidney function that remains a major cause of illness and death, with few specific drugs available. Interest is growing in natural extracts as nephroprotective agents, but some promising foods, such as quinoa, remain scarcely studied in AKI models. AKI is defined as an abrupt decline in renal function, usually detected by rising serum creatinine and blood urea nitrogen, and reduced urine output (Kang *et al.*, 2021; Zeng *et al.*, 2023). The principal etiologies driving AKI encompass renal ischemia-reperfusion injury, sepsis, hemodynamic shock, major surgery, and nephrotoxin exposure, including environmental toxins, radiographic contrast agents, and drugs such as cisplatin and aminoglycoside antibiotics (Ali *et al.*, 2022; Paes *et al.*, 2023). Acute kidney injury (AKI) develops through a multifactorial pathological process that typically begins with hemodynamic alterations and then progresses to tubular ischemia and toxic injury, alongside oxidative stress, inflammation, mitochondrial dysfunction, and eventual cell death; in some cases, fibrosis may also occur (Fang *et al.*, 2021).

Traditional management focuses on treating the cause, optimizing fluids and blood pressure, avoiding nephrotoxins, and using kidney replacement therapy (dialysis); there is no approved targeted drug for AKI (Chen *et al.*, 2025).

Multiple reviews show that plant-derived products (flavonoids, alkaloids, terpenoids, polyphenols, polysaccharides) can reduce oxidative stress, inflammation, and apoptosis in AKI models (Kang *et al*., 2021; Ali *et al*., 2022). In previous studies, Quercetin, a plant-derived flavonoid, has been evaluated in a meta-analysis of animal models of acute kidney injury (AKI), where it significantly reduced serum creatinine and blood urea nitrogen, and exerted marked antioxidant and anti-inflammatory effects, improving overall kidney injury scores (Li *et al.*, 2019). Curcumin, the main phenolic compound from *Curcuma longa*, has shown renoprotective actions in several AKI models, including cisplatin-, lipopolysaccharide- (LPS), and ischemia/reperfusion-induced injury, primarily by modulating key signaling pathways such as NF-κB and Nrf2 and preserving mitochondrial function (Cai *et al.*, 2022).

Ginger (*Zingiber officinale*) extract has been included in animal AKI studies, lowering lipid oxidation and enhancing the oxidant defense system, maintaining kidney health (Rostamkhani *et al.*, 2022). Moreover, in a study of glycerol-induced AKI, pretreatment with *Echinops spinosus* extract reduced oxidative stress by enhancing renal antioxidant enzymes, reduced kidney injury biomarkers such as KIM-1 and NGAL, reduced proinflammatory cytokines, and regulated apoptotic proteins (Rizk *et al.*, 2023). In an acetaminophen-induced AKI mouse model, aqueous extracts of *Moringa oleifera*, *Mucuna pruriens* and milk thistle significantly lowered the kidney profile, improved the activity of superoxide dismutase and CAT, reduced MDA, and decreased inflammatory cytokines IL-6 and TNF-α, also increasing SIRT1 expression (Housseini *et al.*, 2025).

Quinoa (*Chenopodium quinoa* Willd.) is a nutrient-rich source of bioactive compounds with strong antioxidant and anti-inflammatory activities. Recent work highlights its potential as a functional food in conditions characterized by oxidative stress, such as hypertension and kidney injury, although direct data on renal protection remain limited and largely preclinical. Quinoa supplies polyphenols, flavonoids, saponins, peptides, polysaccharides, and dietary fiber with antioxidant, antidiabetic, antihypertensive, and anti-inflammatory activities (Hazzam *et al.*, 2020; Ren *et al.*, 2022). Red and black quinoa seeds and sprouts have particularly high total phenolic and flavonoid contents and show radical-scavenging antioxidant capacity *in-vitro* (Al-Qabba *et al.*, 2020). Thermal processing can significantly increase phenolic content and composite antioxidant indices while keeping antinutrients within safe limits (Sharma *et al.*, 2022). Different plant parts (roots, sprouts, leaves) also concentrate saponins and phenolics and display strong antioxidant activity, suggesting the value of by-products as nutraceutical ingredients (Lim *et al.*, 2019; Casalvara *et al.*, 2024). Across the literature, quinoa shows promising but variable antibacterial activity, with the strongest results coming from husk-derived saponins and alcohol-based extracts rather than aqueous seed extracts (Sun *et al*., 2019; Dong *et al*., 2020; Casalvara *et al*., 2024). Specifically for oral pathogens, alkali-transformed quinoa husk saponins were the most potent, inhibiting halitosis-related bacteria, including *Fusobacterium nucleatum, Porphyromonas gingivalis, and Clostridium perfringens*, apparently by disrupting bacterial membranes (Sun *et al*., 2019; Cai *et al*., 2023).

Quinoa sprouts rich in ferulic acid and quercetin reduced oxidative stress markers (Al-Qabba *et al*., 2020), improved liver enzymes, lipid profile, and antioxidant defenses (GSH, SOD, reduced MDA) in CCl_4-treated rats, indicating strong systemic cytoprotective effects against oxidative injury. Pressurized hot water extracts of black and red quinoa showed potent *in-vitro* antioxidant and cytoprotective activity in endothelial cells, with profiles closely tied to phenolic content (Ong *et al.*, 2020). Reviews of quinoa emphasize its hypolipidemic, hypoglycaemic, and anti-inflammatory properties and highlight its promise for the development of health products, including low-cost by-products (López-Moreno *et al.*, 2023; Guo *et al.*, 2025).

Recent studies have hinted at oxidative stress, inflammation, and direct tubular damage as the main players in AKI (Turgut *et al.*, 2023; Tamargo *et al.*, 2024). Consistently across experimental animal models, phytochemicals, most notably flavonoids, demonstrate pronounced protective effects. These benefits are predominantly mediated through the enhancement of endogenous antioxidant capacity alongside the suppression of key inflammatory pathways (Dera *et al.*, 2019). For instance, a meta-analysis by Paes *et al*. (2023) across multiple AKI models revealed that quercetin significantly reduces serum creatinine, BUN, oxidative stress, inflammation and renal histological damage. Similar protective profiles have been systematically documented in both ischemic and cisplatin-induced AKI. Furthermore, polyphenols and saponins represent highly promising nephroprotective agents due to their synergistic modulation of redox imbalance, inflammatory cascades, and programmed cell death pathways (Fang *et al*., 2021; Kang

et al., 2021). Despite its well-documented bioactivity, *Chenopodium quinoa* remains largely unexamined in standard experimental AKI models. Nevertheless, quinoa seeds are exceptionally rich in quercetin and related flavonoids, as well as complex polyphenols and bioactive saponins. Furthermore, previous investigations have demonstrated its capacity to attenuate renal oxidative stress markers in hypertensive rat models, suggesting a strong pharmacological rationale for evaluating its nephroprotective potential against acute kidney injury (Al-Qabba *et al.*, 2020; López-Moreno *et al*., 2023). These collective mechanistic insights strongly justify the evaluation of *Chenopodium quinoa* seed extract (QE) as a therapeutic candidate for nephroprotection. Therefore, this study aimed to characterize QE phytochemically and investigate its dose-dependent protective effects against hyperuricemia-induced AKI in rats. Following *in-vitro* assessment of its bioactive profile, antioxidant potential, and antimicrobial capacity against pathogenic Gram-positive and Gram-negative bacteria, an *in-vivo* trial was performed to evaluate renal function, oxidative stress markers, early tubular injury indicators, and tissue architecture. Furthermore, we sought to elucidate whether QE activates the Nrf2 signaling axis and its downstream target enzymes, thereby directly linking its nephroprotective benefits to Nrf2-mediated antioxidant defense and anti-inflammatory pathways

MATERIALS AND METHODS

Chemicals and reagents: Potassium oxonate, 2,2-diphenyl-1-picrylhydrazyl (DPPH), and reference standards, including gallic acid, caffeic acid, ferulic acid, rutin, quercetin, and kaempferol, were obtained from Sigma-Aldrich (St. Louis, MO, USA). All other chemicals were standard analytical-grade products.

Extraction and preparation of quinoa seed extract (QE): For the preparation of QE, quinoa seeds were purchased from the local market, washed, then dried, pulverized into a fine powder, and defatted using *n*-hexane. The resulting defatted matrix was extracted with 70% (v/v) ethanol (1:10 w/v) at room temperature for 72 hours with intermittent stirring. Following filtration, the liquid extract was concentrated under vacuum and freeze-dried to obtain a solid powder. The final extract was preserved at -20°C prior to experimental use.

HPLC phytochemical profiling: Bioactive constituents were analyzed using an HPLC system equipped with a C18 reverse-phase column (5 µm, 250 × 4.6 mm) and a diode array detector. The mobile phase comprised two solvents: 0.1% formic acid in water (A) and acetonitrile (B), applied via gradient elution at 1.0 mL/min. Six key phenolic and flavonoid compounds, rutin, quercetin, kaempferol, gallic acid, caffeic acid, and ferulic acid, were identified and quantified by matching retention times and UV spectra against authentic reference standards. Total phenolic content was subsequently calculated and expressed as milligrams per gram of extract.

