

Molecular and Pathological Effect of Lead Acetate Nephrotoxicity in Rats Treated with Quercetin

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ABSTRACT

Lead is a common environmental metal known to cause toxicity to multiple organs, with the kidneys being the primary target of lead poisoning due to their role in lead excretion. Quercetin is a natural flavonoid with reported antioxidant and protective properties. However, despite these properties, its preventive or therapeutic role in lead-induced toxicity has not been fully elucidated. The present study aimed to evaluate the preventive effect of quercetin against lead acetate-induced nephrotoxicity in rats. Twenty adult male rats were randomly divided into four groups: a control group, a lead-treated group administered 241 mg/kg body weight (1/20 LD₅₀) of lead acetate orally, a quercetin-treated group receiving 40 mg/kg body weight of quercetin, and a combined lead plus quercetin group. Renal injury was assessed using biochemical markers of oxidative stress, molecular analysis of metallothionein-2 (MT2) gene expression, and histopathological examination of kidney tissue. The results showed that lead exposure induced significant renal toxicity, evidenced by increased kidney injury molecule-1 (KIM-1) and malondialdehyde (MDA) levels, altered superoxide dismutase (SOD) activity, marked upregulation of MT2 gene expression, and severe histopathological alterations in renal tissue. Co-administration of quercetin significantly attenuated lead-induced oxidative stress, reduced KIM-1 levels, modulated MT2 expression, and alleviated the severity of renal histopathological lesions. However, quercetin did not fully restore biochemical or histological parameters to control levels. Quercetin alone did not induce renal injury and was associated with reduced oxidative stress markers. In conclusion, Lead acetate induces nephrotoxicity by a mechanism mediated by oxidative stress. Quercetin provides partial nephroprotection and may serve as a supportive preventive agent against renal toxicity caused by lead, but does not fully compensate for the renal damage caused by lead.

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1. Introduction

Lead (Pb) is a ubiquitous heavy metal pollutant in the environment. It is used in many industrial activities including mining, refining and producing lead-acid batteries (Jwad, 2012; Salman & Shwaish, 2024). Lead had been associated with serious environmental and public health concerns (Boskabady et al., 2018). The exposure to lead can occur mainly through alimentary and respiratory routes and interferes with at low levels, is associated with a wide range of toxic effects in humans and animals, affecting nearly every organ system (Al-Mzaen et al., 2015; KHUDHAIR, 2024; Nawfal et al., 2024). It is known to induce systemic toxicity by multifaceted mechanism primarily through the generation of reactive oxygen species (ROS), leading to severe oxidative stress and subsequent cellular damage (KHUDHAIR, 2024). Also interfering with antioxidant defense systems, mitochondrial function, and cellular signaling pathways. The kidney is particularly vulnerable to lead-induced damage (Bhatia et al., 2020; Fenga et al., 2017), resulting in nephrotoxicity characterized by biochemical alterations and distinct histopathological lesions. Furthermore, lead exposure is known to compromise the immune system, leading to disturbances in both humoral and cellular immunity, which exacerbates the overall toxicological profile (Mishra, 2009).

Because of the persistent nature of lead toxicity and the limited efficacy of current chelation therapies, attention has increased toward natural compounds with potent antioxidant and protective properties. Quercetin, a natural flavonoid compound with a widespread occurrence throughout the plant kingdom, exhibits a variety of pharmacological activities. Because of the wide spectrum of health-promoting effects, quercetin has attracted much attention of dietitians and medicinal chemists (Wang et al., 2022). Previous studies have suggested that Quercetin can mitigate the toxic effects of

various heavy metals by scavenging free radicals, enhancing endogenous antioxidant defenses, and stabilizing cellular membranes (Al-Zharani et al., 2023; Qi et al., 2023; Qi et al., 2022).

