



Original Article

**Tissue accumulation and pathological impacts of enrofloxacin and ciprofloxacin antibiotics in albino Rats**

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**ABSTRACT**

The presence of antibiotic residues in biological systems has become a growing concern due to their potential health risks in both humans and animals. Antibiotics commonly used in veterinary medicine, persist in animal tissues, blood, and even the environment long after administration. This study investigated the tissue residue levels and histopathological effects of Enrofloxacin and Ciprofloxacin on the heart and muscles of albino rats. Fifteen (15) female albino rats (weighing 150 to 200 g) were obtained from a certified animal breeding center in the University of Ibadan, Oyo State. The heart and muscle samples were tested for antibiotic residues using HPLC (High-Performance Liquid Chromatography). The fixed tissue samples (Heart and Muscle) were processed through standard histological procedures. Findings revealed that the heart tissues of control rats showed only mild damage, while rats treated with enrofloxacin and ciprofloxacin showed serious heart damage like necrosis, inflammation, and bleeding, especially in 0.25µg/g to 0.45µg/g higher-dose groups. The skin of control rats appeared healthy, but rats treated with the drugs showed signs of inflammation such as immune cell buildup and blood vessel issues. Ciprofloxacin generally accumulated at 400mg/l and 120mg/l respectively in skeletal muscle, while Enrofloxacin was more concentrated in the heart. In conclusion, enrofloxacin and ciprofloxacin, though effective antibiotics, can cause significant tissue damage when not properly administered. The heart and skin tissues of albino rats demonstrated visible histopathological changes, highlighting the need for careful dosage control and responsible antibiotic use. Based on the findings, it was therefore recommended that enrofloxacin and ciprofloxacin should be administered only under strict veterinary guidance to avoid heart tissue damage. Regular histological checks should be carried out in animals treated with fluoroquinolones (the active ingredients in enrofloxacin and ciprofloxacin) to monitor cardiac health.

**Keywords:** Tissue residue, Histopathology, Enrofloxacin, Ciprofloxacin, Heart, Muscle and albino rats

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**INTRODUCTION**

Antibiotics are medicines used to fight infections caused by bacteria. They work by either killing the bacteria or stopping them from growing. In veterinary medicine, antibiotics are often given to animals to treat different infections and

illnesses. These drugs help sick animals recover faster and prevent the spread of disease among animals in farms. They are also used to keep animals healthy, especially in places where many animals are raised together [1 & 17]. Two antibiotics that are often used in animals are Enrofloxacin and Ciprofloxacin.

These two belong to a group of antibiotics called fluoroquinolones. Fluoroquinolones are strong antibiotics that work against a wide range of bacteria [2]. Enrofloxacin is mainly used in animals, while Ciprofloxacin is a product formed when Enrofloxacin breaks down inside the animal's body. Both drugs are important in treating serious infections in animals like chickens, cows, and pigs [3 & 18].

Enrofloxacin is a strong antibiotic used mostly in animals. It is part of the fluoroquinolone group of antibiotics, which fight bacteria by stopping them from making DNA. Without DNA, bacteria cannot grow or survive. Enrofloxacin is used a lot in farm animals like chickens, cows, and pigs to treat infections such as respiratory or digestive diseases. After treatment, the animal's body does not remove the drug immediately. Some of the Enrofloxacin stays in the meat, liver, or other tissues. These leftovers are called drug residues, and they can be harmful if the meat is eaten before the drug clears from the body [3]. Ciprofloxacin is another powerful antibiotic. It is closely related to Enrofloxacin and also belongs to the fluoroquinolone family. While Enrofloxacin is mostly for animals, Ciprofloxacin is used in both animals and humans. It works by stopping bacteria from copying their DNA, so the bacteria die [4]. Ciprofloxacin is used to treat many infections in animals, like skin infections, urinary infections, and respiratory problems. It is sometimes found in the tissues of chickens, cows, and other animals after treatment. When this happens, it means residues of the drug are still in the body, which may not be safe for people who eat the meat [5 & 19].

Histological study means looking at tissues under a microscope to see if there is any damage. Sometimes, even if we

cannot see problems with our eyes, the tissue may have changes like cell death, swelling, or bleeding. Enrofloxacin and Ciprofloxacin are known to cause changes in tissues when used for a long time or in high doses [6]. A study by [4] showed that mice exposed to high levels of Ciprofloxacin had changes in their tissues, including the liver and kidneys. Similar damage can happen in the heart and muscles. Damage in the heart may lead to problems in how the heart pumps blood. Damage in muscles may reduce the quality of meat and may also be harmful to people who eat it. According to [8], giving Enrofloxacin with other veterinary drugs affected the liver of rats, making the cells weak and changing their structure. This proves that antibiotics, when not properly used, can harm body organs. In Uganda, [3] studied chicken meat from the market and found that some of the samples had drug residues higher than the safety limit. These residues were from Enrofloxacin and its by-product Ciprofloxacin. This is risky because people eating this meat are consuming antibiotics without knowing. Over time, this can lead to drug resistance. [1] explained that although Enrofloxacin is good at killing bacteria, it can also damage the cells of animals. It can interfere with the DNA of cells and lead to cell death. This is one reason why tissue damage happens after using these drugs.