DPPH radical scavenging activity: The antioxidant activity of QE was assessed using the DPPH radical scavenging assay. A series of extract dilutions (25, 50, 100, 150, and 200 µg/mL) were prepared and mixed with a freshly prepared 0.1 mM DPPH methanolic solution. The reaction mixtures were incubated in the dark at room temperature for 30 min, after which absorbance was recorded at 517 nm using a spectrophotometer. Scavenging percentages were calculated from the decrease in absorbance for each concentration, and a dose–response curve was plotted to determine the IC_{50} via linear regression.

Antimicrobial assay: eight clinically significant uropathogenic strains were used: *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Enterococcus faecalis*, *Staphylococcus saprophyticus*, *Porphyromonas gingivalis*, and *Streptococcus mutans*. Antimicrobial activity was determined by the agar well diffusion method. QE was dissolved in sterile distilled water at different concentrations (50–200µg/mL). After overnight incubation, zones of inhibition were measured. Minimum inhibitory concentrations (MICs) were determined via the broth microdilution method according to CLSI guidelines.

Animal experimental design: Adult male Sprague-Dawley rats (180–220 g) were housed under standard laboratory conditions (25±2°C, 12 h light/dark cycle) with *ad libitum* access to water and standard feed. The experimental protocol was approved by the institutional animal care and use committee. After a 1-week acclimatization period, rats were randomly assigned into six groups (n=8 per group): 1. Normal Control: Received vehicle (saline) orally; 2. Hyperuricemia was induced in groups G2–G6 by daily intraperitoneal injection of potassium oxonate (250mg/kg) to inhibit hepatic uricase, followed 30min later by oral gavage of uric acid (300mg/kg) to elevate circulating levels, over 7 consecutive days. One hour after each oxonate injection, oral treatments were administered as follows: G1 (normal control) and G2 (untreated HUA) received vehicle; G3, G4 and G5 received quercetin extract (QE) at 50, 100 and 200mg/kg, respectively, in the HUA background; and G6 received QE 200 mg/kg in the HUA background. This 1-h interval ensures adequate uricase inhibition before QE intervention, allowing the drug to act upon a stable hyperuricemic state (Fig. 1).

Growth performance evaluation: Body weights of the animals were recorded daily throughout the study. Daily food intake was determined each morning by subtracting the residual diet weight in cage hoppers from the amount provided the previous day. The Feed Efficiency Ratio (FER) was subsequently calculated by dividing the total body weight gain (g) by the corresponding total feed consumption (g) over the same period.

Sample collection: Upon conclusion of the 7-day experimental period, rats were anesthetized with isoflurane. Blood was collected from the retro-orbital plexus into EDTA tubes (for haematology) and plain tubes (for serum biochemistry). Serum was isolated by centrifugation at 3,000 rpm for 15 min. Rats were subsequently euthanized, and kidneys were rapidly harvested. One kidney was fixed in

10% neutral-buffered formalin for histological assessment, while the contralateral kidney was snap-frozen in liquid nitrogen and maintained at −80°C for biochemical and gene expression analyses.

Serum biomarker analysis: Serum levels of uric acid, creatinine, and blood urea nitrogen (BUN) were estimated using commercially available standard diagnostic assay kits following the manufacturer's instructions.

Hematological analysis: Whole blood collected in EDTA tubes was analyzed using an automated hematology analyzer. Red blood cells (RBCs) count, hemoglobin (Hb), hematocrit (Hct), white blood cells (WBCs) count, differential leukocyte counts (neutrophils, lymphocytes), and platelet count were recorded.

Stress markers: Kidney tissues were homogenized (10%w/v) in cold PBS and the homogenates were centrifuged to collect the supernatant. Malondialdehyde (MDA) levels were measured by the thiobarbituric acid reactive substances (TBARS) method. Superoxide dismutase (SOD) activity was determined by inhibition of pyrogallol autoxidation, catalase (CAT) activity by monitoring H_2O_2 decomposition, and glutathione peroxidase (GPx) activity by measuring the oxidation of NADPH.

Gene expression: Total RNA was isolated from kidney tissues using a commercial RNA isolation kit. Complementary DNA (cDNA) was synthesized by reverse transcriptase. Quantitative real-time PCR (qRT-PCR) was performed using SYBR Green Master Mix on a real-time PCR system. Specific primer sequences for rat genes were used, including Nrf2, HO-1, SOD1, catalase, and GAPDH (used as the housekeeping internal control). Relative gene expression levels were calculated using the 2−ΔΔCt method.

Immunological analysis: At the end of the experimental period, rats were euthanized, and kidney tissues were rapidly excised, washed in ice-cold PBS, and homogenized in RIPA lysis buffer containing protease and phosphatase inhibitors. Tissue homogenates were centrifuged at 12,000 × g for 20min at 4°C, and the supernatants were collected. Total protein concentrations were determined using a BCA assay kit, and all samples were normalized to the same protein concentration. Renal levels of pro-inflammatory cytokines (IL-1β and TNF-α) and anti-inflammatory cytokine (IL-10) were measured using commercial rat-specific enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's protocols. All assays were performed in duplicate, and absorbance was read at 450nM using a microplate reader.

Kidney histology: Kidney specimens were dehydrated in graded ethanol, cleared in xylene, and embedded in paraffin. Sections (5µm thick) were stained with Hematoxylin and Eosin (H&E) and examined under a light microscope. A semi-quantitative scoring system was used to assess the severity of renal injury (0 = absent/normal; 1 = mild; 2 = moderate; 3 = severe; 4 = very severe) across the following categories: tubular necrosis, proteinaceous casts with tubular dilatation, interstitial inflammation, and glomerular injury. The total injury score was summed for each group.

Statistical analysis: Data were expressed as mean±standard deviation (SD). Statistical significance between groups was determined using One-way Analysis of Variance (ANOVA) followed by Tukey's multiple comparisons post-hoc test. A P-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using GraphPad Prism software.

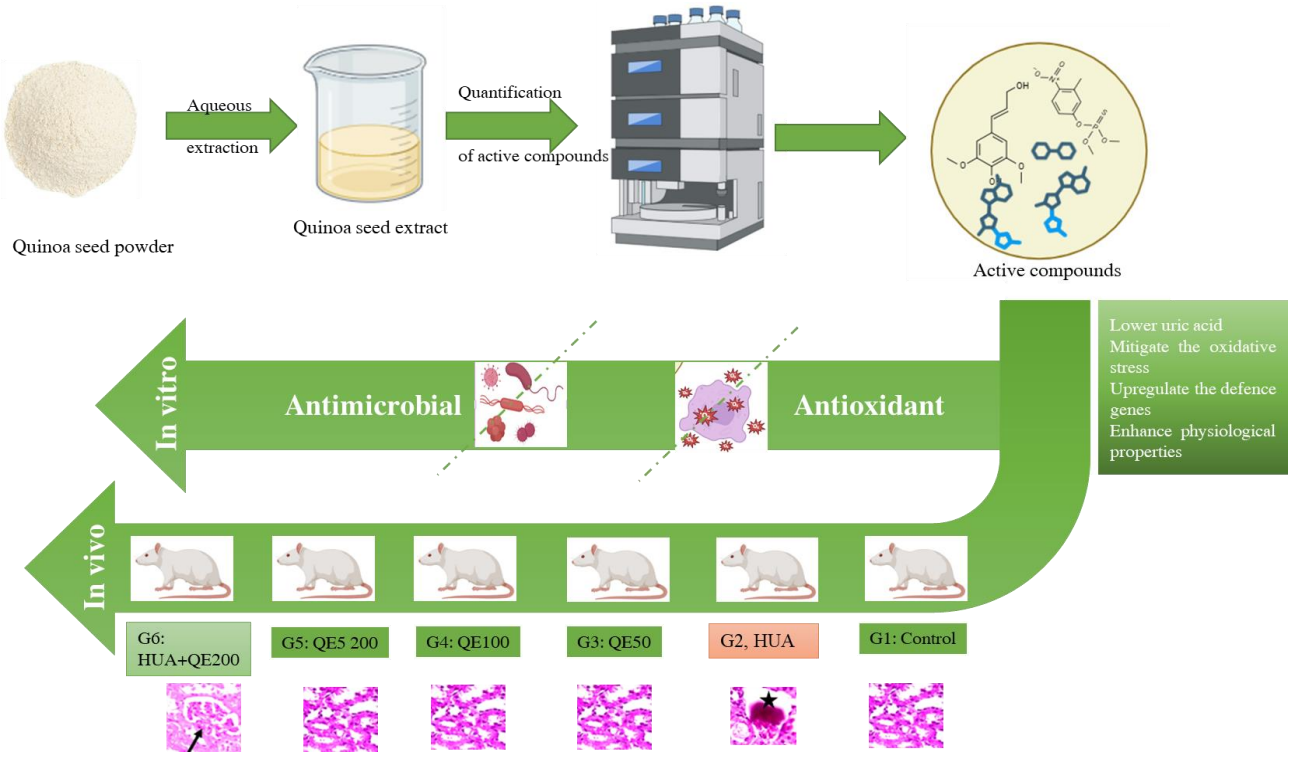

Fig. 1: Experimental design of the protective effect of quinoa seed extract on hyperuricemia in rats.

