



Histopathology of Levofloxacin Induced Toxicity in Kidney and Heart after Repeated Oral Administration in Dual Purpose Chicken

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ABSTRACT

The toxicological effect of the levofloxacin were studied by histopathological changes in kidney and heart of the dual purpose chicken. The experimental birds (35 day old) were randomly allotted into three groups (n=30), Group I birds served as control (Distilled water), Group II and Group III birds were administered with levofloxacin at the dose rate of 10 mg/kg bw and 20 mg/kg bw respectively for 28 days. The section of kidney showed mild tubular epithelial cell degeneration and epithelial cell degeneration with infiltration of inflammatory cells in the interstitium on day 21 and 28 respectively in group II of experimental birds as compared to control group. In group III, section of kidney showed tubular epithelial cell degeneration, necrosis with glomerulus atrophy on day 14. The congestion, tubular epithelial cell degeneration, desquamation and severe hemorrhages in interstitium, tubular epithelial cell degeneration, necrosis along with infiltration of inflammatory cells on day 21 and 28 respectively compared to the control group. In group III, section of heart showed mild congestion, hemorrhages in cardiac muscle and mild myocardial degeneration and infiltration of inflammatory cells between cardiac muscle fibres respectively on day 21 and 28 of the experimental period. This showed that after repeated administration of levofloxacin at the dose rate of 10 mg/kg bw and 20 mg/kg bw for 28 days produced toxicological effect in low dose on day 21, 28 and in high dose on day 14, 21, 28 and in the kidney and heart tissue samples of the dual purpose chicken.

Key words : Kidney, Heart, Dual Purpose Chicken, Toxicity

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INTRODUCTION

Levofloxacin is a third generation fluoroquinolone with broad spectrum nature and is a levo isomer of ofloxacin [1,2]. It's spectrum of activity includes most strains of gram positive and gram negative anaerobic bacterial pathogens responsible for respiratory, urinary tract, gastrointestinal tract, skin and soft tissue infections [3]. It has an excellent broad-spectrum activity against *Mycoplasma* and *Chlamydia* organisms in veterinary medicine [4]. To study the safety evaluation of levofloxacin following repeated oral administration in dual purpose chicken. The histopathological studies of kidney and heart were done to know the toxicological effects of levofloxacin administered at 10 mg/kg bw and 20 mg/kg bw for 28 days of the dual purpose chicken.

MATERIALS AND METHOD

The study was conducted in 30 to 35 days old (n= 90) healthy dual purpose chicken Indian Rock-3(IR-3), a strain of White Plymouth Rock developed by Karnataka Veterinary Animal and Fisheries Sciences University, Bidar . The study was performed at the Department of Poultry Science, Veterinary College, Hebbal, Bengaluru. The birds were kept under observation for one week prior to commencement of experiment and subjected to clinical examination in order to exclude the possibility of disease. The birds

were provided antibiotic-free standard broiler ration for fourteen days. The animal house was maintained at room temperature ($25\pm 2^{\circ}\text{C}$) and at 45 to 65 per cent relative humidity. Food and water were supplied *ad libitum* and standard managerial practices were followed to keep the birds free from stress. The prior approval of the Institutional animal Ethics Committee (IAEC) was obtained before the commencement of the experiment (LPM/IAEC/181/2014, Date: 10/01/2014).

The experimental birds (35 day old) were randomly allotted into three groups (n=30), Group I birds served as control (Distilled water), Group II and Group III birds were administered with levofloxacin at the dose rate of 10 mg/kg bw and 20 mg/kg bw respectively directly into the crop using a thin plastic tube attached to a syringe for 28 days. The food was withheld for 12 h before oral dosing but not water and water was provided *ad libitum* before the drug administration. The selection of the dosage based on levofloxacin at 10 mg/kg bw considered as therapeutic dosage in the poultry birds [5,6]. Therefore 20 mg/kg of levofloxacin was selected as high dose based on the therapeutic dosage of levofloxacin to see the any adverse effect with respect histopathological examination in the dual purpose chicken.