Despite the established toxicity of lead, the protective effects of quercetin and the molecular and immunological mechanisms through which quercetin counteracts lead acetate-induced toxicity remain to be fully elucidated. Specifically, the role of key protective genes such as metallothionein 2 (MT2), which is fundamental in heavy metal detoxification and homeostasis, has not been fully investigated. Therefore, the present study aims to investigate the protective and therapeutic effects of Quercetin against lead acetate-induced toxicity in male albino rats. The findings of this study are expected to provide scientific evidence supporting the use of Quercetin as a potential therapeutic agent to mitigate the adverse health effects associated with chronic lead exposure.

2. Material and Methods

2.1 Ethical Approval

Ethical approval for this study was obtained from the Scientific Committee for Animal Care at the Veterinary Medicine College, the University of Baghdad (Number P.G/51).

2.1.1 Experimental Animals and Animal Housing

Adult albino male rats (*Mus Norvegicus Albinus*) (weight between 200-220 gm) were chosen as the experimental animal model and treated for 30 days. The animals were housed in a dedicated room at the University of Baghdad's Veterinary Medicine College. The standard diet consisted of tap water, and pellets. The animals had a 12/12-hour light/dark cycle and were housed in a clean, air-conditioned room with a temperature of 22 ± 4 °C and a relative humidity of $50 \pm 10\%$. The ventilation vacuum was constantly changing the air in the place. To prevent stress, the area was cleaned every three days, and all the animals were checked daily for any obvious signs of illness or injury. The careful management of their environment ensured that the animals remained healthy and stress-free throughout the study. This attention to detail was crucial for obtaining reliable data on their behavior and overall well-being.

2.2 Experimental Design

Twenty male albino rats were randomly allocated to four experimental groups: a control group; a lead-treated group administered 241 mg/kg body weight of lead acetate ($1/20$ LD₅₀) orally; a quercetin-treated group receiving 40 mg/kg body weight of quercetin; and a combined lead plus quercetin group. The experimental period lasted for one month. Animals from each group were sacrificed at the end of experiment period.

All animals were monitored daily for clinical signs behavioral changes, and all observations were recorded throughout the experimental period.

2.3 Sample Collection

2.3.1 Blood Samples

At the end of the experimental period, rats were anaesthetized with ketamine (9 mg/kg b.w.) and xylazine (10 mg/kg b.w.) intraperitoneally. Blood was collected by cardiac puncture through the diaphragm and immediately placed into plain tubes to obtain serum and plasma. The Serum was separated and stored at -20 °C for biochemical and immunological analyses, including kidney injury molecule-1 (KIM-1), superoxide dismutase (SOD), and malondialdehyde (MDA), which ELISA determined. Plasma obtained from heparinised blood was stored at -80 °C for molecular analysis of metallothionein-2 (MT2) gene expression by PCR.

2.3.2 Tissue Samples

Following blood collection, the brain and kidneys were excised and fixed in 10% neutral buffered formalin, routinely processed, sectioned at 5 μ m, and stained with hematoxylin and eosin (H&E) for gross and histopathological examination.

2.4 Parameters and Laboratory Analyses

2.4.1 Laboratory Analyses

2.4.1.1 Biochemical Analyses

Kidney injury molecule-1 (KIM-1) was determined using a commercial ELISA kit following the manufacturer's protocol. Oxidative and antioxidant markers were also assessed: malondialdehyde (MDA) as a lipid peroxidation marker and

superoxide dismutase (SOD) activity as an enzymatic antioxidant marker, both estimated using ELISA kits.

2.5 Molecular Analysis

2.5.1 Primer Design and Preparation

In this study, specific primers were designed to target the genes of interest using sequences from the National Centre for Biotechnology Information (NCBI) database. The primers were synthesized by MacroGen® (Korea). Each primer was carefully selected to ensure high specificity and optimal amplification efficiency, avoiding secondary structures and dimer formations. Each primer was characterized by its unique nucleotide sequence (5'–3'), the expected amplicon size in base pairs (bp), and the associated NCBI accession number to confirm the target gene identity. Detailed information regarding the primers used in this study is provided in Table 1.

