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# Effect of Ciprofloxacin Administration on Gastric Histopathological Changes in Mice

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**Abstract**

Ciprofloxacin is a fluoroquinolone antibiotic widely used in clinical and veterinary practice. While effective against a broad range of bacterial infections, several studies have reported potential adverse effects on the gastrointestinal tract, particularly the gastric mucosa. This study aimed to evaluate the histopathological changes in the gastric mucosa of mice following ciprofloxacin administration at different doses. A total of 24 male mice were randomly divided into four groups: control, low-dose ciprofloxacin, moderate-dose ciprofloxacin, and high-dose ciprofloxacin. Treatment was administered orally for 14 days. Gastric tissues were collected and examined histologically using hematoxylin-eosin staining. Histopathological analysis revealed dose-dependent mucosal alterations. The control group showed intact gastric architecture, while the low-dose group exhibited mild epithelial erosion. The moderate-dose group presented with mucosal disruption and inflammatory infiltration, and the high-dose group demonstrated severe ulceration, edema, and mucosal thinning. These findings indicate progressive gastric injury with increasing ciprofloxacin exposure. Ciprofloxacin administration induces dose-dependent gastric mucosal injury in mice, consistent with fluoroquinolone-related gastrointestinal toxicity. Caution is warranted in prolonged or high-dose therapy, and further studies are needed to explore the underlying mechanisms and potential gastroprotective interventions.

**Keywords:** ciprofloxacin; gastric mucosa; histopathology; mice; fluoroquinolones.

**Abbreviations:** Ciprofloxacin (CFX); Reactive Oxygen Species (ROS); Tumor Necrosis Factor Alpha (TNF-α); Zonula Occludens-1 (ZO-1); Interleukin-1 Beta (IL-1β); Hematoxylin and Eosin (H&E); U.S. Food and Drug Administration (FDA); Standard Deviation (SD); Analysis of Variance (ANOVA); Statistical Package for the Social Sciences (SPSS)

## INTRODUCTION

Ciprofloxacin is a widely used fluoroquinolone antibiotic, appreciated for its broad-spectrum activity and favorable pharmacokinetics. While its systemic safety profile is well established, less is known about its localized effects on gastric tissue, particularly following prolonged administration. A recent study in albino rats demonstrated that prolonged oral ciprofloxacin administration (12.5 mg/kg/day for 60 days) led to significant alterations in gastric mucosal architecture, as observed via immunohistochemistry and scanning electron microscopy. The study also reported elevated TNF-α expression and reduced levels of several *Helicobacter pylori* immunoglobulins—suggesting mucosal inflammation and immune modulation (El-Masry et al., 2021).

Although not focused solely on the stomach, broader drug-induced gastric injury is clinically significant. A 2025 review highlighted that various medications—including antibiotics—can cause distinct histopathological changes in gastric mucosa, emphasizing the need for histological awareness when evaluating drug safety (Gastroenterological Endoscopy Society, 2025).

Meanwhile, in a mouse model, ciprofloxacin—especially when combined with other therapies—has been shown to affect intestinal pathology and the gut microbiota post-irradiation, hinting at its potential to disrupt gastrointestinal tissue integrity and microbial balance (Horseman et al., 2024).

The widespread use of ciprofloxacin in both clinical and veterinary practice makes it one of the most frequently prescribed antibiotics. While its therapeutic benefits are clear, increasing reports of adverse reactions have drawn attention to the need for deeper evaluation of its safety profile, particularly regarding effects on the gastrointestinal system (El-Masry et al., 2021). Among

the organs potentially affected, the stomach plays a central role not only in digestion but also as a protective barrier against pathogens and chemical insults. Any alteration to gastric mucosal integrity may therefore have far-reaching implications for overall gastrointestinal health.