Albino rats are commonly used in scientific studies because they are easy to handle and their body systems work in ways similar to humans and other animals. Studying rats gives us an idea of how the drugs will act in farm animals and even in humans. The results help in making rules about how long to wait after giving antibiotics before the animal's meat or organs can be eaten [3]. Antibiotics like Enrofloxacin and Ciprofloxacin are useful drugs in veterinary medicine. They help treat and

prevent infections in farm animals. But when these drugs are used carelessly, they can leave residues in the tissues of animals. These residues may be harmful to people who eat the meat or organs. The heart and muscle are important tissues to study because they are commonly eaten. This study, like others before, shows that antibiotic residues can damage tissues and may not be safe for people. Using these drugs in a controlled way, and respecting withdrawal periods before animals are slaughtered, is very important. Government agencies, farmers, and health professionals must work together to make sure food is safe and healthy for everyone. Hence, this study therefore seeks to investigate tissue residue determination and histological study or hispatological effects of enrofloxacin and ciprofloxacin in the heart and muscle of albino rat.

## MATERIALS & METHODS

**Experimental Animals** Female albino rats aged 5–6 weeks and weighing 150–200g were purchased from a registered animal breeding unit at the University of Ibadan, Oyo State. They were housed in clean cages under controlled room temperature (22–25°C), with 12-hour light and dark cycles. The animals were allowed to acclimatise for one week before starting the experiment. They had free access to rat pellets and clean drinking water ad-libitum. The experiment followed ethical rules and were approved by the Animal Ethics Committee of the University of Ibadan.

### Animal Treatments

The 15 rats were divided randomly into three groups:

- Group A (Enrofloxacin-treated, n=5): received 10ml dose of Enrofloxacin orally.

- Group B (Ciprofloxacin-treated, n=5): received 10ml dose of Ciprofloxacin orally.
- Group C (Control, n=5): did not receive any antibiotic (they received distilled water).

### Drug Administration

Both antibiotics were given daily morning and afternoon – (8 hours) by oral gavage (using a feeding needle) for 7 days. The dosage was chosen based on earlier studies that looked at how these drugs act in the body. The control group received the same amount of clean water instead of the antibiotics.

### Collection and Processing of Tissue Samples

After 7 days, all the rats were painlessly sacrificed under light anesthesia. The heart and skeletal muscles were carefully removed. Parts of each organ were stored in clean containers for residue analysis, and the remaining parts were fixed in 10% formalin for histological (tissue structure) studies.

### Tissue Residue Analysis

The heart and muscle samples were tested for antibiotic residues using HPLC (High-Performance Liquid Chromatography) at concentration of 180mg to 400mg/100ml. This test helps check if any Enrofloxacin or Ciprofloxacin were accumulated in the organs after treatment. The amount of residue was compared between the groups.

### Histopathological Studies

After fixing the heart and muscle tissues in 10% formalin for at least 24 hours, the samples were taken through a step-by-step process. First, they were dehydrated by placing them in increasing levels of alcohol to remove water. Next, the tissues were cleared in xylene and then embedded in paraffin wax to make them

firm for slicing. Thin sections (5 microns thick) were cut using a rotary microtome, then placed on slides and stained with hematoxylin and eosin (H&E) to make the tissue parts visible. Finally, the stained tissue slides were observed under a light microscope to check for any damage or changes in the tissue caused by the antibiotics at the  $40\times 100$  magnification.

### Data Analysis

All results were calculated and reported as mean  $\pm$  standard deviation. Data was analyzed using SPSS software version 26. One-way ANOVA was used to check for differences between the groups.