Table 1: Primers Used in this Study, including their Sequences, Expected Product Sizes, and References

Primer Name	Sequence (5'–3')	Product Size (bp)	NCBI Accession Number	Reference
MT2-F	TGCAAAGAGGCTTCGGACAAG	126	NM_001137564.2	MacroGen® (Korea)
MT2-R	AAAGTGTGGAGAACCGGTCAG			
BACT-F	GGTGGGTATGGCCTGAGAAGA	101	NM_031144.3	MacroGen® (Korea)
BACT-R	TGGTGACAATGCCGTGTTTC			

2.5.2 RNA Extraction and cDNA synthesis

Total RNA was isolated from whole blood samples using TRIzol™ reagent (Invitrogen, USA) following the manufacturer's standard protocol, with minor modifications to optimise RNA yield and purity.

2.5.3 RNA Quantification

The concentration and purity of the extracted RNA were determined using the Qubit 4.0 Fluorometer (Invitrogen, USA) with the Qubit™ RNA High Sensitivity (HS) Assay Kit.

2.5.4 cDNA Synthesis

Complementary DNA (cDNA) was synthesized from the isolated total RNA using the ProtoScript® First Strand cDNA Synthesis Kit (NEB, UK).

Quantitative Real-Time PCR (qPCR)

Quantitative real-time PCR (qPCR) was employed to determine the relative expression levels of the target genes using the Luna Universal qPCR Master Mix (NEB, UK).

2.5.5 Pathological Examination

Gross and histopathological examinations were performed on kidney tissues immediately after necropsy to detect abnormalities such as congestion, discolouration, or enlargement. Lesions were recorded, photographed, and compared among groups.

2.5.6 Statistical Analysis

Statistical analysis of data was performed using the Statistical Analysis System (SAS, version 9.1). A two-way analysis of variance (ANOVA) was applied to evaluate the effects of treatment and duration, as well as their interaction. When significant differences were detected, the Least Significant Difference (LSD) post hoc test was employed to compare mean values among groups. All results were expressed as mean $\pm$ standard deviation (SD). A probability level of $p < 0.05$ was considered statistically significant.

3. Result

3.1 MT2 Gene Expression

Expression of the MT2 gene using quantitative PCR (qPCR) data presented in Table 2 was analyzed and the results indicated differential expression of the MT2 gene across the experimental groups. the control group (C) was established a baseline relative fold change of 1.0. though Group L demonstrated a substantial increase in MT2 expression, with an 7.93-fold increase. While, Group Q exhibited showing a 0.67-fold increase. Group LQ showed a 2.57-fold increase compared with the control group.

Table 2: Fold Changes in MT2 Gene Expression Across Groups at 30 Days of Exposure

Group	Mean Ct MT2	Mean Ct β -Actin	Mean Δ Ct (MT2 β -Actin)	$\Delta\Delta$ Ct vs Control	Fold Change
Control	33.75	30.40	3.35	0.00	1.00
Quercetin (Q)	34.87	30.94	3.93	+0.58	0.67
Lead (L)	31.64	31.28	0.36	-2.99	7.93
Lead + Quercetin (LQ)	36.65	34.66	1.99	-1.36	2.57

Values Represent Relative Fold Expression Normalized to β -Actin (Housekeeping Gene)

3.2 Kidney Injury Molecule-1 (KIM-1)

The serum level of KIM-1 in lead-intoxicated rats was significantly increased ($P < 0.05$) compared with the control group. Co-administration of quercetin with lead significantly reduced the elevation of serum KIM-1 concentration when compared with the lead-intoxicated group. No significant difference was observed between the control group and the lead + quercetin-treated group. The serum KIM-1 levels in the experimental groups are presented in Table 3.