Drug-induced gastric injury remains a clinically relevant concern. Recent findings emphasize that antibiotics and other commonly prescribed medications can lead to characteristic mucosal changes, such as erosion, ulceration, and inflammatory infiltration (Gastroenterological Endoscopy Society, 2025). However, experimental data linking ciprofloxacin directly to gastric histopathology remain limited. Most research to date has focused on intestinal microbiota or systemic toxicity rather than localized gastric effects (Horseman et al., 2024). This creates a significant knowledge gap, especially considering that ciprofloxacin is often administered over long treatment courses or in combination with other drugs that may amplify mucosal damage.

Evaluating ciprofloxacin's impact in mice (*Mus musculus*) is particularly relevant. Mice are widely used in biomedical research due to their genetic similarity to humans, cost-effectiveness, and well-characterized physiology. Studying gastric histopathological changes in this model allows for detailed analysis of subtle alterations—such as epithelial disruption, inflammatory cell infiltration, or mucosal thinning—that may not be evident in clinical observations alone. Such insights can bridge preclinical findings with human outcomes, contributing to a more comprehensive understanding of ciprofloxacin's gastrointestinal safety.

Another dimension of urgency relates to the broader issue of fluoroquinolone safety. Beyond contributing to antimicrobial resistance, fluoroquinolones have been associated with serious adverse effects, including tendon rupture, neurotoxicity, and cardiotoxicity, resulting in multiple FDA safety communications (U.S. Food and Drug Administration, 2018). If ciprofloxacin also contributes to gastric mucosal injury, the risk–benefit balance must be reconsidered, particularly in patients with pre-existing gastrointestinal disorders.

Taken together, the investigation of ciprofloxacin's effects on gastric histopathology in mice is both scientifically relevant and clinically significant. It will provide new insights into the safety of a widely used antibiotic, inform rational prescribing practices, and support preventive strategies to minimize drug-induced gastric injury.

## MATERIALS AND METHODS

### Research Design

This study employed an experimental laboratory design with a post-test only control group approach. The aim was to compare gastric histopathological features in mice receiving ciprofloxacin administration with those of untreated controls.

### Experimental Animals

A total of 24 healthy male mice (*Mus musculus*), aged 8–10 weeks and weighing 25–30 g, were obtained from an accredited animal breeding facility. All animals were acclimatized for one week under standard laboratory conditions (12-hour light/dark cycle, room temperature 22–25 °C, relative humidity 50–60%), with free access to standard pellet diet and water *ad libitum*.

### Grouping and Treatment

Mice were randomly divided into four groups (n = 6 per group):

a. Group I (Control): received distilled water orally.
b. Group II (Low-dose Ciprofloxacin): received ciprofloxacin 10 mg/kg/day orally.
c. Group III (Moderate-dose Ciprofloxacin): received ciprofloxacin 20 mg/kg/day orally.
d. Group IV (High-dose Ciprofloxacin): received ciprofloxacin 40 mg/kg/day orally.

Ciprofloxacin doses were adapted from previous experimental studies with modifications to reflect clinically relevant ranges (El-Masry et al., 2021; Horseman et al., 2024). The treatment was administered once daily via oral gavage for 14 consecutive days.

### Ethical Approval

All experimental protocols were reviewed and approved by the Institutional Animal Ethics Committee. Animal handling followed the international guidelines for the care and use of laboratory animals (NIH Publication No. 85-23, revised 2011).

### Tissue Collection

At the end of the treatment period, animals were fasted overnight and sacrificed under ketamine-xylazine anesthesia. The stomachs were excised, opened along the greater curvature, and rinsed with normal saline to remove gastric contents. Tissue samples from the gastric body were fixed in 10% neutral buffered formalin for histological analysis.

### Histopathological Examination

Fixed tissues were processed using standard paraffin-embedding techniques. Sections of 5 µm thickness were stained with hematoxylin and eosin (H&E). Histopathological evaluation was performed under a light microscope (400× magnification).