RESULTS

In vitro characterization of Quinoa seed extract (QE): HPLC analysis (Table 1) revealed rutin as the predominant phenolic constituent (15.2 mg/g extract), followed by quercetin (12.4 mg/g) and kaempferol (8.7 mg/g). Additional phenolic acids, including gallic, caffeic, and ferulic acids, were likewise quantified. Total phenolic content was determined to be 55.6 mg/g extract, underscoring a substantial polyphenolic composition. The DPPH radical scavenging assay was employed to evaluate the antioxidant capacity of QE across 25–200 µg/mL (Fig. 2). A clear concentration-dependent enhancement in scavenging activity was observed, spanning from approximately 28% at the lowest dose to 87% at 200 µg/mL. The corresponding half-maximal inhibitory concentration (IC_{50}) was 42.3 µg/mL, denoting potent scavenging activity comparable to that of reference plant polyphenol extracts.

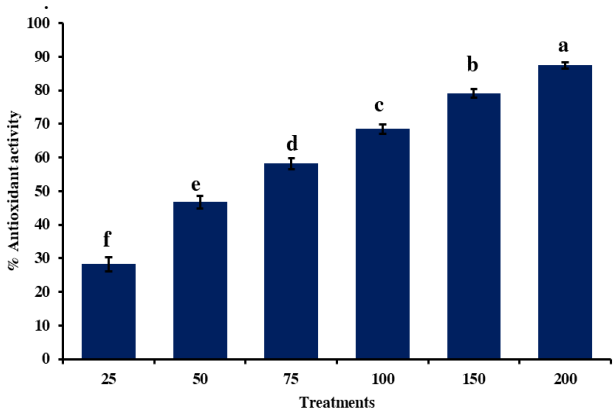

Fig. 2: % Antioxidant activity of quinoa seed extract against DPPH free radicals. Lowercase letters above the column indicate a significant difference, P<0.05.

Table 2 evaluates the antimicrobial activity of QE at concentrations ranging from 25 to 250 µg/mL. Although the title references six uropathogens, the dataset actually includes eight bacterial strains, featuring two notable oral pathogens: *Porphyromonas gingivalis*, a principal contributor to periodontal disease, and *Streptococcus mutans*, the primary etiologic agent of dental caries. Compared to the other tested organisms, the oral pathogens demonstrate the highest resistance to QE treatment. Both *P. gingivalis* and *S. mutans* require a minimum concentration of 75 ug/mL before any visible inhibition zones appear 8.2 and 8.1 mm, respectively), remaining unaffected at lower concentrations. Furthermore, both oral species exhibit the highest Minimum Inhibitory Concentration (MIC) values in the entire group at 65 ug/mL, whereas non-oral strains such as *E. coli*, *S. aureus*, and *K. pneumoniae* show greater sensitivity with MICs of 40 ug/mL. Despite their higher susceptibility thresholds, both oral pathogens exhibit clear dose-dependent inhibition. As the QE concentration increases to 200 µg/mL, inhibition zone diameters expand significantly to 16 mm for *P. gingivalis* and 15.8 mm for *S. mutans*, confirming that higher concentrations effectively suppress their growth.

Growth performance and general health of experimental animals: All animals survived the 7-day experimental period without any apparent signs of toxicity. As shown in Table 3, hyperuricemic rats exhibited significantly reduced weight gain (approximately 9 g vs. 27 g in controls) and lower daily food intake (12.7 vs. 18.4 g/rat), alongside a markedly decreased feed efficiency ratio (0.10 vs. controls). These alterations are indicative of a catabolic state and illness-related behavioral changes induced by acute hyperuricemic kidney injury. Conversely, rats administered QE alone at any dose (50, 100, or 200 mg/kg) demonstrated growth performance comparable to the control group, with final body weights, weight gains, food intake, and feed efficiency ratios all remaining within normal ranges.

Table 1: Major bioactive compounds in quinoa seed extract (QE) by HPLC

Compound	Concentration (mg/g extract)	Retention time (min)
Quercetin	12.4±0.8	8.2
Kaempferol	8.7±0.5	9.6
Rutin	15.2±1.1	7.4
Caffeic acid	5.3±0.3	6.1
Ferulic acid	4.9±0.2	10.3
Gallic acid	9.1±0.6	4.8
Total identified phenolics	55.6±2.7	–

Table 2: Antimicrobial activity of QE against six uropathogens (25–200 µg/mL)

Microorganism	Inhibition zone diameter (mm) at QE concentration (µg/mL)						MIC (ug/mL)
	25	50	75	100	150	200	
Escherichia coli	–	8.8±0.4	11.5±0.6	14.2±0.5	19.8±0.4	22.5±0.5	40
Staphylococcus aureus	–	8.9±0.3	10.2±0.4	12.5±0.6	17.8±0.5	21.1±0.4	40
Klebsiella pneumoniae	–	8.1±0.5	9.4±0.4	11.2±0.5	15.9±0.4	18.3±0.6	40
Pseudomonas aeruginosa	–	–	8.1±0.5	9.8±0.4	13.4±0.5	16.2±0.4	50
Enterococcus faecalis	–	–	8.7±0.3	10.5±0.4	14.3±0.5	18.6±0.6	55
Proteus mirabilis	–	–	8.5±0.5	10.1±0.6	12.8±0.4	16.5±0.5	60
Porphyromonas gingivalis	–	–	8.2±0.4	9.7±0.2	11.9±0.3	16.2±0.7	65
Streptococcus mutans	–	–	8.1±0.6	9.3±0.5	11.7±0.5	15.8±0.3	65

Notes: Values are mean±SD (n=3). MIC = minimum inhibitory concentration.

Table 3: Growth performance of hyperuricemic rats in all experimental groups.

Group	Initial body weight (g)	Final body weight (g)	Weight gain (g)	Daily food intake (g/rat)	Feed efficiency ratio
G1	185.2±6.3	212.5±7.1	27.3±3.2	18.4±1.2	0.21±0.02
G2	186.1±5.9	195.3±6.8*	9.2±2.1*	12.7±1.5*	0.10±0.02*
G3	184.5±7.0	210.8±6.5	26.3±2.9	18.1±1.3	0.20±0.02
G4	185.9±6.2	213.2±7.3	27.3±3.4	18.6±1.1	0.21±0.03
G5	186.5±6.0	214.5±6.9	28.0±3.0	18.8±1.0	0.21±0.02
G6	185.7±6.5	209.4±7.2#	23.7±2.8#	17.2±1.4#	0.19±0.02#

P<0.05 vs. control; #P<0.05 vs. hyperuricemic group. Data are mean±SD (n=6).. G1, Control; G2, Hyperuricemic (HUA); G3-G5, QE 50-200 (alone), G6 HUA + QE 200

Importantly, hyperuricemic rats treated with QE 200mg/kg regained nearly normal growth parameters: weight gain (23.7 g) and feed intake (17.2g/rat) were significantly higher than those of untreated hyperuricemic rats, although they remained slightly below control levels. The feed efficiency ratio (0.19) also approached the controls' value, indicating improved nutrient utilization.

Improvement of renal function and Uric acid homeostasis: Renal dysfunction in hyperuricemic rats was severe (Table 4). Serum uric acid increased from 2.1 mg/dL in controls to 8.4 mg/dL, creatinine exhibited a threefold rise (0.5 to 1.5 mg/dL), and BUN increased approximately threefold (16 to 45 mg/dL). These values confirm the successful induction of acute hyperuricemia and resultant renal dysfunction. Treatment with QE at 200 mg/kg markedly attenuated these markers: uric acid declined to 3.1 mg/dL (a 63% reduction relative to untreated hyperuricemic rats), creatinine to 0.6 mg/dL, and BUN to 18 mg/dL. Notably, these values did not differ significantly from controls, suggesting near-complete restoration of glomerular filtration and uric acid homeostasis. QE alone, at any dose, did not alter renal function parameters in healthy rats, excluding any intrinsic nephrotoxic or uricosuric effects.

