

Protective Effects of Vitamin C and L-Carnitine on Moxifloxacin-Induced Nephrotoxicity in Rats

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ABSTRACT: Moxifloxacin is an essential clinically relevant fluoroquinolone antibiotic that is employed against a great variety of bacterial infections. Nevertheless, its use in clinical practice is linked to nephrotoxicity that is a severe adverse outcome that involves oxidative stress pathways. This paper sought to compare the ameliorative property of two strong antioxidants, Vitamin C and L-Carnitine, to moxifloxacin induced renal injury on a male albino rat model. The rat population was randomly divided into four groups of ten (i.e. a control group, a group treated with moxifloxacin (80 mg/kg), a group treated with moxifloxacin and Vitamin C (500 mg/kg) and a group treated with moxifloxacin and L-Carnitine (600 mg/kg). All therapies were taken in the form of gavage every day and in 30 days. To evaluate the renal damage, the serum urea and creatinine levels were measured, and kidney tissues were examined histopathologically to observe structural changes in tissues. The findings revealed that the serum levels of urea and creatinine were highly increased in moxifloxacin treated rats in isolation of the control group and signified poor kidney functioning. Histopathological analysis showed severe renal injury, such as shrinkage of the glomeruli, tubular necrosis, inflammation of the tissue by cells and cytoarchitectural degeneration. Inflammation and cellular injury were measured using systematic histopathological scoring of tissue sections to measure glomerular integrity, extent tubular necrosis, intensity of inflammatory infiltration and general structural preservation. On the other hand, the serum urea and creatinine levels and the histopathological injury scores in groups co-treated with Vitamin C or L-Carnitine were significantly lower and the levels were much lower as well. The glomerular and tubular organization of the kidney tissues of antioxidant-treated groups was better and the inflammation and cellular damage were significantly lower. This paper proves that moxifloxacin causes acute nephrotoxicity, and the process occurs via oxidative stress. Vitamin C or L-Carnitine co-administration has a significant effect in curing renal biochemical dysfunction and histopathological damage. The results indicate the possibility of the clinical use of antioxidant supplementation as a preventive measure against nephropathy induced by moxifloxacin.

Keywords: L-Carnitine, Moxifloxacin, Nephrotoxicity, Oxidative Stress, Vitamin C



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1. INTRODUCTION

Moxifloxacin is a fourth-generation antibiotic that is fundamentally required in the treatment of different bacterial infections because of its extended-spectrum important and potency [1]. Its clinical usefulness could be, however, compromised by its adverse effects of which drug induced nephrotoxicity is a significant concern [2]. Kidneys in particular are susceptible to toxic damage because of the high blood perfusion rate and the important concentration and excretion of xenobiotics. The primary avenue of the necrosis of the kidney induced by moxifloxacin is supposed to be the occurrence of oxidative stress in which the surplus generation of reactive oxygen species (ROS) overpowers the natural supply of the antioxidants in the kidney [3]. The process triggers widespread renal cellular injury in a variety of oxidative processes, including membrane lipid peroxidation, protein oxidation and DNA oxidative modification, which culminates in tubular necrosis, interstitial nephritis, and progressive renal dysfunction. [4, 5].

Oxidative stress agents, which produce surplus reactive oxygen species (ROS), are the major mediators of moxifloxacin-induced nephrotoxicity in renal tubular cells [6]. The structure of fluoroquinolone contributes to the chelation of vital metal ions, in particular magnesium and iron, which in turn induce mitochondrial dysfunction and ROS production in the high-energy setting of renal tubules [7]. These ROS target several cellular targets at the same time:

oxidation of lipid peroxidation affects membrane integrity, oxidation of proteins disrupts enzyme activity and structural proteins, and oxidative alteration of the DNA leads to genomic instability [8]. These molecular damages exceed the capacity of cellular antioxidant defense mechanisms, such as superoxide dismutase, catalase, and glutathione peroxidase, resulting in significant loss of cellular glutathione and vitamin C stocks [8]. The end result of this oxidative cascade is cellular dropout tubular necrosis with loss of brush border, cytoplasmic eosinophilia, and interstitial nephritis with inflammatory cell infiltration and eventually has a clinical consequence of renal dysfunction due to increased serum creatinine and urea concentrations [8, 9].