After the collection of the blood for serum biochemical analysis, six birds from each group were randomly selected and sacrificed at weekly interval on day 0, 7, 14, 21 and 28 during the study period. The birds were subjected to a detailed post mortem examination and gross lesions if any were recorded. The samples of kidney and heart were collected, washed with normal saline and then collected in 10 percent neutral buffered formalin (NBF). They were processed through routine paraffin embedding technique. All the organs were processed for histopathology by cutting sections of $4\mu\text{m}$ thickness and stained with Haematoxylin and Eosin [7]. The histopathological lesions were observed in sections of various organs were systematically recorded and photomicrographs were taken using Zeiss AxioCam Erc5s microscope [H&E x 200].

RESULTS AND DISCUSSION

Histopathology of the Kidney

The Group I, section of kidney showed normal architecture of renal tubular epithelial cells (Fig.1), sections of kidney in Group II did not reveal any histopathological changes on day 0, 7, 14 and in group III on day 0, 7 throughout the experimental period compared to the control group.

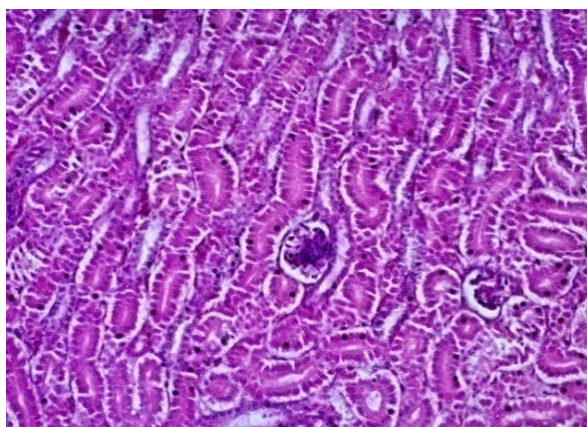


Fig.1: Section of kidney in control group showing normal architecture of renal tubular epithelial cells

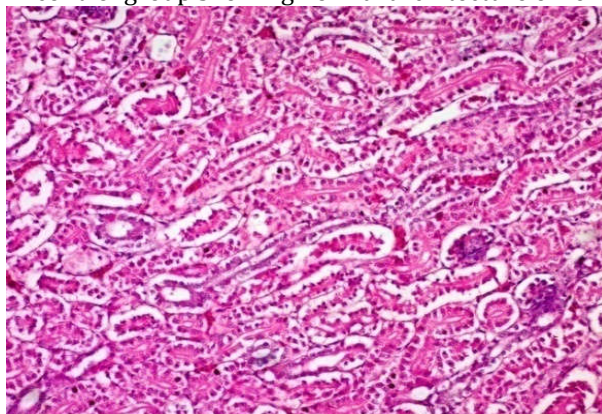


Fig. 2: Section of kidney on day 21 administered with levofloxacin (10 mg/kg bw) showing mild tubular epithelial cell degeneration

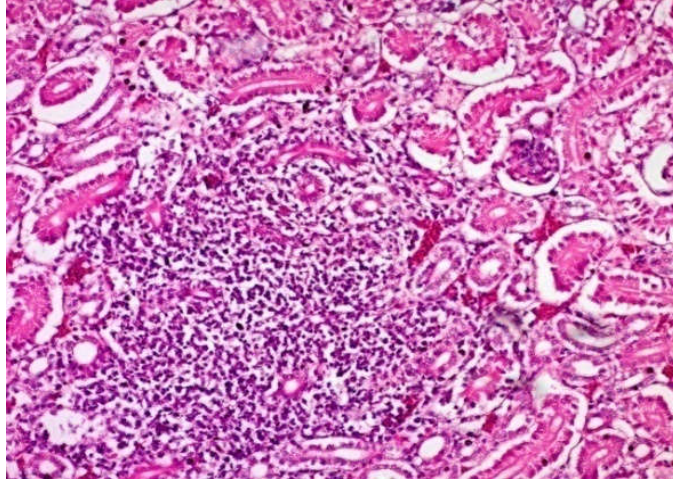


Fig. 3: Section of kidney on day 28 administered with levofloxacin (10 mg/kg bw) showing tubular epithelial cell degeneration and inflammatory cells infiltration in the interstitium