Table 3: Concentration of Kidney Injury Molecule-1 (KIM-1), Mean $\pm$ SD (n = 5)

Group	Kidney Injury Molecule-1 (KIM-1) Level
Control	166.89 $\pm$ 32.12 ^C
Lead Acetate	1368.84 $\pm$ 108.44 ^A
Lead + Quercetin	548.22 $\pm$ 11.84 ^B
Quercetin	260.24 $\pm$ 11.54 ^C
LSD	117.91

Note. Values are Presented as Mean $\pm$ SD (n=5). Different Superscript Letters Indicate Statistically Significant Differences Among Groups ($p < 0.05$)

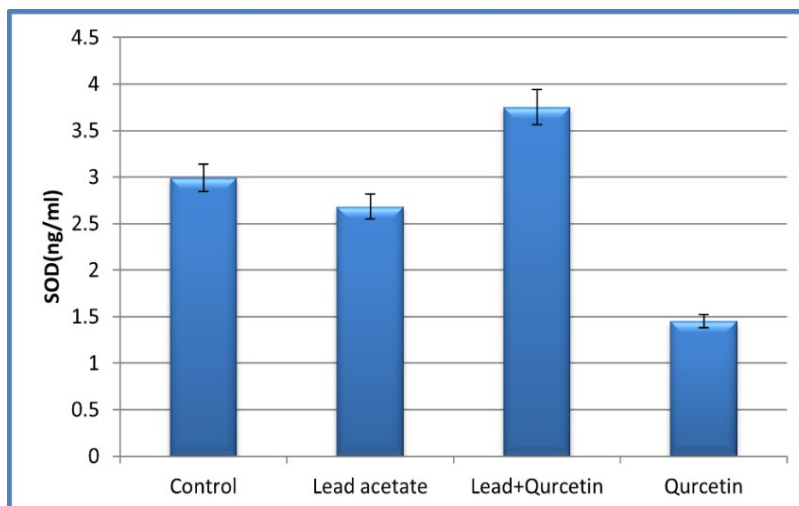
3.3 Superoxide Dismutase (SOD)

The serum activity of superoxide dismutase (SOD) in lead acetate-treated rats was significantly decreased ($P < 0.05$) compared with the control group. Co-administration of quercetin with lead significantly increased SOD activity when compared with the lead-intoxicated group. No significant difference was observed between the lead acetate-treated group and the quercetin-treated group. The serum SOD levels in the experimental groups are presented in Table 4.

Table 4: Concentration of Superoxide Dismutase (SOD) in Different Treatment Groups.

Group	Superoxide Dismutase (SOD) Levels
Control	2.99 $\pm$ 0.97 ^B
Lead Acetate	2.48 $\pm$ 0.20 ^B
Lead + Quercetin	3.75 $\pm$ 0.39 ^A
Quercetin	1.45 $\pm$ 0.13 ^C
LSD	1.12

Note. Values are Presented as Mean $\pm$ SD (N=5). Different Superscript Letters Indicate Statistically Significant Differences among Groups ($P < 0.05$)

**Figure 2:** Superoxide Dismutase (SOD) Levels Across Experimental Groups. Values are Mean $\pm$ SD ($p < 0.05$)

3.4 Malondialdehyde (MDA)

Malondialdehyde levels were significantly elevated in the lead acetate-treated group compared with all other groups ($P < 0.05$). Co-administration of quercetin with lead significantly reduced MDA levels compared with the lead-intoxicated group, although values remained significantly higher than those of the control group. Quercetin alone significantly reduced MDA levels compared with all other groups. The MDA levels in the experimental groups are presented in Table 5.

Table 5: Concentration of Malondialdehyde (MDA) in Different Treatment Groups

Group	Malondialdehyde (MDA)
Control	6.25 ± 0.60^c
Lead Acetate	60.99 ± 0.72^a
Lead + Quercetin	37.41 ± 0.91^b
Quercetin	2.96 ± 0.31^d
LSD	1.55

Note. Values are Presented as Mean $\pm$ SD ($n=5$). Different Superscript Letters Indicate Statistically Significant Differences Among Groups ($p < 0.05$)