## RESULTS

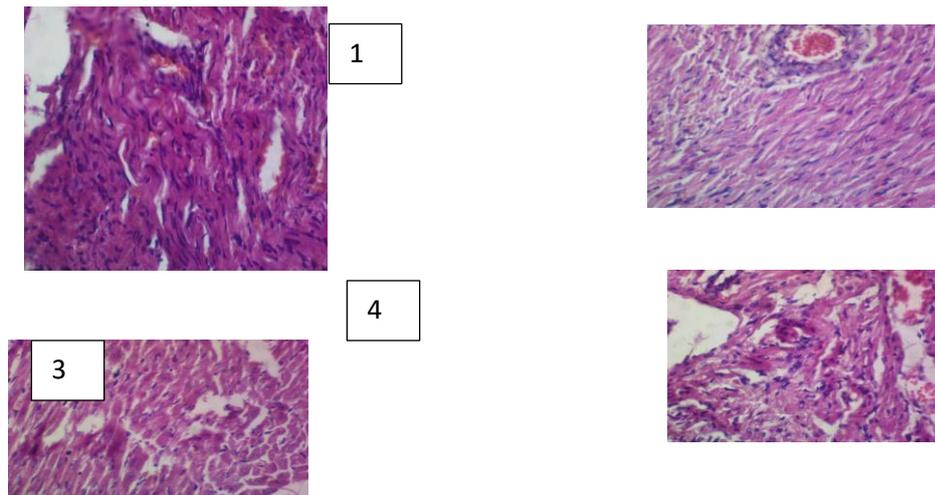
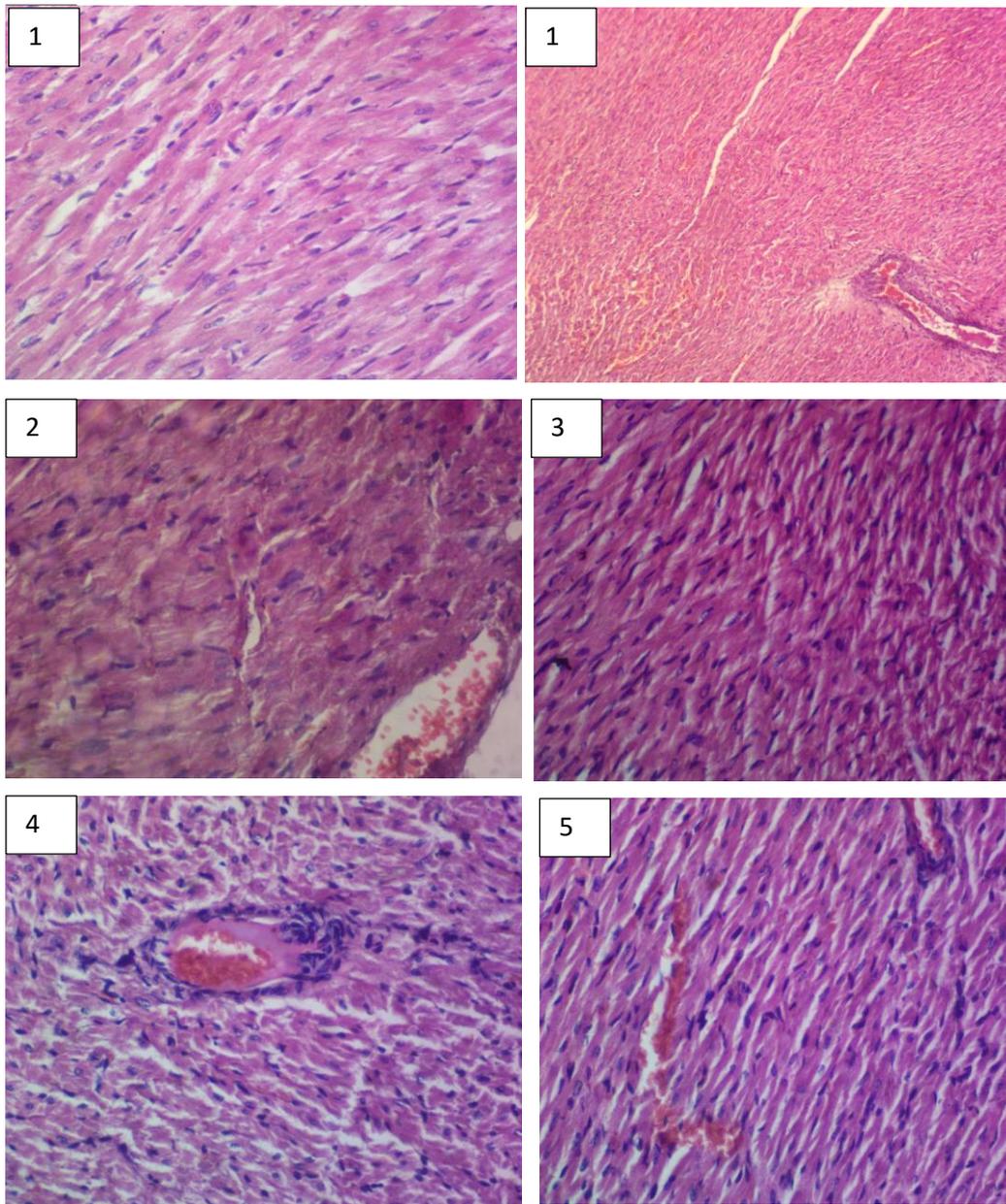