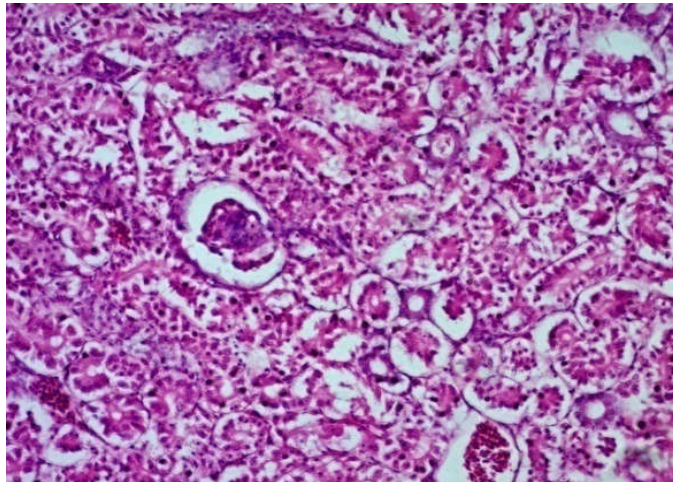


Fig. 4: Section of kidney on day 14 administered with levofloxacin (20 mg/kg bw) showing tubular epithelial cell degeneration, necrosis and glomerulus atrophy.

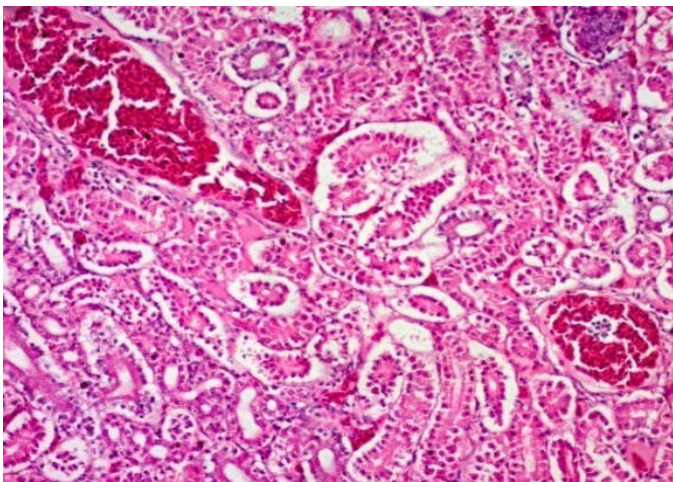


Fig.5: Section of kidney on day 21 administered with levofloxacin (20 mg/kg bw) showing severe congestion of vessels, tubular epithelial cell degeneration and desquamation.

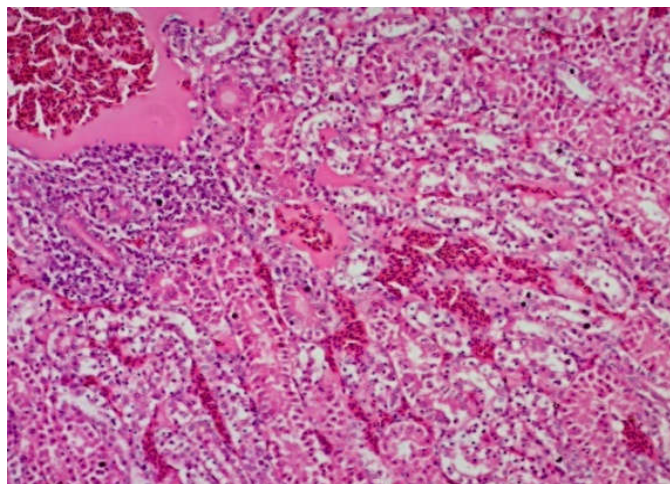


Fig.6: Section of kidney on day 28 administered with levofloxacin (20 mg/kg bw) section showing severe hemorrhages in the interstitium, tubular epithelial cell degeneration and necrosis along with infiltration of inflammatory cells.