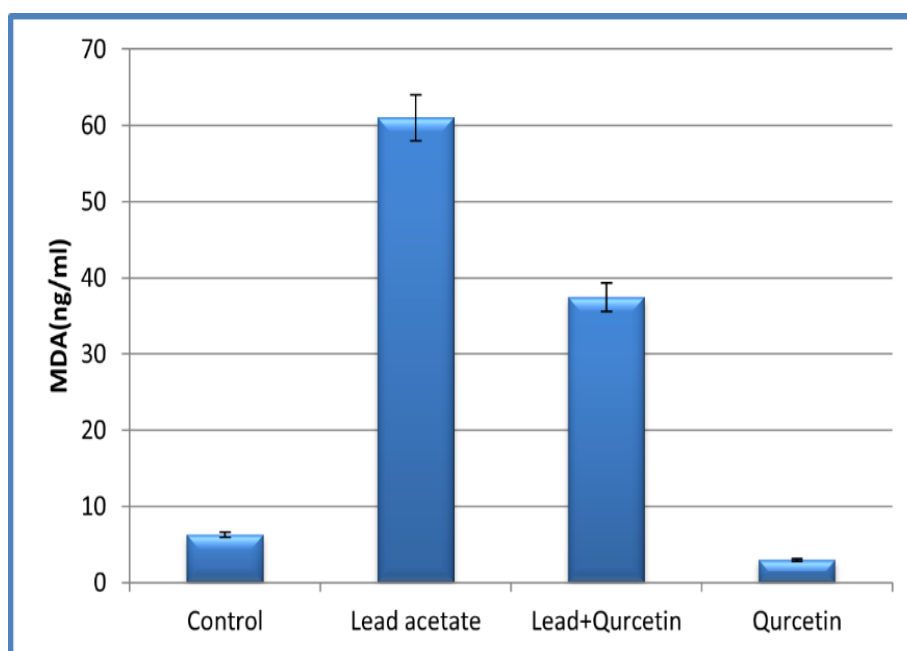


Figure 3: Malondialdehyde (MDA) Levels Across Experimental Groups. Values are Mean $\pm$ SD ($p < 0.05$)

3.5 Histopathological Findings of the Kidney (H&E Stain)

In the lead acetate-treated group, the kidney showed prominent pyknosis of tubular epithelial cells, accompanied by hyaline droplets within the tubular cytoplasm (Figure 4A). In addition, massive vacuolation of tubular epithelium with intranuclear inclusion in some proximal tubules was observed, accompanied by focal mononuclear cell infiltration (Figure 4C).

In the quercetin-treated group, kidney sections revealed obvious perivascular mononuclear cell cuffing with mild hyperemia of the glomerular capillaries, while renal tubules appeared largely intact (Figure 4D). Mild interstitial hemorrhage was observed in some sections, together with vascular congestion and dilation. Obvious cellular swelling with vacuolation of the tubular epithelium was also recorded (Figure 4B).

In the mixed lead acetate plus quercetin group, kidney sections showed hyperemia of the glomerular tuft capillaries with moderate mononuclear cell infiltration adjacent to swollen tubular epithelium (Figure 4F). Aggregation of mononuclear cells, occasionally admixed with neutrophils, was observed between swollen renal tubules (Figure 4H). Periglomerular mononuclear cell infiltration associated with cystic dilatation of some renal tubules was also detected (Figure 4E). Focal interstitial mononuclear cell infiltration between swollen tubules was evident in several sections.