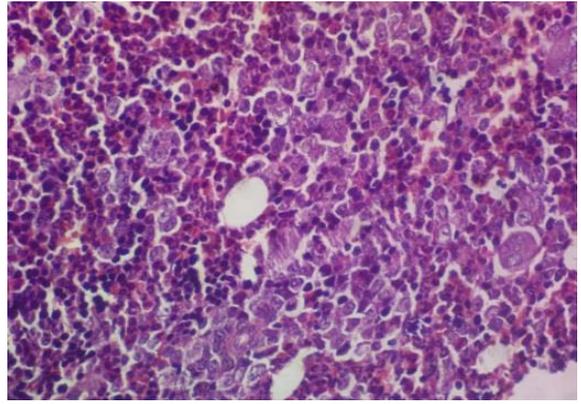
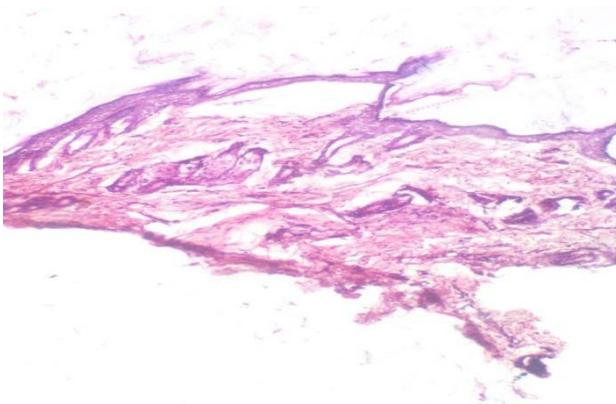
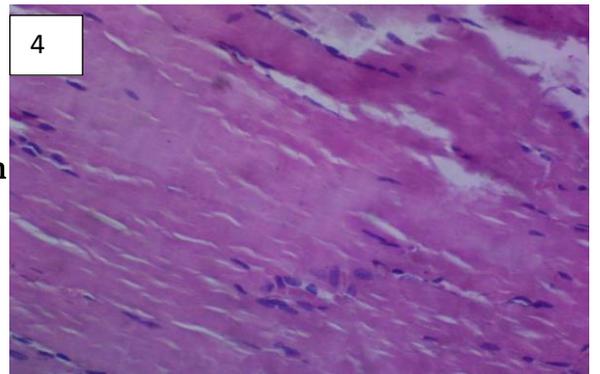
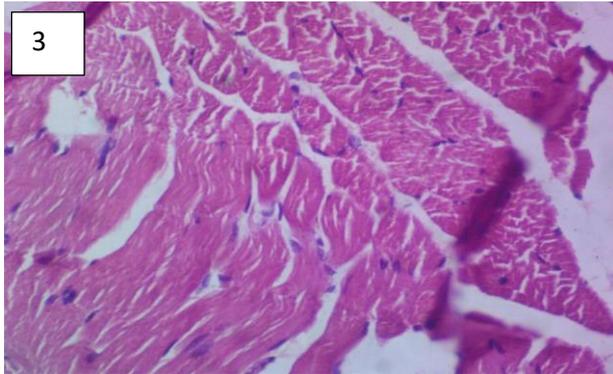
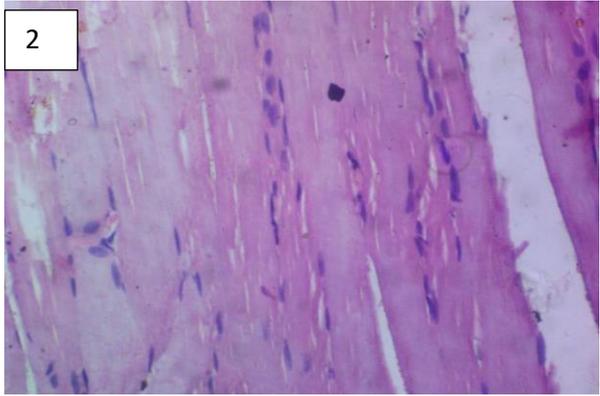
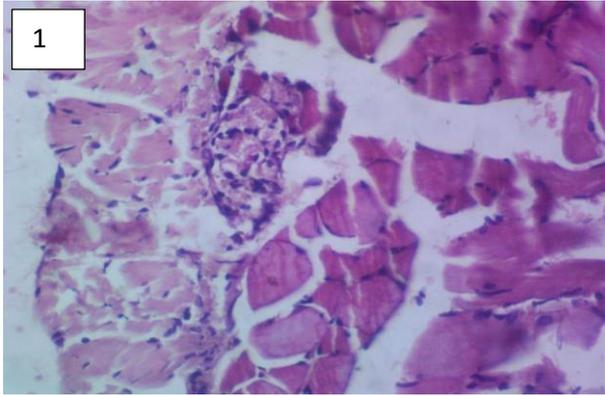
Figure 1: Different micrograph of the section of Heart & with control at  $40\times$  magnification