Table 4: Renal function markers of hyperuricemic rats in all experimental groups

Group	Uric acid (mg/dL)	Creatinine (mg/dL)	BUN (mg/dL)
Control	2.1±0.3	0.5±0.1	16±2
Hyperuricemic (HUA)	8.4±0.6*	1.5±0.1*	45±3*
QE 50 (alone)	2.0±0.2	0.5±0.1	15±2
QE 100 (alone)	1.9±0.2	0.4±0.1	15±1
QE 200 (alone)	1.9±0.2	0.4±0.1	14±2
HUA + QE 200	3.1±0.4#	0.6±0.1#	18±2#

*P<0.01 vs. control; #P<0.01 vs. hyperuricemic group. Data are mean±SD (n=6). BUN = blood urea nitrogen; MDA = malondialdehyde; SOD = superoxide dismutase; CAT = catalase; GPx = glutathione peroxidase. * G1, Control; G2, Hyperuricemic (HUA); G3-G5, QE 50-200 (alone), G6 HUA + QE 200

Restoration of renal oxidative stress balance: Hyperuricemia induced a marked oxidative insult in renal tissue (Fig. 3A-D). Malondialdehyde (MDA), a lipid peroxidation product, increased from 1.8 nmol/mg protein in controls to 5.6 nmol/mg protein in hyperuricemic rats (a 3.1-fold elevation). The activities of the three major antioxidant enzymes, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), decreased to approximately one-third of control levels (e.g., SOD decreased from 12.4 to 4.1 U/mg protein).

QE treatment at 200 mg/kg reversed this oxidative imbalance. Renal MDA decreased by 65% relative to the hyperuricemic group (1.9 vs. 5.6 nmol/mg), while SOD, CAT, and GPx activities returned to near-control levels (11.2, 7.9, and 8.7 U/mg protein, respectively). The protective effect was dose-dependent, as lower QE doses (50 and 100mg/kg) produced intermediate improvements (Fig. 3A-D).

Upregulation of renal antioxidant defense genes: To investigate the molecular mechanism underlying the restoration of enzyme activities, mRNA expression of key transcription factors and antioxidant genes was quantified (Fig. 4A-D). In hyperuricemic rats, Nrf2 expression, the master regulator of antioxidant defense, decreased to 42% of control levels, while downstream targets HO-1, SOD1, and catalase were suppressed to 35%, 48%, and 52% of control levels, respectively, thereby accounting for the observed enzymatic depletion. QE treatment at 200 mg/kg upregulated Nrf2 expression 3.5-fold relative to untreated hyperuricemic rats, reaching absolute levels higher than controls; HO-1 showed the greatest induction (4.2-fold), followed by SOD1 (2.8-fold) and catalase (2.4-fold). These findings are consistent with Nrf2/ARE pathway activation, which drives transcription of phase II detoxification and antioxidant enzymes. QE alone elicited mild, dose-dependent increases in these genes (up to 1.2-fold for Nrf2 at 200 mg/kg), indicating a modest tonic effect without pathological overactivation.

Hematological recovery: The hyperuricemic rats developed a systemic inflammatory and anemic state (Table 5). Their white blood cell count was elevated nearly twofold (12.8 vs. 7.2 × 10^3/μL), with a marked left shift (neutrophils increased from 24.4% to 58.7%, lymphocytes decreased from 68.2% to 34.1%), indicative of acute inflammation. Concurrently, red blood cell count, hemoglobin, and hematocrit fell by approximately 20–25%, consistent with anemia of chronic disease or possible hemolysis. Platelets were also reduced (620 vs. 850 × 10^3/μL), suggesting consumptive thrombocytopenia.

Treatment with QE 200mg/kg significantly attenuated these hematological disturbances. WBCs count dropped to 8.5×10^3/μL, neutrophil percentage fell to 32.5%, and lymphocyte percentage rose to 60.3%. RBCs count, hemoglobin, hematocrit, and platelet counts all improved substantially, although they did not fully normalize to control levels within the 7-day treatment period. This partial recovery is expected given the short duration of therapy. QE alone had no effect on hematological parameters in healthy rats, confirming its safety.

Immunological parameters: Hyperuricemic rats (G2) exhibited a marked pro-inflammatory renal milieu, characterized by significantly elevated IL-1β and TNF-α alongside suppressed IL-10 compared with healthy controls (G1) (*P<0.05) (Table 6). Administration of QE alone (G3–G5) at any dose did not appreciably alter cytokine levels relative to controls, indicating no inherent immunostimulatory or adverse effects in normouricemic animals. In contrast, treatment with QE at 200mg/kg in hyperuricemic rats (G6) potently reversed the inflammatory state, reducing IL-1β by 58% and TNF-α by 62%, while increasing IL-10 by 3.1-fold compared with the untreated HUA group (#P<0.05). Notably, IL-10 in G6 (56.4 pg/mL) exceeded even the healthy control level (42.1 pg/mL).

Table 5: Hematological parameters in all experimental groups

Group	WBC (×10^3/μL)	RBC (×10^6/μL)	Hemoglobin (g/dL)	Hematocrit (%)	Platelets (×10^3/μL)	Neutrophils (%)	Lymphocytes (%)
G1	7.2±0.6	8.1±0.4	14.5±0.6	42.3±2.1	850±45	24.4±2.1	68.2±3.2
G2	12.8±1.1*	6.5±0.5*	10.2±0.5*	31.6±2.0*	620±38*	58.7±3.4*	34.1±2.8*
G3	7.4±0.7	8.0±0.4	14.3±0.7	41.8±2.2	845±50	25.1±2.3	67.5±3.5
G4	7.1±0.5	8.2±0.5	14.7±0.5	42.5±1.9	860±42	23.8±2.0	69.0±3.0
G5	6.9±0.6	8.3±0.4	14.8±0.6	43.0±2.0	870±48	23.2±1.9	69.8±3.1
G6	8.5±0.8#	7.8±0.4#	13.9±0.6#	39.7±2.0#	810±40#	32.5±2.6#	60.3±3.4#

*P<0.05 vs. control; #P<0.05 vs. hyperuricemic group. Data are mean±SD (n=6). WBC = white blood cells; RBC = red blood cells.G1, Control; G2, Hyperuricemic (HUA); G3-G5, QE 50-200 (alone), G6 HUA + QE 200

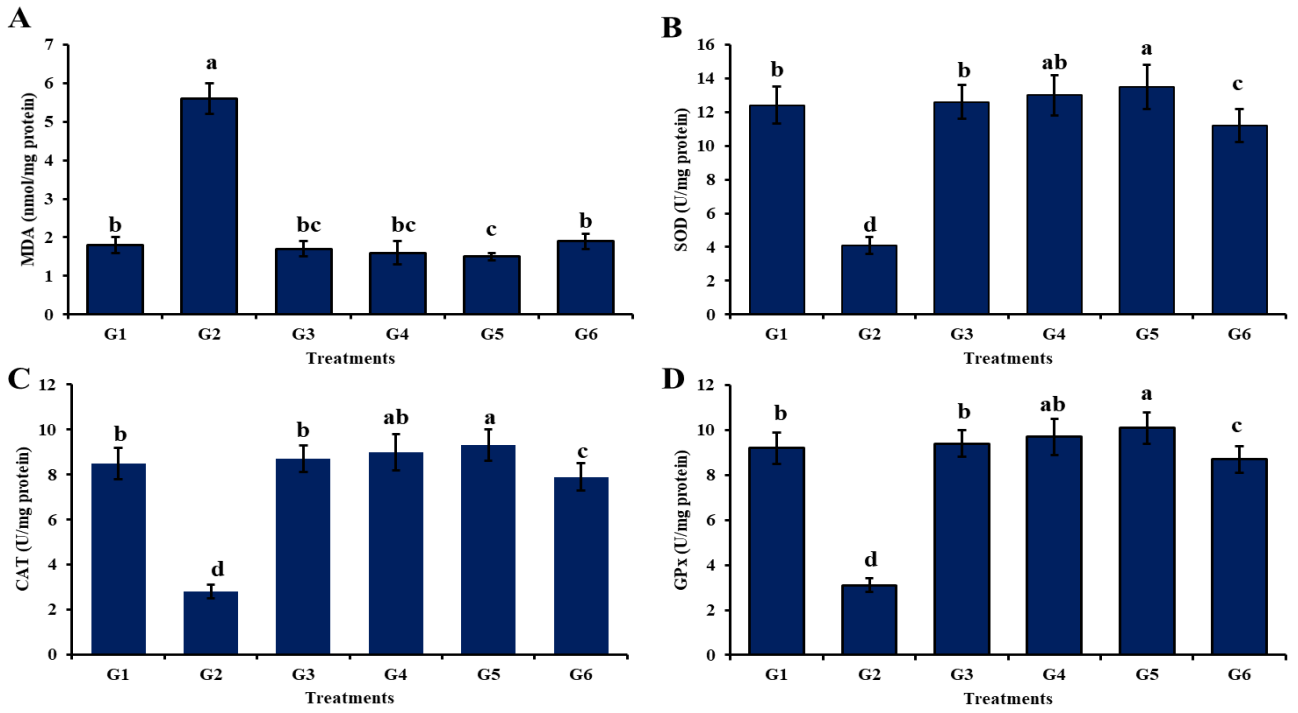

Fig. 3: The effect of quinoa seed extract on the oxidative stress markers in hyperuricemic rats. Lowercase letters above the column indicate a significant difference, P<0.05 (A) malondialdehyde levels, (B) superoxide dismutase, (C) catalase levels, (D) glutathione peroxidase. G1, Control; G2, Hyperuricemic (HUA); G3-G5, QE 50-200 (alone), G6 HUA + QE 200.