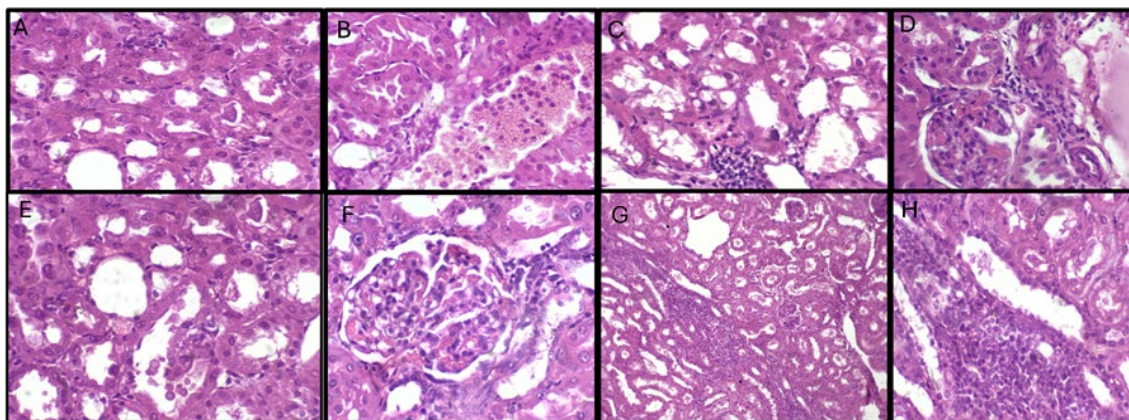


Figure 4: Histological Examination of Kidney Sections of Rats at 30 Days Post-Treatment (H&E Stain, ×40). (A) Kidney Section of a Rat from the Lead Acetate Group Showing Prominent Pyknosis of Tubular Epithelial Cells Associated with the Presence of Hyaline Droplets. (B) Kidney Section of a Rat from the Quercetin-Treated Group Showing Obvious Cellular Swelling of Tubular Epithelium with Vascular Congestion and Mild Interstitial Fibroplasia. (C) Kidney Section of a Rat from the Lead Acetate Group Showing Massive Vacuolation of Tubular Epithelium with Intranuclear Inclusion in Some Proximal Tubules and Focal Mononuclear Cell Infiltration. (D) Kidney Section of a Rat from the Quercetin-Treated Group Showing Obvious Perivascular Mononuclear Cell Cuffing with Mild Hyperemia of Glomerular Capillaries, While Renal Tubules Appeared Intact. (E) Kidney Section Showing Cystic Dilatation of Some Renal Tubules with Obvious Cytoplasmic Enlargement and the Presence of Several Crystalline Bodies. (F) Kidney Section of a Rat from the Mixed (Lead Acetate Plus Quercetin) Group Showing Hyperemia of Glomerular Tuft Capillaries with Mild Mononuclear Cell Infiltration, Associated with Periglomerular Mononuclear Cell Infiltration Between Swollen Tubules and Cystic Dilatation of Some Renal Tubules. (H) Kidney Section of a Rat from the Mixed Group Showing Marked Aggregation of Mononuclear Cells, Occasionally Admixed with Neutrophils, Between Swollen Renal Tubules.

4. Discussion

Lead is a ubiquitous environmental pollutant with no known physiological benefit, and exposure occurs through contaminated air, water, soil, and food, posing a significant public health risk to both humans and animal ([Balachandar et al., 2024](#)). The presented study investigated the toxic effects of lead acetate on male Wistar rats, focusing on its impact on renal toxicity. Concurrently, the study evaluated the potential protective effects of quercetin in lead exposed animals. We first examined the effect of lead exposure on the expression of the MT2 gene, which is responsible for the regulation of the metallothionein 2 (MT2) protein. metallothionein 2 protein, is a member of a family of low molecular weight, cysteine-rich proteins that bind to heavy metals, protecting cells from toxicity and oxidative stress, and maintenance of metal ion homeostasis ([Yang et al., 2024](#)). Our finding revealed a 7.93-fold increase in metallothionein 2 (MT2) gene expression, suggesting an increase in MT2 protein production in the lead-exposed group compared with the control group. This finding is consistent with previous studies showing a positive correlation between metallothionein induction and increased heavy-metal burden, including Pd²⁺. Induction of MT2 expression has been shown to increase severalfold in response to various heavy metals or oxidative stress, including Pb exposure ([Chen et al., 2014](#); [Yamada & Koizumi, 1991](#); [Yu et al., 2009](#)). The upregulation of MT2 is a molecular-level response to lead exposure, aimed at detoxifying and protecting cells from the toxic effects of lead acetate. The mechanism underlying the interaction between lead and MT2 has been suggested to involve MT2 binding to lead ions to form a protein-lead complex and the reduction of their intracellular levels ([GoERING, 1993](#); [Wong et al., 2017](#)). In contrast, the group administrated quercetin alone showed a downregulation of MT2 gene expression 0.67-fold in comparison to control group, such finding suggesting the reduced MT2 expression may reflect a lower requirement for metallothionein-mediated defense due to the antioxidant and free radical-scavenging properties of quercetin ([Soudani et al., 2019](#)), which are known to reduce basal oxidative stress (BOS) levels. Similar findings were in experimental models showing that MT expression is linked to oxidative and metal-induced stress rather than to antioxidant supplementation per se ([Gulcin, 2020](#); [Jomova et al., 2024](#); [Zhu et al., 2017](#)). In the lead–quercetin group, MT2 gene expression was higher than in the control group but lower than in the lead-only group, suggesting a modulatory rather than synergistic effect. This pattern may be attributed to quercetin's ability to reduce lead-induced oxidative stress, thereby attenuating MT2 induction relative to lead exposure alone. However, quercetin did not abolish the effect of lead on MT2 activation; rather, it partially mitigated it by reducing oxidative stress and lipid peroxidation. A similar pattern has been reported previously, in which co-administration of quercetin with cadmium increased metallothionein expression compared