In a setting of centrality to oxidative stress in the nephrotoxicity of moxifloxacin, it follows that antioxidant supplementation is a logical preventive approach. Vitamin C (ascorbic acid), a strong water-soluble antioxidant, directly reacts with hydroxyl radical, superoxide anions, and other reactive species (ROS) produced during the metabolism of moxifloxacin, which prevents live cell membrane lipid peroxidation and maintains tubular integrity of the kidneys [8]. Vitamin C also restores the other antioxidants e.g., vitamin E and glutathione and enhances the total antioxidant defense mechanism and prevents antioxidant injury caused by fluoroquinolone [10]. The complementary protective actions of L-Carnitine are stabilizing mitochondrial membranes, β -oxidation of fatty acids to stabilize cellular energy homeostasis, and the Nrf2/Keap1 antioxidant signaling pathway, which increases the expression of endogenous antioxidant enzymes [11]. Also, L-carnitine suppresses the formation of mitochondrial ROS at its origin by enhancing efficiency of the electron transport chain and inhibiting mitochondrial permeability transition, which is especially important in the renal proximal tubules that are metabolically active [12]. Latest research illustrates that administration of either vitamin C or L-carnitine concomitantly with moxifloxacin is very much effective in diminishing hepatotoxicity and oxidative injury indicators, which enumerate on similar protective powers against nephrotoxicity [13]. Although the nephrotoxic effects of moxifloxacin have been acknowledged, there is still very little to effective use of clinical approaches to mitigate drug-induced renal injury. Thus, the hypothesis of the given study is that co-administration of either vitamin C or L-carnitine will play a significant role in reducing the biochemical and histopathological indicators of moxifloxacin-induced renal damages in a rat model.

Since oxidative stress is at the center of moxifloxacin nephrotoxicity, antioxidant supplementation is a plausible preventive approach to the condition [5,14]. Vitamin C (ascorbic acid), an effective water-soluble antioxidant, is a direct scavenger of hydroxyl radicals, superoxide anions and other ROS that are produced during the metabolism of moxifloxacin and prevents cellular membrane lipid peroxidation, and maintains renal tubular integrity [6,15,16]. As well, vitamin C also restores other antioxidants like vitamin E and glutathione, increasing the total antioxidant defense response and preventing oxidative damage caused by fluoroquinolone [15,16,17]. L-Carnitine demonstrates complementary protective systems involving stabilization of mitochondrial membranes, promoting fatty acid 2-oxidation to guarantee energy homeostasis in the cell and Nrf2/Keap1 antioxidant signaling pathway, which increases the expression of endogenous antioxidant enzymes [11,18,19,20]. Moreover, L-carnitine decreases the production of ROS in the mitochondrion by increasing the efficiency of electron transport chains and reducing mitochondrial permeability transition, which is especially significant in the renal proximal tubules of high metabolic activity [11,19, 20]. Recent reports indicate that the concomitant use of either vitamin C or L-carnitine and moxifloxacin can greatly reduce the effects of hepatotoxicity and oxidative damage, implying the same point of protection against nephrotoxicity [21,22].

Although the nephrotoxicity of moxifloxacin is well-established and the role of oxidative stress in its pathogenesis has been recognized, there is a major gap in knowledge on how to prevent it in clinical practice [23,24]. Although antioxidants have demonstrated potential on the alleviation of drug toxicity in different organs, there is paucity of studies that specifically analyzes the protective effect of vitamin C and L-carnitine against the moxifloxacin induced renal toxicity [6,25]. The given gap is especially worrying considering the prevalent clinical application of moxifloxacin and that there are no standard prophylactic practices of preventing nephrotoxicity among at-risk patients [2,24]. Thus, the purpose of this study was to assess the ameliorative properties of vitamin C and L-carnitine in comparison with nephrotoxicity caused by moxifloxacin in a rat model. This objective was accomplished by a thorough measuring of the biochemical indices of kidney function i.e. serum levels of urea and creatinine in conjunction with detailed histopathological study of kidney tissues to describe structural damage and measure the protective potential of these antioxidants at cell and tissue levels [23,15].

2. MATERIALS AND METHODS

2.1 MOXIFLOXACIN PREPARATION

Moxifloxacin (pharmaceutical grade) was acquired in Scilife Pharma, Pakistan. The drug was made by dissolving the right amount in a normal physiological saline (0.9% NaCl, which was bought in The Nile.co, Egypt) to get a final concentration of 80 mg/kg body weight. Daily fresh dosing solutions were made with the help of a magnetic stirrer (Etec, Japan) in room temperature to ensure full dissolution. The solution was thoroughly mixed for approximately 10 minutes. Prepared solutions were used immediately for oral administration via gavage.

2.2 VITAMIN C AND L-CARNITINE PREPARATION

Vitamin C (L-ascorbic acid) was purchased from a USA supplier in powder form. Fresh dosing solutions of vitamin C were prepared daily by dissolving the appropriate amount in physiological normal saline (0.9% NaCl) to achieve a final concentration of 500 mg/kg body weight using a magnetic stirrer (Etec, Japan). The solution was prepared immediately before administration to prevent oxidative degradation.