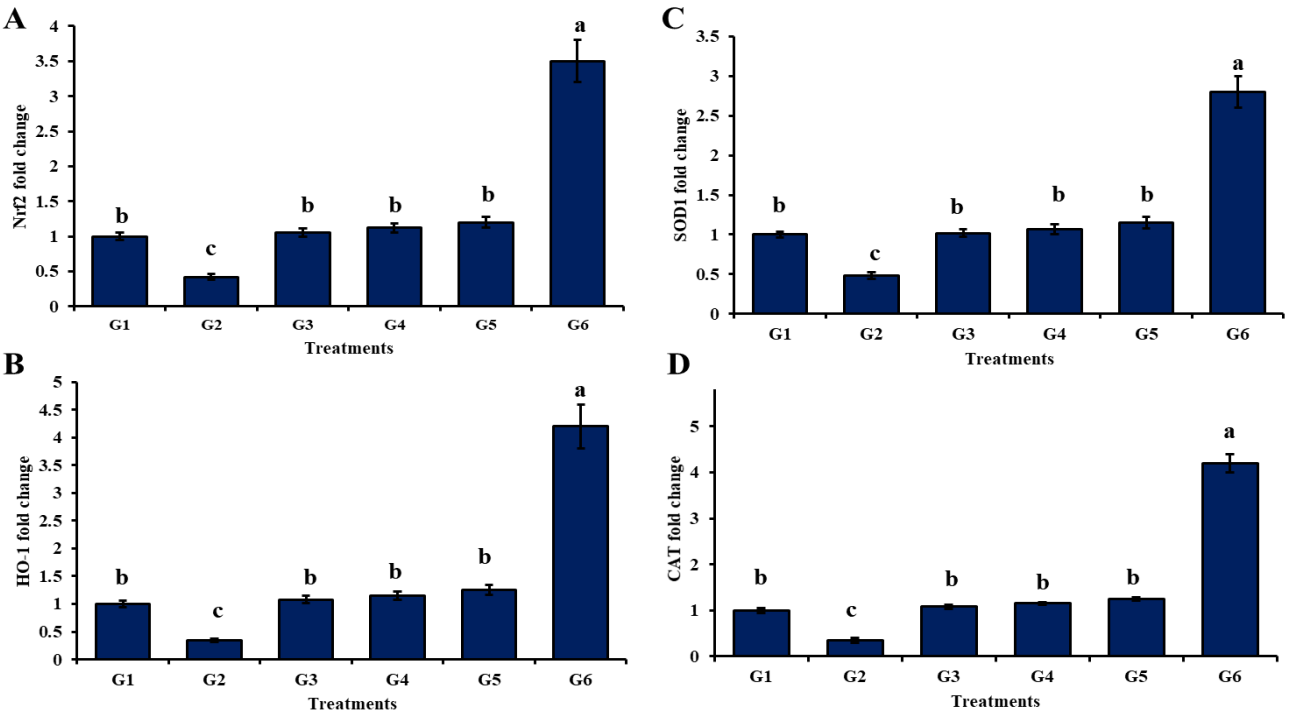

Fig. 4: The effect of quinoa seed extract on the defence genes in hyperuricemic rats. Lowercase letters above the column indicate a significant difference, P<0.05 (A) Nrf2 levels, (B) superoxide dismutase 1, (C) HO-1, (D) Catalase. G1, Control; G2, Hyperuricemic (HUA); G3-G5, QE 50-200 (alone), G6 HUA + QE 200.

Table 6: Immunological parameters in renal tissue of all experimental groups

Group	IL-1β (pg/mL)	TNF-α (pg/mL)	IL-10 (pg/mL)
G1 (Control)	28.4±3.2	45.2±4.5	42.1±3.8
G2 (HUA)	120.5±8.3*	245.7±12.1*	18.2±2.5*
G3 (QE 50 alone)	26.5±2.8	42.3±4.1	44.5±4.0
G4 (QE 100 alone)	25.1±3.0	40.1±3.9	46.2±4.2
G5 (QE 200 alone)	23.8±2.5	38.5±3.6	48.7±4.5
G6 (HUA + QE 200)	50.6±4.1#	93.4±5.9#	56.4±4.8#

P<0.05 vs. control; #P<0.05 vs. hyperuricemic group. Data are mean±SD (n=8).G1, Control; G2, Hyperuricemic (HUA); G3–G5, QE 50, 100, and 200 mg/kg alone, respectively; G6, HUA + QE 200 mg/kg; QE, quercetin extract.

Histological evidence of nephroprotection: Histological examination demonstrated that the renal tubules and glomeruli in normal rats that underwent histological investigation were in good condition, as histological examination did not reveal any pathological abnormalities and revealed a normal histological structure (negative control group) (Fig. 5a). The current study showed the most prominent pathological abnormalities through histopathological evaluation of the tissues in the Hyperuricemic rats' group, which showed cloudy swelling, vascular degeneration, and desquamation of the pre-lining epithelium of the renal tubules. Renal tubules contracted, the epithelial brush border disappeared, and the glomeruli developed significant cytoplasmic hydropic degeneration (free form), abundant of vacuolated epithelial cells in the glomerulus (hexagonal shapes) and a distinct foamy appearance (horizontal oval shape) (Fig. 5b). Renal tissue sections exhibited severe structural damage, characterized by tubular constriction, widespread disruption of the apical brush border, and prominent hydropic degeneration throughout the glomerular cytoplasm. The lipid droplets found inside these cells caused vacuolation. The proximal tubules, loop of Henle, distal tubules, and collecting tubules all showed identical abnormalities. However, corticomedullary junction structures were partially restored in hyperuricemic rat kidneys treated with normal QE. The third group (Fig. 5c) showed less hydropic degeneration (lower right third) than the positive groups, but there was still some modest capillary congestion, increased intertubular cellularity, desquamation, and a few erythrocytes in some tubule lumens (Fig. 5b). The histopathological changes observed in this study could be linked to the overproduction of ROS caused by the use of potassium oxonate.

Kidney histology (Table 7) provided direct morphological confirmation of the biochemical findings. Control rats showed normal renal architecture with intact proximal tubules, no casts, and minimal interstitial or glomerular changes (total injury score 0.2/16). In contrast, hyperuricemic rats exhibited severe, widespread damage: extensive tubular necrosis (score 3.5/4), numerous proteinaceous casts with tubular dilatation (3.2/4), marked interstitial inflammation (3.0/4), and mild-to-moderate glomerular injury (2.8/4). The composite total injury score of 12.5 reflects a severely compromised kidney. Rats treated with QE 200mg/kg showed a striking reduction in all injury parameters. Tubular necrosis fell to a score of 1.0, casts and dilatation to 0.8, interstitial inflammation to 0.7 and glomerular injury to 0.5, resulting in a total score of 3.0 – an approximately 75% reduction compared to the untreated hyperuricemic group. Importantly, the residual damage was predominantly mild and focal, with many areas appearing normal. None of the QE-alone groups showed any histological abnormalities, with total scores ranging from 0.0 to 0.4, further confirming the absence of nephrotoxicity.

Table 7: Semi-quantitative histological scoring of kidney injury

Group	Tubular necrosis	Tubular dilatation/cast formation	Interstitial inflammation	Glomerular injury	Total score (0–16)
G1	0.0±0.0	0.2±0.2	0.0±0.0	0.0±0.0	0.2±0.2
G2	3.5±0.5*	3.2±0.4*	3.0±0.5*	2.8±0.4*	12.5±1.1*
G3	0.0±0.0	0.2±0.2	0.2±0.2	0.0±0.0	0.4±0.3
G4	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
G5	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
G6	1.0±0.3#	0.8±0.3#	0.7±0.3#	0.5±0.2#	3.0±0.6#

*P<0.01 vs. control; #P<0.01 vs. hyperuricemic group. Data are mean±SD (n=6, scoring was performed on 3 sections per rat). Histological changes were assessed in H&E-stained kidney sections. Histological scoring system (0–4): 0 = normal; 1 = mild (<25% involvement); 2 = moderate (25–50%); 3 = severe (51–75%); 4 = very severe (>75%).