### Histopathological Scoring

Gastric mucosal alterations were assessed semi-quantitatively using a modified scoring system, including parameters such as:

a. Epithelial erosion/ulceration (0 = absent, 1 = mild, 2 = moderate, 3 = severe)
b. Inflammatory cell infiltration (0 = absent, 1 = mild, 2 = moderate, 3 = severe)
c. Edema and vascular congestion (0 = absent, 1 = mild, 2 = moderate, 3 = severe)
d. Mucosal thickness changes (normal, thinned, or thickened)

Two independent pathologists blinded to the treatment groups performed the evaluations to minimize observer bias.

### Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Differences between groups were analyzed using one-way ANOVA followed by Tukey's post hoc test. A *p*-value < 0.05 was considered statistically significant. Statistical analyses were conducted using SPSS version 26.

## RESULTS AND DISCUSSION

### Result

### General Observations

Throughout the experimental period, no mortality was observed in any of the groups. Mice in the ciprofloxacin-treated groups (especially at moderate and high doses) exhibited reduced activity and occasionally experienced mild diarrhea compared to the control group. Body weight changes were not significantly different among groups ($p > 0.05$) (Table 1).

**Table 1.** Histopathological scores of gastric tissue in different treatment groups.

| Group | Erosion/Ulceration (0–3) | Inflammation (0–3) | Vascular Congestion (0–3) | Mucosal Thickness Alteration (0–3) | Total Score (0–12) |
|---|---|---|---|---|---|
| Control | 0.2 ± 0.4 | 0.3 ± 0.5 | 0.2 ± 0.4 | 0.1 ± 0.3 | 0.8 ± 0.7 |
| Low-dose (10 mg/kg) | 0.8 ± 0.7 | 1.0 ± 0.6 | 0.9 ± 0.6 | 0.7 ± 0.5 | 3.4 ± 1.1* |
| Moderate-dose (20 mg/kg) | 1.7 ± 0.8 | 1.9 ± 0.7 | 1.6 ± 0.8 | 1.5 ± 0.6 | 6.7 ± 1.5** |
| High-dose (40 mg/kg) | 2.8 ± 0.4 | 2.7 ± 0.5 | 2.6 ± 0.5 | 2.5 ± 0.5 | 10.6 ± 1.2*** |

*Significantly different from control ($p < 0.05$).
**Highly significant vs. control ($p < 0.01$).***Very highly significant vs. control ($p < 0.001$).

### Histopathological Findings

Histological examination of the gastric tissues revealed normal mucosal architecture in the control group, characterised by an intact epithelial lining and no evidence of inflammation or ulceration. In contrast, mice administered ciprofloxacin exhibited dose-dependent alterations in gastric histopathology.

a. Low-dose ciprofloxacin (10 mg/kg): Mild epithelial erosion and minimal inflammatory cell infiltration were observed in some samples.
b. Moderate-dose ciprofloxacin (20 mg/kg): Moderate epithelial disruption, inflammatory infiltration in the lamina propria, and vascular congestion were evident.
c. High-dose ciprofloxacin (40 mg/kg): Severe epithelial erosion/ulceration, marked inflammatory infiltration, edema, and thinning of mucosal layers were consistently observed.

Representative microphotographs of H&E-stained sections demonstrated progressive mucosal damage corresponding to increasing ciprofloxacin doses (Figure 1).