with control animals but failed to prevent tissue injury (Soudani et al., 2019). The primary mechanism of lead toxicity is oxidative stress, whereby lead disrupts the balance between reactive oxygen species (ROS) and antioxidant system, resulting in cellular damage, lipid peroxidation, DNA damage, and dysfunction of major organs (Jafarzadeh et al., 2022). In the present study, the biochemical analysis of oxidative stress biomarkers, including malondialdehyde (MDA) and Superoxide dismutase (SOD), was performed. Our results revealed that MDA levels were significantly elevated in the lead acetate-treated group compared with all other groups ($P < 0.05$), suggesting increased lipid peroxidation and oxidative stress, indicating damage to cell membranes and loss of cellular function as a consequence of lead toxicity. These results are in agreement with previous studies where reports similar findings (Nawfal & Al-Okaily, 2022; Salman & Shwaish, 2024; Shirazinia et al., 2021; Sutaria et al., 2022; Velaga et al., 2014). While Co-administration of quercetin with lead acetate significantly reduced MDA levels compared with the lead acetate group; however, this reduction only partially mitigated the toxic effects of lead. These findings are supported by previous studies reporting the antioxidant properties of quercetin, which acts through scavenging reactive oxygen species (ROS). The antioxidant activity of quercetin is attributed to its active phenolic hydroxyl groups and conjugated double bonds (Nguyen & Bhattacharya, 2022). In addition, the B-ring of natural flavonoids represents the main active site responsible for antioxidant activity and ROS scavenging (Chen et al., 2023). Interestingly, the level of MDA in quercetin only group showed a significant reduction compared with the control group suggesting modulatory effect on oxidative status through its antioxidant activity (Al-Sammarae, 2025; Khalaf & Salih, 2023; Mohammed & Al-Hayany, 2020; Nawfal et al., 2024; Remigante et al., 2022; Xu et al., 2019). The investigation of effect of lead acetate on SOD levels was carried out and results showed that there was no significant reduction in SOD levels after 30 days of exposure in comparison with the control group. Such finding may interpreted by the fact the exposure to lead in sublethal dosing scenario is time dependent, where the lead required time to replacement of Cu, Zn cofactors, and thiol binding subsequently lowering SOD levels which reported in previous studies (Nawfal et al., 2024). Moreover, co-administered lead acetate and quercetin group showed significant increase in SOD levels, while, in quercetin group showed significant reduction SOD comparable with other groups (Ramezani & Monikh, 2017; Xu et al., 2019).

The investigation of the effect of lead acetate on SOD activity revealed no significant reduction in SOD levels after 30 days of exposure compared with the control group. This finding may be attributed to the time-dependent nature of lead-induced oxidative toxicity, as sublethal exposure requires a longer duration to disrupt SOD function through displacement of essential Cu and Zn cofactors and binding to sulfhydryl groups, ultimately leading to enzymatic inhibition as reported in previous studies. In contrast, co-administration of lead acetate with quercetin resulted in a significant increase in SOD activity, indicating a protective antioxidant effect of quercetin against lead-induced oxidative stress. Interestingly, SOD levels in the quercetin-only group revealed a significant reduction compared with the control group, suggesting a modulatory effect of quercetin on SOD activity. This reduction may reduce the oxidative burden due to its antioxidant and direct free-radical scavenging properties, thereby bolstering endogenous antioxidant capacity (Aghababaei & Hadidi, 2023; Cizmarova et al., 2023; Qi et al., 2022).