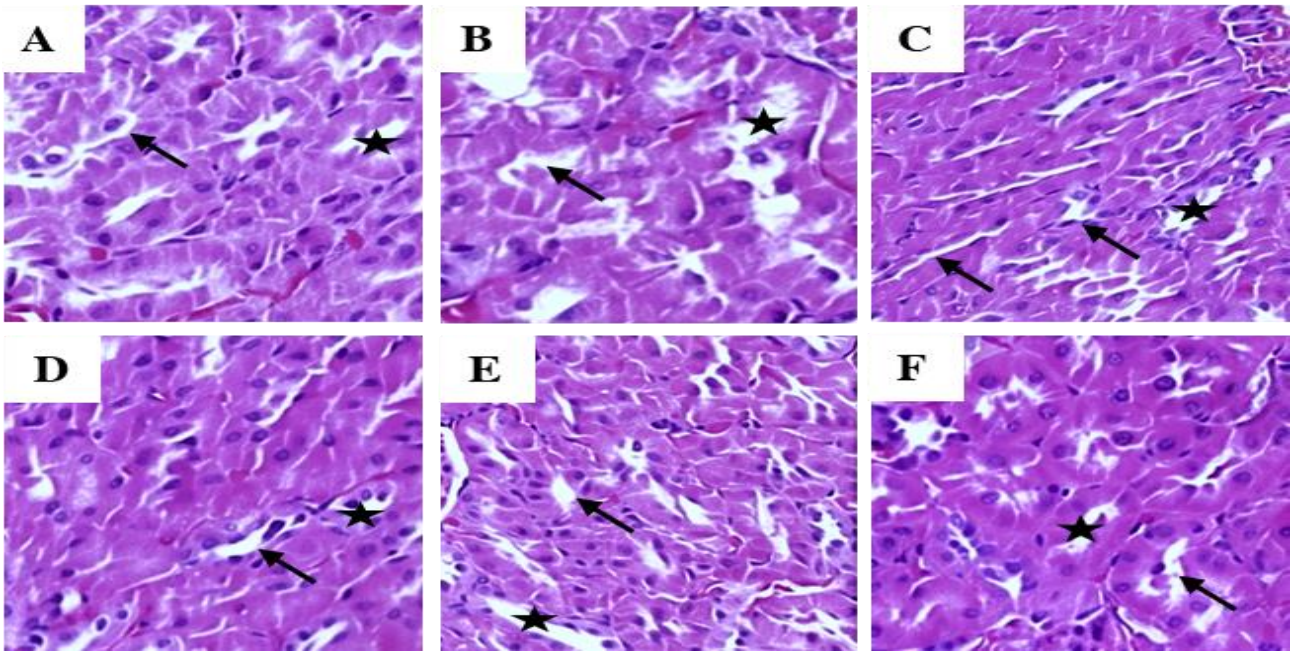

Fig. 5: Protective effects of quinoa seed extract (QE) on the renal histopathology of hyperuricemic rats. (A) Control group showing normal histological architecture of the glomeruli and renal tubules; (B) Hyperuricemic group showing significant tubular necrosis, vacuolation, and cast formation; (C) Groups treated with QE 200mg/kg howing normal histological architecture of the glomeruli and renal tubules (D) UAC+QE 200mg/kg showing marked restoration of renal corpuscles and tubular epithelium (E) UAC+QE 400 mg/kg group: Demonstrates near-complete structural normalization, displaying intact glomerular capillary tufts (arrow), well-preserved Bowman's spaces, and healthy renal tubular epithelial lining with minimal pathological alterations. (F) Positive Control (Allopurinol / Standard drug) group: Shows substantial protection of kidney architecture with well-maintained glomeruli (arrow) and intact renal parenchyma, alongside mild focal tubular lumen dilation (star) (H&E, x400). G1, Control; G2, Hyperuricemic (HUA); G3-G5, QE 50-200 (alone), G6 HUA + QE 200.

DISCUSSION

The current findings demonstrate that quinoa seed extract exhibits robust in vitro antioxidant and antimicrobial activities. When administered orally at 200mg/kg to rats with acute hyperuricemic kidney injury, QE improves growth performance, normalizes renal function markers, reduces oxidative stress, upregulates the Nrf2/HO-1 antioxidant gene pathway, corrects hematological, inflammatory, and anemic changes, and substantially attenuates renal tubular necrosis and inflammation. The protective effects are specific to the treatment group – QE alone does not alter any measured parameter in healthy animals. These data provide a solid mechanistic and functional basis for considering QE as a candidate nutraceutical against hyperuricemia-induced acute kidney injury.

Beyond its role as a biomarker, hyperuricemia independently contributes to kidney damage, with oxidative stress serving as the principal underlying mechanism (Du *et al.*, 2024). The rat model of hyperuricemic nephropathy faithfully recapitulated the hallmark disease features, manifested by elevated serum uric acid, depleted antioxidant defenses, pronounced lipid peroxidation, and significant renal tubular injury (Wang *et al.*, 2016). In untreated hyperuricemic rats, MDA levels were elevated by over 200%, whereas SOD, CAT, and GPx activities declined to approximately one-third of normal levels. This pattern aligns with previous evidence that uric acid promotes mitochondrial ROS production, thereby provoking tubular injury and facilitating apoptosis (Verzola *et al.*, 2014). Hyperuricemia is recognized as an independent risk factor for kidney disease initiation and progression, with oxidative stress serving as a central pathogenic mechanism. The potassium oxonate-induced rat model employed herein reliably recapitulates hyperuricemic nephropathy, characterized by elevated serum uric acid, diminished antioxidant defenses, enhanced lipid peroxidation, and tubular injury. In the present hyperuricemic rats, MDA levels increased by over 200%, while SOD, CAT, and GPx activities fell to approximately one-third of control values—findings consistent with prior reports linking uric-acid-driven mitochondrial ROS production to tubular cell damage and pro-apoptotic signaling (Lin et al., 2023). The substantial restoration of these parameters following QE treatment consequently positions QE as an effective countermeasure against uric-acid-mediated oxidative renal injury (Lin *et al.*, 2023).

In this study, a hydroalcoholic extract of whole quinoa seeds was investigated, and a rich phenolic profile (187.6mg GAE/g), including quercetin, kaempferol, rutin, caffeic acid, ferulic acid, and gallic acid, which are well known for their antioxidant and anti-inflammatory bioactivities, was identified. In a 2023 study by Lin and colleagues, quinoa bran saponins (QBS4) were explored in a hyperuricemic mouse model (induced by adenine and potassium oxonate) and similarly found reduced uric acid, BUN, creatinine, and renal inflammation, with mechanistic involvement of the PI3K/AKT/NF κB signaling pathway (Lin *et al*., 2023). While both studies support the nephroprotective potential of quinoa-derived components, the present work extends these observations by demonstrating that a whole-seed, phenolic-rich extract, rather than saponins alone, can upregulate the Nrf2/HO1 axis, a key antioxidant defense pathway. This distinction is important as different quinoa fractions may activate complementary cytoprotective mechanisms.

Similarly, in high fructose-fed rats, dietary quinoa supplementation decreased plasma MDA levels and improved antioxidant capacity in the kidney, heart, and other tissues, which is similar to our observation that QE decreased renal MDA and increased SOD and CAT activities (Pasko *et al.*, 2010). However, that study did not specifically examine hyperuricemia or the Nrf2 pathway. The present findings thus provide more detailed mechanistic insight into how quinoa phenolics protect the kidney under uric acid overload. A cardinal finding of this study is the marked upregulation of Nrf2, HO-1, SOD1, and catalase mRNA in hyperuricemic rats treated with QE 200mg/kg. These genes were downregulated (42–52% of control) in untreated hyperuricemic rats, indicating impaired antioxidant transcription.

In challenged rats, Nrf2 and HO-1 were markedly downregulated, an effect reversed by QE treatment, which elicited 3.5- and 4.2-fold increases, respectively, relative to untreated hyperuricemic animals. These findings corroborate the established role of the Nrf2/HO-1 axis as a critical protective pathway against hyperuricemic kidney injury (Qiao *et al.*, 2023). For instance, Chiang *et al.* (2025) recently showed that it not only protected renal tubular cells from H_2O_2-induced ROS, but also improved renal function and mitigated MDA in a rat model of hyperuricemia, all through Nrf2/HO-1 activation. Similarly, Yu *et al*. (2024) showed that luteolin alleviates hyperuricemic nephropathy in mice by enhancing urate excretion, upregulating the Nrf2/HO-1/NQO1 antioxidant cascade, and suppressing liver xanthine oxidase activity. The frequent targeting of the Nrf2/HO-1 axis by structurally varied natural products emphasizes its central function in maintaining cellular redox homeostasis and validates its potential as a crucial therapeutic target (Uddin *et al.*, 2021; Zhang *et al.*, 2026).

The HPLC analysis of QE turned up substantial amounts of quercetin, kaempferol, and rutin, all flavonols that have individually been tied to lowering uric acid and reining in oxidative stress (Pandya *et al.*, 2023; Putri and Putra, 2024). These findings are supported by various studies; a systematic review synthesizing 15 *in-vivo* studies demonstrated that various flavonoids, including kaempferol, luteolin, apigenin, rutin, and quercetin, consistently attenuate hyperuricemia through the dual mechanisms of xanthine oxidase (XO) inhibition and the modulation of renal urate transporters (Haidari *et al.*, 2011). Haidari and colleagues (2011) showed that quercetin and kaempferol at 5 mg/kg not only reduced serum uric acid in oxonate-treated rats but also suppressed liver xanthine oxidoreductase activity, increased total antioxidant capacity, and reduced MDA levels. These observations closely align with the pattern exhibited by QE. Furthermore, the aglycone derivatives—luteolin, apigenin, kaempferol, and quercetin—have been identified as potent xanthine oxidase (XO) inhibitors, with IC50 values below 5 μM (Pereira *et al*., 2020; Xi *et al*., 2024). Although XO activity was not quantified directly in the present study, the marked decline in serum uric acid levels—from 8.4 mg/dL to 3.1mg/dL, suggests that QE attenuates hyperuricemia by suppressing uric acid synthesis, enhancing renal clearance, or exerting a dual regulatory mechanism.