L-Carnitine was obtained from a commercial supplier in powder form. Dosing solutions were prepared daily by dissolving L-carnitine in physiological normal saline (0.9% NaCl) to achieve a final concentration of 600 mg/kg body weight. All solutions were mixed thoroughly using a magnetic stirrer (Etec, Japan) for approximately 10 minutes and used fresh for administration.

2.3 EXPERIMENTAL ANIMALS AND ANIMAL CARE

Forty adult male albino Wistar rats, aged between 10 and 14 weeks with body weights ranging from 200 to 230 grams, were used in this experimental study. The animals were housed in standard plastic boxes (China) in the Science Laboratory of the College of Pure Sciences at Wasit University, Kut, Iraq. A controlled environment was ensured in the housing conditions where the temperature was 22-25 °C, adequate AC was provided and light/dark cycle was 12 hours. During the duration of the experiment all the animals were fed on standard pellets and given tap water ad libitum. An acclimatization process was administered to the animals before the initiation of the experimental procedures to reduce the effects of stress in physiological differences. All experimental protocols were conducted in accordance with the guidelines for the care and use of laboratory animals [26].

2.4 EXPERIMENTAL DESIGN AND TREATMENT PROTOCOL

This study was conducted in the Science Laboratory of the College of Pure Sciences at Wasit University during the period from October 19, 2024 to November 19, 2024. After the acclimatization period, the forty rats were randomly allocated into four experimental groups (n=10 per group):

- Group 2 (Moxifloxacin Group): Administered moxifloxacin at a dose of 80 mg/kg body weight daily via oral gavage for 30 consecutive days. This dose was selected based on previous studies demonstrating nephrotoxic effects in rodent models [26].
- Group 3 (Moxifloxacin + Vitamin C Group): Administered moxifloxacin (80 mg/kg) together with vitamin C (500 mg/kg body weight) simultaneously via oral gavage daily for 30 days.
- Group 4 (Moxifloxacin + L-Carnitine Group): Administered moxifloxacin (80 mg/kg) together with L-carnitine (600 mg/kg body weight) simultaneously via oral gavage daily for 30 days.

All treatments were administered once daily via oral gavage using a stainless steel gavage needle (HBG, China) for a duration of 30 consecutive days. The animals were put under observation during the experimental time, and the general health, behavioral changes, and body weight were monitored.

2.5 BLOOD COLLECTION AND SERUM PREPARATION

All experimental animals had blood samples taken at the end of the 30-day treatment period. Before the blood was drawn, the rats were not fasted. Using a disposable plastic syringe (5 ml, HBG, China), approximately 1.5–2 ml (or 5 ml, depending on some procedures) of blood was drawn straight from the heart via cardiac puncture. Following the animals' anaesthesia, the cardiac puncture was carried out to enable direct collection from the site of the puncture. Following collection, the blood samples were promptly placed in sterile, anticoagulant-free gel tubes (ALS, Japan) and left to clot for 15 to 20 minutes at room temperature (or 30 to 60 minutes, depending on certain protocols). To extract the serum, the clotted blood samples were centrifuged in a chilled centrifuge (Kottermann, Germany) for 10 to 15 minutes at 3000 rpm. Using a micropipette, the clear serum (roughly 250–500 µL) was carefully aspirated and then transferred into sterile, labelled Eppendorf tubes (2 ml, HBG, England). Prior to biochemical analysis, serum samples were kept in a refrigerator (Media, China) at -20°C. All ensuing biochemical analyses used undiluted serum, and samples were examined without additional dilution or concentration.

2.6 BIOCHEMICAL ANALYSIS OF RENAL FUNCTION MARKERS

The Mindray BS-430 automated clinical chemistry analyser (China) and commercially available diagnostic kits were used to measure the concentrations of serum urea and creatinine, which are biochemical indicators of renal function. Samples of frozen serum were brought to room temperature and gently vortexed prior to analysis.

Serum Urea: The urease-based enzymatic colorimetric method was used to measure urea. Urea is hydrolysed by the urease enzyme to produce ammonia, which undergoes a sequence of coupled reactions to produce a coloured product. The colour intensity is directly proportional to the serum's urea concentration, and the absorbance is measured photometrically.

Serum Creatinine: The Jaffe's kinetic alkaline picrate method, which is based on the formation of a coloured creatinine-picric acid complex when creatinine reacts with picric acid in an alkaline medium, was used to measure creatinine. The colour intensity is proportional to the creatinine concentration, and the absorbance is measured at particular wavelengths (490-510 nm).

Using the Mindray BS-430 analyser, all biochemical analyses were carried out in accordance with the manufacturer's instructions. Every parameter depended on particular enzymatic reactions that produced colour shifts that could be photometrically measured at particular wavelengths. Throughout the analysis, quality control was upheld. Both urea and creatinine results were reported as mg/dl.