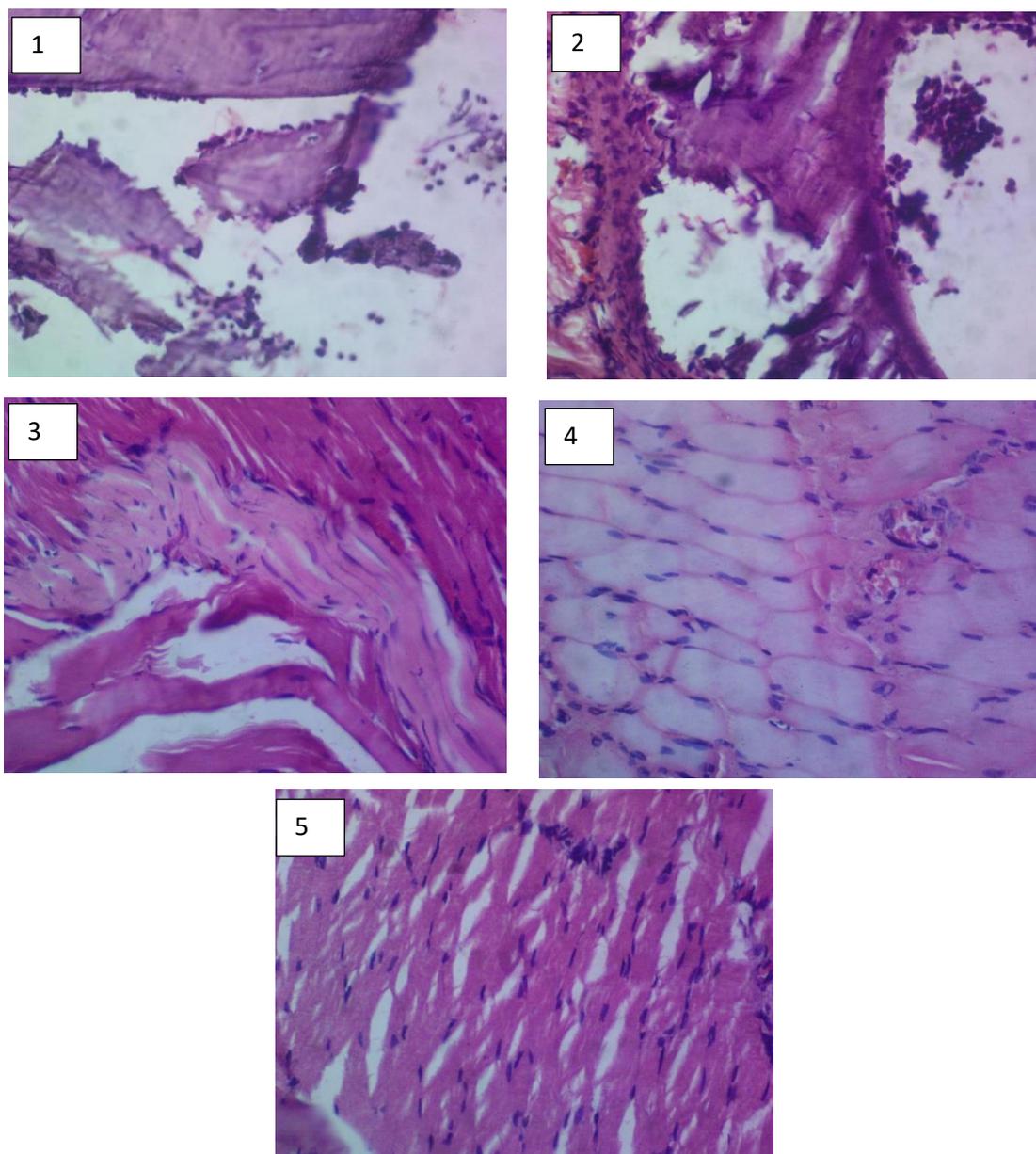
Figure 1 and 2 showed that control group rats showed myocardial alterations, with some rats presenting focal degeneration and congestion. Enrofloxacin (Group E) and Ciprofloxacin treatments resulted in more visible changes, such as myocardial necrosis, hypertrophy, inflammation (vasculitis), and hemorrhages, especially in groups E2–E5.