An underappreciated aspect of hyperuricemic kidney injury is the increased susceptibility to urinary tract infections, which can exacerbate renal damage. QE exhibited concentration-dependent antimicrobial activity against six uropathogens, with inhibition zones ranging from 12.5mM (*P. mirabilis*) to 19.5mM (*E. coli*) at 200µg/mL and MIC values of 2.5–5.5mg/mL. These data suggest that QE may offer dual protection: directly reducing oxidative and inflammatory renal injury and limiting bacterial colonization, which could complicate AKI (Li *et al.*, 2025a). To our knowledge, this is the first study to explicitly link the antimicrobial activity of a quinoa extract with its nephroprotective effects in hyperuricemia. Future *in-vivo* infection models will be needed to confirm whether these *in-vitro* antimicrobial effects translate to a reduced bacterial burden in the kidney.

The increased awareness of the ability of plant polyphenols to reduce uric acid levels safely and to protect the kidney has stimulated the investigation of many natural products, often using the potassium oxonate model (e.g., sugarcane polyphenols (SP) at low, medium, and high doses decreased serum uric acid by 19.77, 27.42 and 45.54%, respectively, in hyperuricemic rats, with improvements in BUN, creatinine, and inhibition of the PI3K/AKT/NF κB pathway (Li *et al.*, 2025b); dandelion leaf aqueous extract (high in polyphenols) also decreased serum UA and inhibited NLRP3/Caspase 1 and TLR4/MyD88/NF κB pathways, and downregulated IL 1β, IL 6, and TNF α (Zhou *et al.*, 2025); and naringenin (100 mg/kg) reduced serum UA levels, apoptosis, inflammation, and DNA damage, while increasing antioxidant activity in a PO-induced hyperuricemic rat model (Calis *et al.*, 2023). Furthermore, a flavonoid-rich fraction of *Monolluma quadrangula* suppressed XO activity, reduced serum uric acid, urea, creatinine, and pro-inflammatory cytokines, downregulated URAT1 and GLUT9 and upregulated OAT1 in PO-induced rats, demonstrating the feasibility of targeting urate transporters with plant flavonoids (ALRashdi *et al.*, 2022). Collectively, these studies, together with our findings on QE, support the concept that dietary polyphenols can ameliorate hyperuricemic nephropathy through overlapping mechanisms: XO inhibition, modulation of urate transporters, NF-κB-mediated anti-inflammation, and Nrf2-driven upregulation of antioxidant genes.

The observed increases in WBC count, neutrophil percentage, RBC count, hemoglobin, and platelets in the HUA + QE group suggest that QE attenuated the systemic inflammatory and anemic responses associated with severe hyperuricemia. Such observations are rarely reported in similar studies, but are clinically relevant, as AKI induced by hyperuricemia is frequently associated with leukocytosis and anemia, which may worsen the outcomes. Histologically, QE treatment reduced the total kidney injury score from 12.5 to 3.0 (a 75% reduction), primarily by ameliorating tubular necrosis and interstitial inflammation. This histological improvement supports the biochemical data and confirms that QE can effectively preserve renal architecture.

All doses of QE alone (50, 100 and 200mg/kg) were well tolerated, with no effects on growth, renal function, oxidative markers, hematology, or histology. This safety profile, together with the efficacy at 200mg/kg, makes QE an appealing candidate for dietary supplementation or as adjunct therapy. Similar studies on hydrolyzed quinoa extract in Wistar rats showed no hepatic or renal toxicity and a decrease in food intake, body weight and fat deposition, which could be beneficial for hyperuricemic patients with metabolic syndrome (Meneguetti *et al.*, 2011).

Integrating the experimental outcomes with the current literature allows us to delineate a plausible mechanism underlying the ameliorative effect of QE in hyperuricemic nephropathy. Consistent with that, Li *et al*. (2024) found that piperine improves hyperuricemic nephropathy by inhibiting URAT1/GLUT9 and the AKT-mTOR pathway, while Alghamdi (2018) stated the protective effect of quinoa (*Chenopodium Quinoa* Willd.) seeds against hypercholesterolemia in male rats. Hyperuricemia triggers excessive mitochondrial ROS accumulation while blunting the Nrf2 antioxidant signaling axis, thereby impairing SOD, CAT and GPx activities and inducing severe lipid peroxidation; protein-rich plants, *i.e.*, soybeans, white beans and fenugreek seeds, enhance antioxidant enzymes, indicating a lowering of oxidative stress from hyperuricemia (Al-Masri, 2016; Utami *et al*., 2026). The bioactives in QE, particularly quercetin, kaempferol, rutin, and related phenolic acids, mitigate this injury via a multi-faceted approach. QE inhibits xanthine oxidase to curb hyperuricemia at its source, upregulates Nrf2 signaling (likely through KEAP1 modification or PI3K/Akt activation) to drive HO-1 and phase II enzyme expression, restores intracellular antioxidant capacity to suppress MDA buildup, and provides concurrent antimicrobial coverage to mitigate secondary nephric infections.

Conclusions: Quinoa seed extract possesses intrinsic antioxidant and antimicrobial properties, as confirmed by *in-vitro* assays. In an *in-vivo* model of acute kidney injury induced by hyperuricemia, dietary supplementation with quinoa seed extract demonstrated protective effects against renal damage. These benefits are associated with the upregulation of key renal defense genes involved in oxidative stress responses, as well as improvements in renal function markers and antioxidant status. The antimicrobial activity of the extract may provide additional protection against secondary infections that commonly complicate kidney injury. Although further studies are needed to establish clinical translation, the present findings position quinoa seed extract as a promising nutraceutical candidate for preventing or mitigating hyperuricemia-associated acute kidney injury, with potential applications in functional foods or supportive therapy.

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REFERENCES

Alghamdi ES, 2018. Protective effect of quinoa (*Chenopodium quinoa* Willd.) seeds against hypercholesterolemia in male rats. Pharmacophore 9(6-2018): 11-21.

Al-Qabba M, El-Mowafy M, Althwab S, *et al*., 2020. Phenolic profile, antioxidant activity and ameliorating efficacy of Chenopodium quinoa sprouts against CCl_4-Induced oxidative stress in rats. Nutrients 12:2904.

Ali A, Sampaio TL, Khan H, *et al*., 2022. Plants with therapeutic potential for ischemic acute kidney injury: A Systematic Review. Evidence-based Complementary and Alternative Medicine 2022:6807700.

ALRashdi BM, Elgebaly HA, Germoush MO, *et al*., 2022. A flavonoid-rich fraction of Monolluma quadrangula inhibits xanthine oxidase and ameliorates potassium oxonate-induced hyperuricemia in rats. Environmental Science and Pollution Research 29:63520-63532.

Al-Masri SA, 2016. Beneficial role of high plant proteins in the treatment against hyperuricemia in experimental rats. Journal of Animal and Plant Sciences 26(3): 619-626.

Cai Y, Huang C, Zhou M, *et al*., 2022. Role of curcumin in the treatment of acute kidney injury: research challenges and opportunities. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology 104:154306.

Cai YQ, Gao H, Song LM, *et al.,* 2023. Optimization of green deep eutectic solvent (DES) extraction of *Chenopodium quinoa* Willd. husks saponins by response surface methodology and their antioxidant activities. RSC Advances 13: 29408 - 29418.

Calis Z, Dasdelen D, Baltaci AK, *et al*., 2023. Naringenin prevents renal injury in experimental hyperuricemia through suppressing xanthine oxidase, inflammation, apoptotic pathway, DNA damage, and activating antioxidant system. Metabolic Syndrome and Related Disorders 21:275-281.

Casalvara R, Ferreira BMR, Gonçalves JE, *et al*., 2024. Biotechnological, nutritional, and therapeutic applications of Quinoa (*Chenopodium quinoa* Willd.) and its by-products: A Review of the Past Five-Year Findings. Nutrients 16(6):840.

Chen L, Deng Y, Hu J, *et al*., 2025. Nephroprotective effects of substances of medicine food homology and traditional Chinese medicine phytochemicals against acute kidney injury. Frontiers in Pharmacology 2025.1539886.

Chiang YF, Huang KC, Huang YJ, *et al*., 2025. Hinokitiol modulates Nrf2/HO-1 signaling, autophagy, and URAT1 in hyperuricemia and oxidative stress models of renal injury. Free Radical Biology and Medicine 238:169-178.