2.7 TISSUE COLLECTION AND HISTOPATHOLOGICAL EXAMINATION

The animals were put to death under deep anaesthesia as soon as the blood was drawn. The liver and kidneys were quickly removed, the surrounding tissue was cut off, and cold physiological saline was used to rinse them. For 24 to 48 hours at room temperature, representative tissue samples from the liver and kidneys were immediately fixed in 10% neutral buffered formalin (Chemanol, Saudi Arabia) at a tissue-to-fixative ratio of at least 1:10 (v/v).

Tissue Processing:

The tissue samples were subjected to standard histological processing after fixation.

A. Washing: After fixation, samples were washed with running tap water for 30 minutes to remove excess formalin.

B. Dehydration: Tissues were dehydrated through a graded series of ascending ethanol concentrations (Merck, USA):

- 70% ethanol - 1 hour
- 80% ethanol - 1 hour
- 90% ethanol - 1 hour
- 100% ethanol - 1 hour (twice, fresh ethanol each time)

C. Clearing: Tissues were cleared in xylene (Merck, Germany) for 2 changes of 30 minutes each to remove alcohol and render tissue transparent.

D. Embedding: Samples were infiltrated with molten paraffin wax (Elabsience, China) at 58-60°C inside metal molds for 2 changes of 45 minutes each, then allowed to cool and solidify at room temperature.

E. Sectioning: Using a rotary microtome (Histo-line MRS3500, Italy), tissue sections were cut at 4-5 µm thickness and transferred to clean glass slides (Sail Brand, China) coated with adhesive such as albumin.

F. Mounting: Slides were placed in a water bath (Hot plate, Hysh1, Korea) at 40-45°C to flatten sections, then mounted on glass slides and dried in an oven (Mommert, Germany) at 40°C for at least one hour.

G. Staining - Hematoxylin and Eosin (H&E):

The standard H&E staining protocol was performed using an automated staining procedure with commercially available hematoxylin and eosin stains (Merck Company, UK) :

1. Deparaffinization: Xylene - 2 changes × 5 minutes each
2. Rehydration: Descending alcohol series (100%, 95%, 90%, 80%, 70%) - 2-3 minutes each
3. Rinsing in distilled water
4. Hematoxylin staining - 5-10 minutes (stains nuclei blue-purple)
5. Differentiation in 1% acid alcohol
6. Bluing in tap water
7. Eosin counterstaining - 1-2 minutes (stains cytoplasm pink-red)
8. Dehydration through ascending alcohols
9. Clearing in xylene
10. Mounting with DPX mounting medium (India) under glass coverslips

The stained sections were examined under a light microscope (MEJI, Japan) at various magnifications (×40, ×100, ×200, and ×400). The glomerular architecture, tubular integrity, interstitial changes, vascular congestion, inflammatory cell infiltration, cellular necrosis, and overall renal and hepatic cytoarchitecture were all evaluated histopathologically. An 8-megapixel digital camera was mounted on the microscope in specific regions to take representative photomicrographs of common histological alterations.

2.8 STATISTICAL ANALYSIS

All data were collected, organized, and entered for preliminary management. Software called SPSS (Statistical Package for Social Sciences) was used to conduct the statistical analysis. The mean ± standard error (SE) was used to express the quantitative data for the serum biochemical parameters (creatinine and urea).

An F-test and one-way analysis of variance (ANOVA) were used in the statistical analysis to ascertain the general differences between the four experimental groups. Fisher's Least Significant Difference (LSD) test was used to perform post-hoc multiple comparisons in order to pinpoint specific group differences when ANOVA showed significant differences between groups. For every analysis, a probability value of $p < 0.05$ was deemed statistically significant. Every statistical test had two tails.

The thorough approach that combines biochemical markers and histopathological examination, as well as the assessment of two antioxidants with different protective mechanisms, are some of this study's strong points.

It is necessary to recognise a few limitations, though. Dose-response analysis was not possible because the study only used one dose of moxifloxacin. The use of only male rats restricts direct extrapolation to human clinical scenarios and generalisability to both sexes. Mechanistic understanding is limited by the lack of direct measurements of oxidative stress biomarkers, such as malondialdehyde, glutathione, and antioxidant enzymes. Prior to clinical translation, future research should incorporate molecular analyses, both sexes, dose-escalation protocols, and validation in larger animal models.

3. RESULTS

3.1 BIOCHEMICAL FINDINGS

Renal function was significantly impaired in the moxifloxacin-treated group (G1), according to the biochemical analysis. Serum urea and creatinine levels were significantly higher ($p \leq 0.05$) in this group than in the control group, as indicated in Table 1. These increases were considerably reduced by concurrent vitamin C (G2) administration. The mean creatinine level of the L-Carnitine group (G3) was surprisingly higher than that of the control group, despite the fact that it also displayed lower urea levels. This finding warrants more discussion.