Results in figure 3 and 4 showed that skin from the controlled group was generally healthy, showing complete reepithelization and limited inflammatory changes. However, samples from Group E exhibited inflammatory responses including lymphocytic infiltration, capillary congestion, and vasculitis, particularly in E3 and E4



**Figure 2: Micrographs of different sections of Heat at x40 magnification**





**Figure 4: Different Photomicrographs of Skin section at x40, x100 Magnification respectively**

Result in Table 1 revealed the presence of residues of Enrofloxacin and Ciprofloxacin in the tissues of albino rats, particularly in the heart and skeletal muscle. The control group showed no detectable residues in either the heart or muscle tissues, confirming that the rats had no background drug contamination prior to the experiment. Rats treated with Enrofloxacin showed higher residue concentrations in the heart compared to skeletal muscle. The average concentration of Enrofloxacin Residual detected in the heart was  $1.85 \pm 0.22 \mu\text{g/g}$ , while the skeletal muscle recorded a lower value of  $0.97 \pm 0.18 \mu\text{g/g}$ . For Ciprofloxacin, the residue pattern was slightly different. The skeletal muscle showed a higher concentration of  $2.34 \pm 0.27 \mu\text{g/g}$ , while the heart recorded a lower concentration of  $1.28 \pm 0.20 \mu\text{g/g}$ .

Hence, Ciprofloxacin generally accumulated at higher levels in skeletal muscle, while Enrofloxacin was more concentrated in the heart.

Table 1: Levels of Tissue Residues of Enrofloxacin and Ciprofloxacin in the heart and muscle of Albino Rats

Group / Treatment	Tissue	Detected Residue ( $\mu\text{g/g}$ )
Control	Heart	ND (no residues detected)
Control	Muscle	ND (no residues detected)
Enrofloxacin (10 mg/kg)	Heart	1.85 $\pm$ 0.22
Enrofloxacin (10 mg/kg)	Muscle	0.97 $\pm$ 0.18
Ciprofloxacin (20 mg/kg)	Heart	1.28 $\pm$ 0.20
Ciprofloxacin (20 mg/kg)	Muscle	2.34 $\pm$ 0.27

Note: ND = Not Detected (below HPLC detection limit)

## DISCUSSION

The study showed that the heart tissues of controlled rats showed only mild damage probably due to stress. Rats treated with Enrofloxacin and Ciprofloxacin showed serious heart damage like necrosis, inflammation, and bleeding, especially at 250mg/L to 400mg/L higher-dose groups; which implies that these drugs may harm the heart by affecting blood vessels or causing stress in the cells. This finding aligns with the study of [8] who asserted that high doses of azithromycin caused severe heart tissue damage in rats, showing inflammation and cell death. It also aligns with [7] who found that enrofloxacin combined with other drugs resulted in high levels of liver enzymes and tissue congestion, suggesting similar toxic effects in vital organs like the heart. Similarly, [9] showed that ciprofloxacin caused damage to tissues in poultry, including shrinking of organs and damage to heart-like tissues. This finding is supported by the work of [10] who reported that fluoroquinolones may damage mammalian cells at high doses due to enzyme disruption. [11] also observed structural changes in heart tissue following fluoroquinolone treatment, including swelling and necrosis.

The study revealed that the skin of control rats appeared healthy, but rats treated with the drugs showed signs of

inflammation such as immune cell buildup and blood vessel issues; which implies that Enrofloxacin and Ciprofloxacin can cause skin irritation or deeper tissue reactions. This finding aligns with the study of [12] who asserted that fluoroquinolones can cause tissue inflammation and bleeding, especially in soft tissues, when used in high doses. Similarly, [9] reported visible signs of tissue damage in the breast muscle of chickens treated with ciprofloxacin, where nerves and fibers appeared inflamed and broken—suggesting a systemic reaction that could also affect the skin. This is supported by [13] who found that high doses of doxycycline caused inflammation and oxidative stress across multiple organs, indicating that antibiotic use may lead to immune cell buildup, including in surface tissues like skin. [14] also discovered that increased doses of a fungicide led to swelling and inflammation across organs, highlighting how chemical exposure can activate immune responses. The observation in this study aligns with the work of [15], who warned that misuse or overuse of enrofloxacin in animals can lead to harmful drug residues, which may cause tissue irritation including skin reactions.