Dera A, Rajagopalan P, Alfhili M, *et al*., 2019. Thymoquinone attenuates oxidative stress of kidney mitochondria and exerts nephroprotective effects in oxonic acid-induced hyperuricemia rats. BioFactors 46(2):292-300.

Dong S, Yang X, Zhao L, et al., 2020. Antibacterial activity and mechanism of action saponins from *Chenopodium quinoa* Willd. husks against foodborne pathogenic bacteria. Industrial Crops and Products. 149: 112350.

Du L, Zong Y, Li H, *et al*., 2024. Hyperuricemia and its related diseases: mechanisms and advances in therapy. Signal Transduction and Targeted Therapy 9:212.

Fang C, Lou D, Zhou LQ, *et al*., 2021. Natural products: potential treatments for cisplatin-induced nephrotoxicity. Acta Pharmacologica Sinica 42:1951-1969.

Guo Z, Deng X, Ping C, *et al*.,. 2025. Quinoa: Nutritional and phytochemical value, beneficial effects, and future applications. Applied Food Research 5(1):100766.

Haidari F, Keshavarz SA, Mohammad Shahi M, *et al*., 2011. Effects of parsley (*Petroselinum crispum*) and its flavonol constituents, kaempferol and quercetin, on serum uric acid levels, biomarkers of oxidative stress and liver xanthine oxidoreductase activity inoxonate-induced hyperuricemic rats. Iranian Journal of Pharmaceutical Research 10:811-819.

Hazzam KE, Hafsa J, Sobeh M, *et al*., 2020. An insight into saponins from quinoa (*Chenopodium quinoa* Willd): A review. Molecules 25(5):1059.

Housseini IA, Dakdouk H, Borjac J, 2025. Nephroprotective effect of *Mucuna pruriens*, *Moringa oleifera* and milk thistle extracts against Acetaminophen-induced acute kidney injury in mice. Kidney and Blood Pressure Research 50:523-532.

Kang H, Lee H, Cho KB, *et al*., 2021. A review of natural products for prevention of acute kidney injury. Medicina 57(11):1266.

Li HD, Meng XM, Huang C, *et al*., 2019. Application of herbal traditional chinese medicine in the treatment of acute kidney injury. Frontiers in Pharmacology 10:376.

Li, L, Zhao K, Luo J, *et al.,* 2024. Piperine improves hyperuricemic nephropathy by inhibiting URAT1/GLUT9 and the AKT-mTOR pathway. Journal of Agricultural and Food Chemistry 72(12):6565-6574.

Li J, Diao L, Li M, *et al*., 2025a. Unraveling the mysteries of the gut-kidney axis: the protective role of traditional Chinese medicine in chronic kidney disease. Frontiers in Microbiology 16:1642377.

Li K, Han Y, Wang Y, *et al*., 2025b. Urate-lowering and renal-protective effects of sugarcane polyphenols in hyperuricemia: mechanisms and key components. Food and Function 16:6760-6772.

Lim J, Park H-M, Yoon K, 2019. Analysis of saponin composition and comparison of the antioxidant activity of various parts of the quinoa plant (*Chenopodium quinoa* Willd.). Food Science and Nutrition 8:694-702.

Lin X, Zhou Q, Zhou L, *et al*., 2023. Quinoa (*Chenopodium quinoa* Willd) bran saponins alleviate hyperuricemia and inhibit renal injury by regulating the PI3K/AKT/NFκB signaling pathway and uric acid transport. Journal of Agricultural and Food Chemistry 71:6635-6649.

López-Moreno M, Jiménez-Moreno E, Gallego AM, *et al*., 2023. Red quinoa hydrolysates with antioxidant properties improve cardiovascular health in spontaneously hypertensive rats. Antioxidants 12(6):1291.

Meneguetti QA, Brenzan MA, Batista MR, *et al*., 2011. Biological effects of hydrolyzed quinoa extract from seeds of *Chenopodium quinoa* Willd. Journal of Medicinal Food 14:653-657.

Ong E, Pek CJN, Tan J, *et al*., 2020. Antioxidant and cytoprotective effect of Quinoa (*Chenopodium quinoa* Willd.) with pressurized hot water extraction (PHWE). Antioxidants 9(11):1110.

Paes A, De Carvalho R Koga R, *et al*., 2023. Phytocompounds from amazonian plant species against acute kidney injury: Potential nephroprotective effects. Molecules 28(17):6411.

Pandya A, Thiele B, Köppchen S, *et al*., 2023. Characterization of bioactive phenolic compounds in seeds of *Chilean quinoa* (*Chenopodium quinoa* Willd.) Germplasm. Agronomy 13(8):2170.

Pasko P, Barton H, Zagrodzki P, *et al*., 2010. Effect of diet supplemented with quinoa seeds on oxidative status in plasma and selected tissues of high fructose-fed rats. Plant Foods for Human Nutrition 65:146-151.

Pereira E, Cadavez V, Barros L, *et al*., 2020. Chenopodium quinoa Willd.(quinoa) grains: A good source of phenolic compounds. Food Research International 137:109574.

Putri DP, Putra KWR, 2024. Flavonoids for anti-hyperuricemia: A literature review. Nurse and Health: Journal of Keperawatan 13:109-126.

Qiao P, Sun Y, Wang Y, *et al*., 2023. Activation of NRF2 signaling pathway delays the progression of hyperuricemic nephropathy by reducing oxidative stress. Antioxidants 12(5):1022.

Ren G, Teng C, Fan X, *et al*., 2022. Nutrient composition, functional activity and industrial applications of quinoa (*Chenopodium quinoa* Willd.). Food Chemistry 410:135290.

Rizk S, Moneim AA, Abdel-Gaber R, *et al*., 2023. Nephroprotective efficacy of *Echinops spinosus* against a Glycerol-induced acute kidney injury model. ACS Omega 8:41865-41875.

Rostamkhani H, Faghfouri AH, Veisi P, *et al*., 2022. The protective antioxidant activity of ginger extracts (*Zingiber Officinale*) in acute kidney injury: A systematic review and meta-analysis of animal studies. Journal of Functional Foods 94:105111.

Sharma S, Kataria A, Singh B, 2022. Effect of thermal processing on the bioactive compounds, antioxidative, antinutritional and functional characteristics of quinoa (*Chenopodium quinoa*). LWT - Food Science and Technology 160:113256.

Sun X, Yang X, Xue P, *et al.,* 2019. Improved antibacterial effects of alkali-transformed saponin from quinoa husks against halitosis-related bacteria. BMC Complementary and Alternative Medicine 19:46.

Tamargo C, Hanouneh M, Cervantes C, 2024. Treatment of acute kidney injury: a review of current approaches and emerging innovations. Journal of Clinical Medicine 13(9):2455.

Turgut F, Awad A, Abdel-Rahman E, 2023. Acute kidney injury: medical causes and pathogenesis. Journal of Clinical Medicine 12(1):375.

Uddin MJ, Kim EH, Hannan MA, *et al*., 2021. Pharmacotherapy against oxidative stress in chronic kidney disease: promising small molecule natural products targeting Nrf2-HO-1 signaling. Antioxidants 10(2):258.

Utami PD, Setianingsih H, Sari DRT, 2026. Hepatorenal protective role of encapsulated Holothuria atra in a mice model of *Plasmodium berghei* ANKA inoculation. Journal of Advanced Veterinary and Animal Research 13(1):55-66.

Verzola D, Ratto E, Villaggio B, *et al*., 2014. Uric acid promotes apoptosis in human proximal tubule cells by oxidative stress and the activation of NADPH oxidase NOX 4. PloS one 9:e115210.

Wang M, Zhao J, Zhang N, *et al*., 2016. Astilbin improves potassium oxonate-induced hyperuricemia and kidney injury through regulating oxidative stress and inflammation response in mice. Biomedicine and Pharmacotherapy 83:975-988.

Xi X, Fan G, Xue H, *et al*., 2024. Harnessing the potential of quinoa: Nutritional profiling, bioactive components, and implications for health promotion. Antioxidants 13(7):829.

Yu H, Huang L, Gui L, *et al*., 2024. Luteolin ameliorates hyperuricemic nephropathy by activating urate excretion and Nrf2/HO-1/NQO1 antioxidant pathways in mice. Food Science and Nutrition 12:8053-8066.

Zeng YF, Li JY, Wei XY, *et al*., 2023. Preclinical evidence of reno-protective effect of quercetin on acute kidney injury: a meta-analysis of animal studies. Frontiers in Pharmacology 4:1310023.

Zhang L, Huang X, Xiong H, *et al*., 2026. The Nrf2/HO-1 signaling pathway in arthritis: from molecular mechanisms to therapeutic potential. Frontiers in Cell and Developmental Biology 14:1728679.

Zhou X, Liu T, Xu B, *et al*., 2025. Dandelion leaf aqueous extract relieves hyperuricemia and its complications via modulating uric acid metabolism, renal inflammation, and gut microbes. Foods 14(22):3843.