Table 1. - Serum Urea and Creatinine Levels in Different Experimental Groups.

Group	Urea (mg/dl)	Creatinine (mg/dl)
Control	40.20 ± 6.20	0.040 ± 0.00
G1 (Moxifloxacin)	55.40 ± 0.20	0.055 ± 0.02
G2 (Moxi + Vit C)	45.50 ± 0.60	0.030 ± 0.01
G3 (Moxi + L-Carnitine)	46.65 ± 2.15	0.110 ± 0.03

3.2 HISTOPATHOLOGICAL FINDINGS

The control group's kidneys showed normal histological structure. The renal corpuscles were undamaged and had Bowman's capsules and distinct glomeruli. Normal renal architecture was reflected by the clear lumina and normal cuboidal epithelium lining the proximal and distal convoluted tubules (Figures 1).

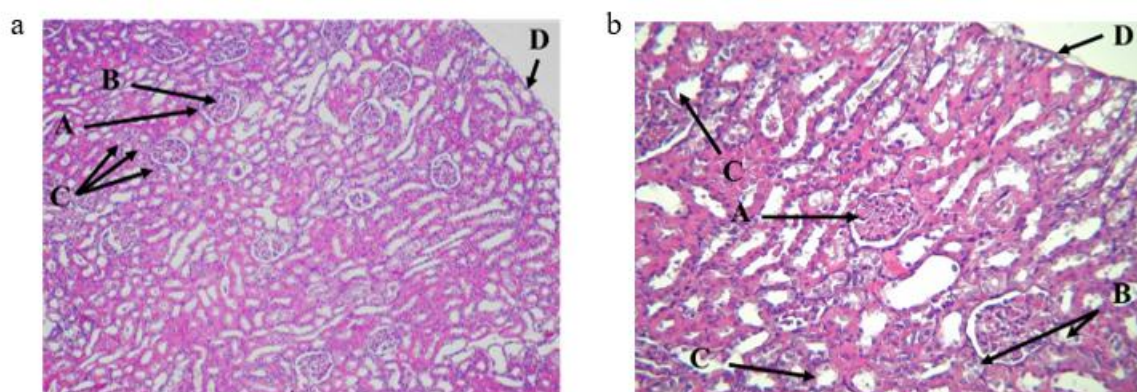


FIGURE 1. Normal Kidney Histological Architecture from Control Group. (a) Normal renal architecture which includes the outer kidney capsule (D), normal renal convoluted tubules (C), and an intact renal corpuscle (A) with its glomerulus (B) (100X H&E stain). (b) A higher magnification view that shows a normal glomerulus (A) and makes a clear distinction between the kidney capsule (D), which encloses the proximal (B) and distal (C) convoluted tubules.

Conversely, the kidneys of rats treated with moxifloxacin alone showed extensive and severe histopathological damage. There was a marked distortion of the renal cytoarchitecture, with hypercellularity and shrinkage of the glomeruli (Figure 2). The renal tubules exhibited widespread degenerative changes, including cloudy swelling, cytoplasmic vacuolation, and extensive necrosis, with cellular debris filling the tubular lumina (Figure 3). Congestion of blood vessels and infiltration of inflammatory cells in the interstitium were also prominent, alongside the accumulation of amyloid-like material in some tubules (Figures 4).

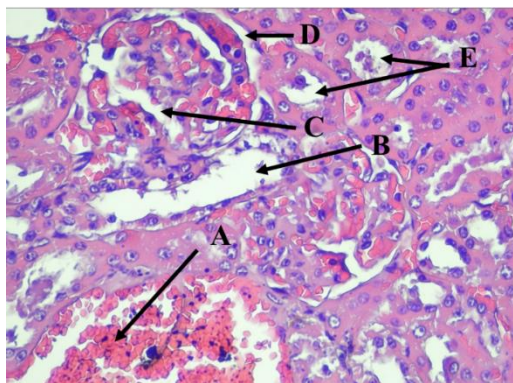


FIGURE 2. Moxifloxacin-Induced Nephrotoxicity in Rat Kidney. Kidney of adult male Rats effected with (moxifloxacin 80 mg/kg) noticed destruction of kidney tissue, increase of Congestion of blood vessels (A), renal tubules dilatation (B), destructure of glomerulus (C), increase of Bowman's spaces (D) & cellular depressing of tubular kidney (E) (H&E 100x).