The study revealed that ciprofloxacin generally accumulated at higher levels in skeletal muscle, while enrofloxacin was more concentrated in the heart; this implies that the two drugs have different

patterns of tissue distribution and affinity for certain organs. The higher concentration of ciprofloxacin in skeletal muscle indicates that the drug may bind strongly to muscle fibers, which is a concern because muscle is the main edible part of animals. This finding aligns with the study of [5] who reported that both enrofloxacin and ciprofloxacin residues were found in different parts of chicken meat, with ciprofloxacin showing higher accumulation in muscle tissue. Their study revealed that over 45% of the samples contained residue levels above the safe limit, which poses a significant risk to consumers. Similarly, [4] found that ciprofloxacin tends to remain in body tissues like the liver, kidney, muscles, and intestines after prolonged use. This supports the present finding that ciprofloxacin may persist in skeletal muscles, leading to harmful health effects if consumed by humans. [16] also stated that drug residues remain in organs like the liver, kidneys, heart, and muscles after treatment, which shows why withdrawal periods are crucial before animals are slaughtered for consumption.

### CONCLUSION

Enrofloxacin and Ciprofloxacin, though effective antibiotics, can cause significant tissue damage when not properly administered. The heart and skin tissues of albino rats demonstrated visible histopathological changes, highlighting the need for careful dosage control and responsible antibiotic use.

Based on the findings of this research, it was recommended that enrofloxacin and Ciprofloxacin should be administered only under strict veterinary guidance to avoid heart tissue damage. Lower and shorter-duration doses should be prioritized to reduce the risk of necrosis and bleeding in heart tissues. Alternative drugs with lower risks of skin tissue

reaction should be considered when inflammation is a concern. Ciprofloxacin use in food animals should be strictly regulated to prevent excessive residues in edible tissues. Enrofloxacin treatment should include proper withdrawal periods to reduce harmful residues in vital organs. Farmers and veterinarians should be trained on the safe and controlled use of veterinary antibiotics.

Enrofloxacin and ciprofloxacin accumulated in the rat heart and muscle with higher ciprofloxacin residuals (heart:  $0.2 \pm 0.03 \mu\text{g/g}$  and  $0.15 \pm 0.02 \mu\text{g/g}$ ).

Histopathology showed Myocardial fiber disruption and muscle necrosis at  $\geq 400\text{mg/kg}$  doses. This data indicate potential cardiotoxicity and myotoxicity necessitating careful therapeutic use and monitoring

### DECLARATION

#### Ethics Approval and Informed Consent

All experimental procedures involving animals were carried out in strict compliance with internationally accepted guidelines for animal welfare and use in research. Ethical approval was obtained from the Animal Ethics Committee of the University of Ibadan, Oyo State, Nigeria (Approval No: UI/ACUREC/2025/044). Efforts were made to minimize animal suffering, and the number of animals used was kept to the minimum required to achieve scientific validity. Since this study did not involve human participants, informed consent was not applicable.

#### Authors' Contributions

The author: Adewoga, T. O. S. conceived and designed the study. The author was responsible for experimental design, animal treatment, sample collection, and laboratory analysis. Data interpretation, histopathological examination, and

statistical analysis were carried out by the author with technical input from departmental laboratory staff. Mr. Friday of Dept. of Biological Sciences and Mr. Ambrose of Veterinary Pathology Dept., UI. The author drafted the manuscript, revised it critically for intellectual content, and approved the final version for submission.

#### Disclosure of Conflict of Interest

The author declares that there is no conflict of interest related to this study. The research was conducted independently, and no personal, financial, or institutional interests influenced the design, execution, analysis, or reporting of the work.

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In summary, ethical standards were strictly maintained, the contribution of the author is clearly acknowledged, no conflicts of interest are declared, and the work was self-funded. These declarations affirm the transparency, independence, and academic integrity of the research presented in this article.