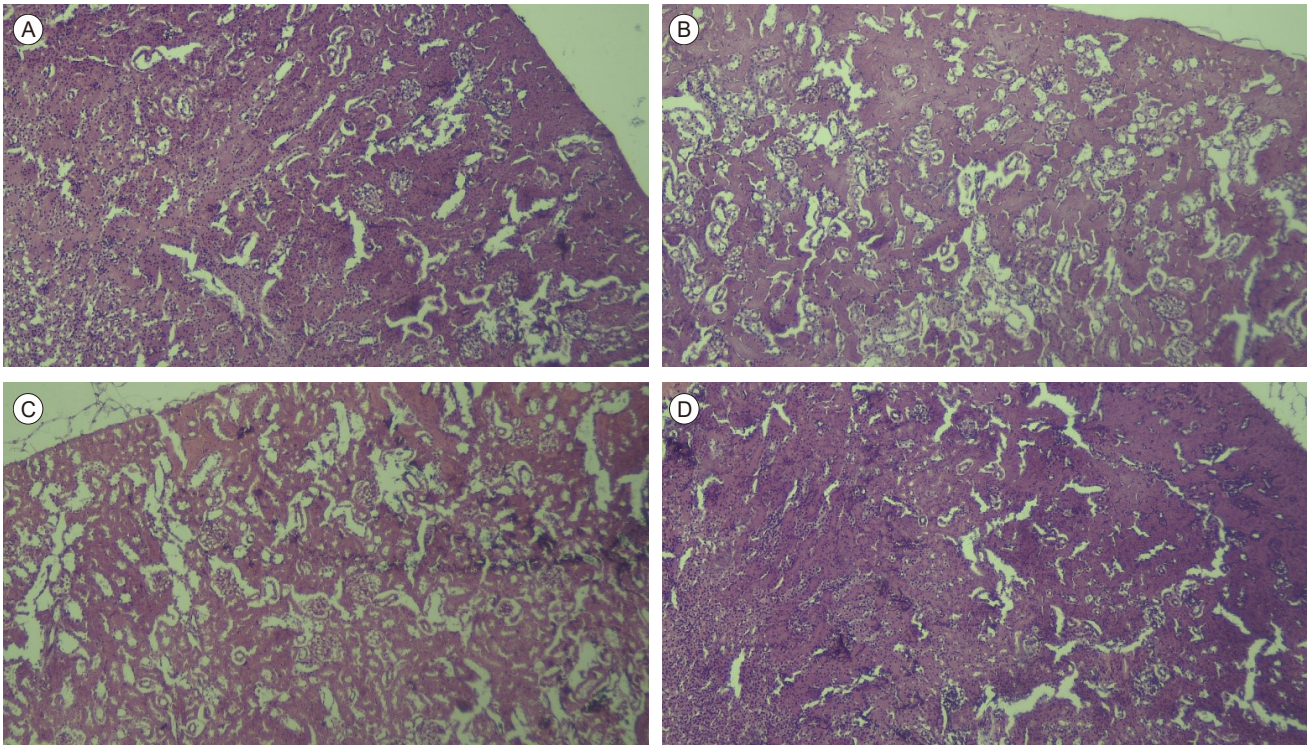


**Figure 1.** Histopathological scores of gastric tissue in different treatment groups. A. Group I (Control): received distilled water orally, B. Group II (Low-dose Ciprofloxacin): received ciprofloxacin 10 mg/kg/day orally, C. Group III (Moderate-dose Ciprofloxacin): received ciprofloxacin 20 mg/kg/day orally, and D. Group IV (High-dose Ciprofloxacin): received ciprofloxacin 40 mg/kg/day orally.

## Discussion

This study demonstrated that ciprofloxacin administration induced dose-dependent gastric mucosal alterations in mice. The control group exhibited normal gastric architecture, while low-dose ciprofloxacin caused mild epithelial erosion. Moderate doses resulted in mucosal disruption with inflammatory infiltration, and high doses produced severe ulceration, edema, and mucosal thinning (Islam et al., 2024). These findings suggest that repeated administration of ciprofloxacin may compromise gastric mucosal integrity (Ge et al., 2020).

Our results are in agreement with prior research in rodents. El-Masry, El-Baz, and Ibrahim (2021) reported that prolonged ciprofloxacin exposure in rats resulted in epithelial disruption, vascular congestion, necrosis, and elevated TNF-α expression. These histopathological changes mirror the patterns we observed, suggesting that ciprofloxacin exerts direct toxic effects on gastric mucosa. Furthermore, Horseman et al. (2024) showed that ciprofloxacin, particularly when combined with supportive agents, altered intestinal structure and microbiota following irradiation in mice. While that study focused on the intestine, the disruption of mucosal architecture and immune balance supports our observations of the gastric vulnerability (Horseman et al., 2024).