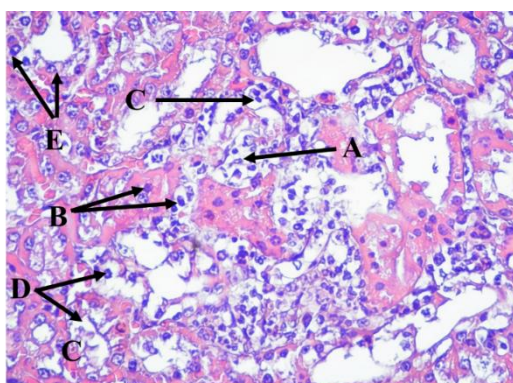


FIGURE 3. Severe Cellular Damage in Moxifloxacin-Treated Rat Kidney. Kidney of adult male rats affected with (moxifloxacin 80 mg/kg) appeared destructured of glomerulus (A), highly cellular pyknotic (B), highly cellular Karyohexis (C), separation of endothelial cells (D), & cellular cloudy degeneration (E) (H&E 200X).

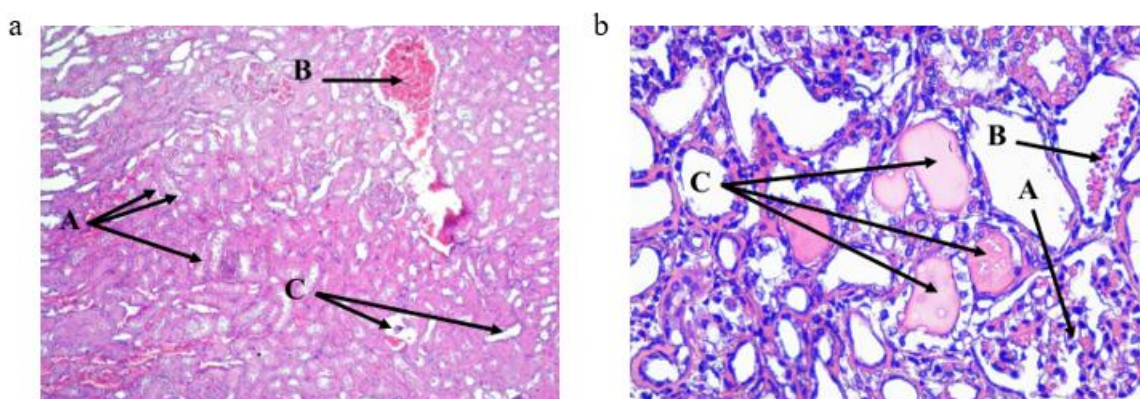


FIGURE 4. Severe Histopathological Damage in Moxifloxacin-Treated Rat Kidney. Severe histopathological damage in the kidneys of rats treated with moxifloxacin (80 mg/kg). (a) reveals widespread tissue destruction, including endothelial cell proliferation (A), vascular congestion (B), and dilation of the tubular lumina (C). (40X H&E stain). (b) a high-magnification view of the damage, showing a destructured glomerulus (A), congestion (B), and the aggregation of amyloid-like material within the renal tubules (C) (400X H&E stain).

The co-administration of Vitamin C or L-Carnitine with moxifloxacin resulted in a remarkable restored of the renal architecture. In the Vitamin C group, the glomeruli appeared more intact, tubular degeneration was reduced, and there was minimal inflammatory infiltration (Figures 5). Similarly, the L-Carnitine group showed a substantial protective effect, with a near-normal appearance of the glomeruli and renal tubules and a marked reduction in necrotic and degenerative changes (Figures 6). Both antioxidant groups demonstrated a amelioration of the nephrotoxic effects of moxifloxacin.

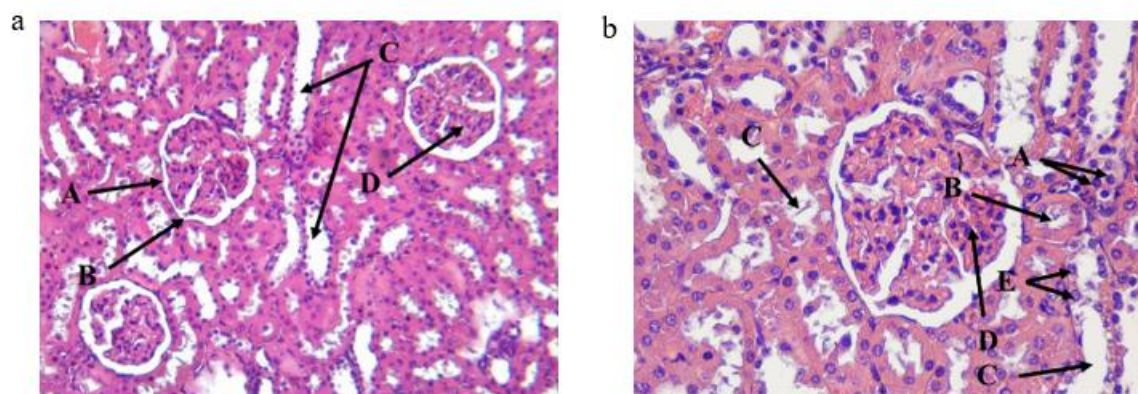


FIGURE 5. Nephroprotective Effect of Vitamin C Against Moxifloxacin-Induced Renal Damage.