The kidney is the primary target of lead toxic effect because its role in excretion of lead. In our study we investigate the effect of lead exposure on the Kidney Injury Molecule-1, a type I cell membrane glycoprotein and mucin-containing molecule that upregulate significantly in acute and chronic kidney disease due to tubule-interstitial damage (Hussein et al., 2021). KIM-1 level significantly elevated in lead-intoxicated group in comparison with control group, indicates significant kidney injury caused by lead. Lead acetate is known to induce nephrotoxicity, causing damage to the renal tubules (Sudjarwo et al., 2017). This damage leads to an increase in KIM-1 expression (Ichimura et al., 2004). In co-administrated quercetin and lead group showed a significant reduce in KIM-1 levels suggest that quercetin has a protective effect against lead-induced kidney injury (Zeng et al., 2023). Quercetin is a flavonoid with antioxidant and anti-inflammatory properties that can help alleviate renal toxicity, apoptosis, fibrosis, and inflammation (Zeng et al., 2023). While in quercetin-only Group there was no significant changes in KIM-1 levels in comparison with control group. Quercetin has been suggested that it may exert protective effects against acute against injury (AKI) through various mechanisms (Liu et al., 2010). However, due to the diverse etiology of AKI and the variability in animal models used, there is still a significant gap between experimental models and clinical pathology (Rui et al., 2022).

The Histological examination of renal tissue showed different histological changes. In the lead treated group, nuclear pyknosis was observed in the epithelial cells accompanied by hyaline droplets and cellular necrosis, which indicates tubular epithelial injury, particularly affecting proximal tubules also vacuolar and cloudy swelling in renal tubule epithelial cells, tubular dilation, interstitial inflammatory cells with hemorrhage and glomerulus's hypercellularity, which attributed to partial excretion of lead through the kidney and oxidative damage of lead induced generation of reactive oxygen species. Hyaline droplets in the tubular cytoplasm have been described as a response to changes in protein handling and stress to the tubular cells in nephrotoxic conditions (Sato et al., 2005). In contrast, the quercetin group at 30 days showed mainly vascular and perivascular changes, including mild glomerular hemorrhage and limited mononuclear cell involvement, while the tubular architecture remained largely preserved. This pattern indicates the absence of obvious tubular injury at this

stage. Comparable observations have been described in quercetin-treated rats, where renal morphology was generally maintained despite the presence of mild vascular or inflammatory alterations (Almaghrabi, 2015; Gomes et al., 2014). In the mixed lead plus quercetin group at 30 days, glomerular hyperemia, moderate mononuclear cell infiltration, tubular epithelial swelling, and focal interstitial inflammation were still evident, indicating that renal injury and inflammatory changes persisted despite co-treatment. Similar studies have reported that quercetin can attenuate, but not fully prevent, lead-induced renal damage, with residual inflammatory infiltration and tubular alterations frequently observed during early or sub-chronic exposure periods (Al-Omair et al., 2017; Awad & Al-Okaily, 2023; Liu et al., 2012).

Collectively, these findings support the concept that quercetin confers partial nephroprotection against lead-induced renal injury, reducing lesion severity while not fully restoring normal renal histology at this stage of exposure.

5. Conclusion

Lead acetate caused a clear renal toxicity in the animal model, shown by increased KIM 1 and MDA, altered SOD activity, marked MT2 upregulation, and consistent histopathological injury. Quercetin reduced oxidative stress, lowered KIM 1, moderated MT2 expression, and lessened kidney injury. Overall, these results support oxidative stress mediated nephrotoxicity from lead and indicate that quercetin provides partial renal protection during sub chronic exposure.

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