#### REFERENCES

1. Grabowski, L., Gaffke, L., Pierzynowska, K., Cyske, Z., Choszcz, M., Wegrzyn, G. and Wegrzyn, A. (2022). Enrofloxacin—The ruthless killer of eukaryotic cells or the last hope in the fight against bacterial infections? *International Journal of Molecular Sciences*, **23**: 3648.
2. Yang, F., Yang, F., Wang, D., Zhang, C.S., Wang, H., Song, Z.-W., Shao, H.-T., Zhang, M., Yu, M.L. and Zheng, Y. (2021). Development and application of a water temperature-related physiologically based pharmacokinetic model for enrofloxacin and its metabolite ciprofloxacin in rainbow trout. *Frontiers in Veterinary Science*, **7**, 608348.
3. Munanura, E. I., Ntale, M., Wasswa, J. and Kaggwa, B. (2023). Assessment of enrofloxacin usage and residue levels of enrofloxacin-ciprofloxacin in breast and liver tissues of commercial broilers sold in Kampala-Uganda. *Infection and Drug Resistance*, **16**, 7629–7639.
4. Islam, S., Belal, B., Dash, S., Islam, S., Hasan, M., Rafiq, K. and Islam, Z. (2024). Chronic exposure of ciprofloxacin antibiotic residue above the MRL level and its pathophysiological effects in mice. *Current Research in Complementary and Alternative Medicine*, **8**, 249.
5. Verma, M. K., Ahmad, A. H., Pant, D., Rawat, P., Sharma, S. and Arya, N. (2020). Screening of enrofloxacin and ciprofloxacin residues in chicken meat by high-performance liquid chromatography. *Journal of Pharmaceutical Research International*, **32**(21), 64–69.
6. Mathew, U., Charles, I., Kingsly, A., Trevor, H. and Ernest, A. (2020). Histological effect of ciprofloxacin on the kidney histology of adult rats. *International Journal of Healthcare Sciences*, **7**(2), 360–369.
7. Luan, Y., Zhao, J., Han, H., Shen, J., Tang, S. and Cheng, L. (2021). Toxicologic effect and

- transcriptome analysis for short-term orally dosed enrofloxacin combined with two veterinary antimicrobials on rat liver. *Ecotoxicology and Environmental Safety*, **220**, 112398.
8. **El-Kader, M.A.** (2019). Evaluation of azithromycin induced cardiotoxicity in male albino rats and the possible protective role of *Nigella sativa* oil. *Egyptian Journal of Histology*, **43**(2), 465–476.
  9. **Hameed, B.K., Hameed, M.A., Hussein, H.M. and Wadee, S.A.** (2025). Histological study of antibiotic effect on liver, kidney and breast muscle in poultry. *Egyptian Journal of Veterinary Sciences*, **56**(1), 39–46.
  10. **Hooper, D.C. and Jacoby, G.A.** (2021). Topoisomerase inhibitors: Fluoroquinolone mechanisms of action and resistance. *Cold Spring Harbor Perspectives in Medicine*, **6**, a025320.
  11. **Chen, C.R., Malik, M., Snyder, M. and Drlica, K.** (2021). DNA gyrase and topoisomerase IV on the bacterial chromosome: Quinolone-induced DNA cleavage. *Journal of Biological Chemistry*, **258**, 627–737.
  12. **Karakurt, I., Ozaltin, K., Vargun, E., Kucerova, L., Suly, P., Harea, E., Minařík, A., Štěpánková, K., Lehocky, M. and Humpolíček, P.** (2021). Controlled release of enrofloxacin by vanillin-crosslinked chitosan-polyvinyl alcohol blends. *Materials Science and Engineering C: Materials for Biological Applications*, **126**, 112125.
  13. **El-Sanhoury, I.A., Oda, S.S., Elbelehi, S.S. and El-Karim, D.G.** (2021). Doxycycline toxicity in rats: Clinicobiochemical and histopathological studies. *Alexandria Journal of Veterinary Sciences*, **69**(1), 123–131.
  14. **Ahmed, M.S., Massoud, A.H., Derbaleh, A.S., Al-Brakati, A., Al-Abdawani, M.A., Eltahir, H.A., Yanai, T. and Elmahallawy, E.K.** (2020). Biochemical and histopathological alterations in different tissues of rats due to repeated oral dose toxicity of cymoxanil. *Animals*, **10**, 2205.
  15. **Sun, S., Hu, R., Zhang, C. and Shi, G.** (2019). Do farmers misuse pesticides in crop production in China? Evidence from a farm household survey. *Pest Management Science*, **75**, 2133–2141.
  16. **Arsene, M.M., Davares, A.K., Viktorovna, P.I., Andreevna, S.L. and Sarra, S.** (2022). The public health issue of antibiotic residues in food and feed: Causes, consequences, and potential solutions. *Veterinary World*, **15**, 662–671.
  17. **Edem E.O. et al** (2020), The effect of Ciprofloxacin on Naemotological and Biochemical parametics in Albino Rats. *Nigerian Journal of Pharmaceutical and Applied Science Research, University of Uyo*. **5** (1) 61-64.
  18. **Okuwakpam et. al.** (2023). Haemotological and Cardiac Marker Values of Adult male Wistar Rats Administered a combination of common Antimalarial drugs and Ciprofloxacin. *Asian Journal of Research in Biochemistry*. Rivers State University **12** (2) 40-49
  19. **Kennedy I. Amagon et al** (2023). Antibiotics in food aniamls: determination of enrofloxacin residual in chicken tissue. *West*

*African Journal of Pharmacy,*  
Univrsity of Lagos. 28 (1), 98-10