Reno-protective effect of Vitamin C (500 mg/kg) against moxifloxacin-induced damage. (a) shows an improved renal architecture, with a more intact renal corpuscle (A), less distention of the glomerular space (B), reduced endothelial cell damage (C), and a near-normal sized glomerulus (D). (100X H&E stain). (b) provides a closer view, demonstrating a marked decrease in necrotic (A) and degenerated (B) cells, preserved renal tubules (C), a less-damaged glomerulus (D), and an overall increase in normal cells (E). (400X H&E stain).

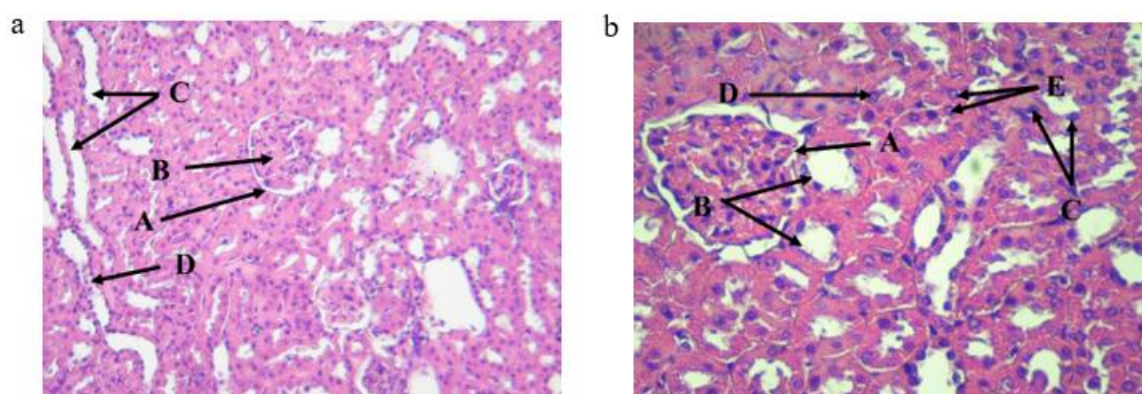


FIGURE 6. Nephroprotective Effect of L-Carnitine Against Moxifloxacin-Induced Renal Damage.

Reno-protective effect of L-Carnitine (600 mg/kg) against moxifloxacin-induced damage. (a) shows a decrease in overall tissue destruction, with less distention of Bowman's space (A), reduced glomerular shrinkage (B), better-preserved renal tubules (C), and less cellular debris (D). (100X H&E stain). (b) provides a more detailed view, revealing a near-normal glomerulus (A) and tubules (B), a marked decrease in pyknotic (C) and karyorrhectic (D) cells, and a notable increase in the population of healthy, normal cells (E). (200X H&E stain).

4. DISCUSSION

As evidenced by increased serum urea and creatinine levels as well as significant histopathological damage to kidney tissues, the results of this study clearly show that moxifloxacin causes significant nephrotoxicity [14]. The moxifloxacin-treated group's higher serum urea and creatinine levels suggest a lowered glomerular filtration rate and a compromised kidney's capacity to eliminate waste products from metabolism [14,23]. Severe histopathological changes, such as glomerular shrinkage with hypercellularity, widespread tubular necrosis with cytoplasmic vacuolation and cloudy swelling, inflammatory cell infiltration in the interstitium, and vascular congestion, are consistent with these biochemical changes. This injury pattern is in line with earlier findings showing fluoroquinolone-induced nephrotoxicity in both clinical and experimental settings through acute interstitial nephritis or crystal nephropathy [23,24].

4.1 OXIDATIVE STRESS MECHANISMS

The main mechanism by which moxifloxacin causes nephrotoxicity is oxidative stress, where the medication increases the generation of reactive oxygen species (ROS) to the point where the endogenous antioxidant defence systems of renal cells are overpowered [5,27]. In the high-energy environment of renal tubules, the fluoroquinolone structure promotes the chelation of essential metal ions, especially iron and magnesium, which in turn causes mitochondrial dysfunction and an excess of reactive oxygen species [1,24]. Lipid peroxidation damages membrane integrity, protein oxidation hinders enzymatic activity, and DNA oxidative modifications cause genomic instability, all of which contribute to tubular necrosis and interstitial nephritis [4,5]. This oxidative cascade depletes endogenous antioxidant defenses including superoxide dismutase, catalase, and glutathione peroxidase, leading to accumulation of oxidative damage that manifests as clinically significant renal dysfunction [3,5,14].