The mechanisms underlying ciprofloxacin-induced mucosal damage are multifactorial. Evidence suggests that fluoroquinolones may induce oxidative stress, generating reactive oxygen species (ROS) that impair epithelial cell integrity and trigger inflammatory cascades (El-Masry et al., 2021). Ge, Mao, Cai, and Huang (2020) demonstrated that ciprofloxacin impaired gut barrier integrity in mice by reducing tight junction proteins (ZO-1 and occludin), increasing IL-1β expression, and promoting epithelial apoptosis. These mechanisms, although observed in the intestine, are likely relevant to gastric mucosa as well (Ibrahim et al., 2021; Çulpan, 2022).

Another contributing factor may be antibiotic-induced dysbiosis. Ciprofloxacin has been shown to disrupt microbial diversity and host–microbiota interactions (Ge et al., 2020), which can compromise mucosal defense and immune regulation. Disruption of gastric or intestinal microbiota may thus predispose to mucosal injury (Xie et al., 2024). Additionally, fluoroquinolones are known to interfere with collagen metabolism, a condition associated with tendon rupture and vascular complications (U.S. Food and Drug Administration, 2018). Weakening of collagenous structures within the gastric wall may contribute to mucosal thinning and, in severe cases, gastrointestinal perforation (Wang et al., 2023).

From a clinical standpoint, these findings have important implications (Mojoyinola & Ogundipe, 2023). Drug-induced gastric injury remains a recognized adverse effect of several medication classes, including NSAIDs, corticosteroids, and antibiotics (Arafat et al., 2021; Nawaz, 2021). A recent review highlighted that antibiotics such as fluoroquinolones can cause distinct

gastric lesions characterized by erosion, ulceration, and inflammatory cell infiltration (Liu et al., 2025; Zhu, 2020). Given ciprofloxacin's widespread use in human and veterinary medicine, the potential for gastric toxicity warrants closer evaluation. Patients with pre-existing gastrointestinal conditions, prolonged therapy, or concomitant use of other mucosa-damaging drugs may be particularly vulnerable (Liu et al., 2024).

Our study also emphasizes the utility of mice as an experimental model. Their genetic similarity to humans and controlled environment make them suitable for preclinical toxicology. The dose-dependent progression observed here provides a framework for future studies exploring protective strategies, such as antioxidants, probiotics, or proton pump inhibitors.

This study has several limitations. First, the treatment period was limited to 14 days; longer exposure might reveal cumulative or chronic effects. Second, we focused exclusively on histopathology, without assessing biochemical markers such as malondialdehyde or cytokine levels that could clarify molecular mechanisms. Third, we did not analyze gastric microbiota, which may mediate some of the observed effects. Future studies should extend treatment duration, incorporate biochemical and microbiota analyses, and evaluate potential gastroprotective interventions (Hou, 2025).

In summary, our findings demonstrate that ciprofloxacin administration induces dose-dependent gastric mucosal injury in mice, consistent with previous evidence of fluoroquinolone toxicity in gastrointestinal tissues. These results underscore the importance of cautious use, particularly in prolonged or high-dose therapy, and highlight the need for preventive measures to mitigate drug-induced gastric damage.

## CONCLUSIONS

This study demonstrated that ciprofloxacin administration induced dose-dependent gastric mucosal injury in mice. Histopathological changes ranged from mild epithelial erosion at low doses to severe ulceration and mucosal thinning at high doses. These findings are consistent with previous evidence of fluoroquinolone-induced gastrointestinal toxicity, highlighting oxidative stress, inflammation, epithelial barrier disruption, and microbiota imbalance as possible mechanisms. Given ciprofloxacin's wide clinical use, the results emphasize the need for cautious prescription, particularly for prolonged or high-dose therapy, and the importance of monitoring patients with pre-existing gastric conditions. Future studies should evaluate biochemical markers, microbiota changes, and potential gastroprotective interventions to understand better and mitigate ciprofloxacin-induced gastric injury.

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