4.2 PROTECTIVE EFFECTS OF ANTIOXIDANTS

Significant nephroprotection was achieved by co-administering either vitamin C (500 mg/kg) or L-carnitine (600 mg/kg), which considerably reduced histopathological damage and biochemical indicators of renal dysfunction [6,15]. By directly scavenging hydroxyl radicals, superoxide anions, and other ROS produced by the metabolism of moxifloxacin, vitamin C, a strong water-soluble antioxidant, prevents lipid peroxidation of cellular membranes and maintains renal tubular integrity [27,19]. Furthermore, vitamin C increases the antioxidant defence capacity and guards against oxidative damage brought on by fluoroquinolones by regenerating other antioxidants like glutathione and vitamin E [6,15]. The effectiveness of this direct antioxidant mechanism in preventing cellular damage is demonstrated by the preserved glomerular and tubular architecture seen in the group that received vitamin C treatment [15].

Stabilising mitochondrial membranes, promoting fatty acid β -oxidation to preserve cellular energy homeostasis, and lowering mitochondrial ROS production at the source by increasing electron transport chain efficiency are all ways that L-carnitine demonstrates complementary protective mechanisms [18,19]. Additionally, it has been demonstrated that L-carnitine inhibits the mitochondrial permeability transition and activates antioxidant signalling pathways, both of which are crucial in the metabolically demanding renal proximal tubules [18,19]. The effectiveness of these mitochondrial-focused protective mechanisms is confirmed by the near-normal kidney architecture and decreased cellular necrosis preserved in the L-Carnitine co-treated group [19]. Future research is necessary because the L-Carnitine group's unexpectedly high mean serum creatinine level, despite positive histological results, could be due to individual animal variability, blood collection timing, or possible interference with creatinine measurement assays [18].

4.3 CLINICAL IMPLICATIONS AND STUDY LIMITATIONS

The potential clinical use of antioxidant supplementation as a preventive measure against fluoroquinolone-induced renal injury is highlighted by the effective reduction of moxifloxacin-induced nephrotoxicity by both vitamin C and L-carnitine [6,15,18]. These results are especially important for patients who need long-term fluoroquinolone treatment or who already have nephrotoxicity risk factors like diabetes, chronic kidney disease, or concurrent use of other nephrotoxic drugs [2,24]. Both antioxidants are good candidates for preventative use in clinical practice because they are widely accessible, reasonably priced, and well-tolerated supplements with proven safety profiles [6,7].

It is necessary to recognise a number of limitations. Dose-response evaluation was not possible because the study only used one dose of moxifloxacin (80 mg/kg) [23,25]. Generalisability to both sexes and direct extrapolation to human clinical scenarios are limited by the use of exclusively male rats [25]. Mechanistic depth is limited by the lack of direct measurements of oxidative stress biomarkers, such as malondialdehyde, glutathione, and antioxidant enzymes [4,5]. Dose-escalation protocols, both sexes, molecular analyses of inflammatory cytokines and oxidative stress markers, time-course assessments, and validation in larger animal models prior to clinical translation should all be included in future research [3,24].

5. CONCLUSION

This study shows that giving male albino rats 80 mg/kg of moxifloxacin for 30 days causes severe nephrotoxicity, which is manifested by much higher serum urea and creatinine levels as well as extensive histopathological damage, such as glomerular shrinkage, tubular necrosis, and inflammatory cell infiltration. These results demonstrate that the main mechanism of moxifloxacin-induced renal injury is oxidative stress-mediated mechanisms. Importantly, prophylactic co-administration of either L-Carnitine (600 mg/kg) or Vitamin C (500 mg/kg) resulted in significant nephroprotection, significantly reducing both structural damage and biochemical dysfunction through complementary antioxidant mechanisms: L-Carnitine stabilises mitochondria, while Vitamin C scavenges direct radicals.

These findings lend credence to the possible clinical use of antioxidant supplements as an affordable, easily accessible method of preventing fluoroquinolone-induced nephrotoxicity in patients who need prolonged antibiotic treatment, especially those who already have renal vulnerability. Given the protective effectiveness of both antioxidants, regular preventative use may improve patient safety while maintaining the therapeutic value of this crucial class of antibiotics. Future investigations should evaluate dose-response relationships, sex-specific responses, molecular mechanisms of protection, and ultimately translate these findings into clinical trials to establish evidence-based guidelines for antioxidant co-therapy during fluoroquinolone treatment.

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