Fig. 7: Section of heart in control group showing normal architecture of cardiac muscle fibers.

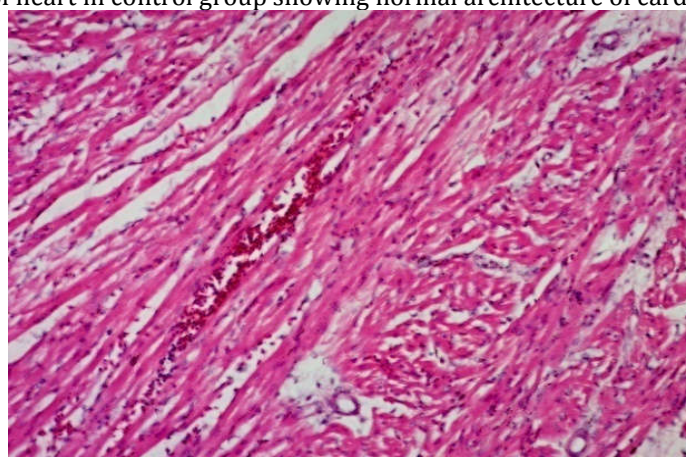


Fig.8: Section of heart on day 21 administered with levofloxacin(20 mg/kgbw)showing mild congestion and hemorrhages in thecardiac muscle.

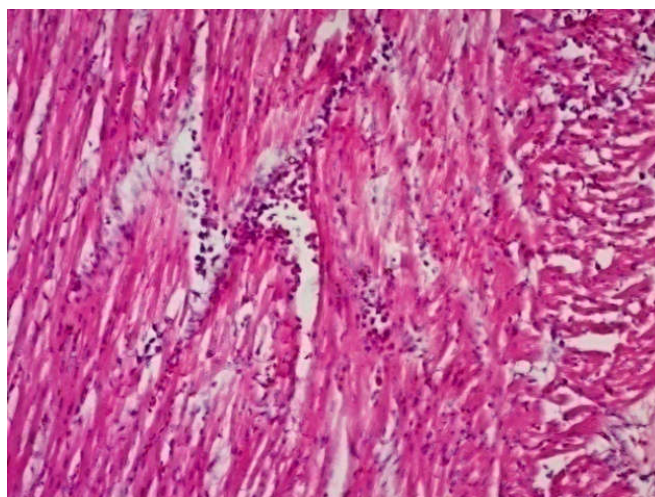


Fig.9: Section of heart on day 28 administered with levofloxacin(20 mg/kg bw)showing mild myocardial degeneration and infiltration of inflammatory cells between cardiac muscle fibers.

The section of kidney showed mild tubular epithelial cell degeneration (Fig. 2) and epithelial cell degeneration with infiltration of inflammatory cells in the interstitium (Fig. 3) on day 21 and 28 respectively in group II of experimental birds as compared to control group.

In group III, section of kidney showed tubular epithelial cell degeneration, necrosis with glomerulus atrophy on day 14 (Fig. 4). The congestion, tubular epithelial cell degeneration, desquamation (Fig. 5) and severe hemorrhages in interstitium, tubular epithelial cell degeneration, necrosis along with infiltration of inflammatory cells (Fig. 6) on day 21 and 28 respectively compared to the control group.

Microscopically in Group II and Group III of experimental birds, section of kidney showed tubular epithelial cell degeneration, desquamation, congestion, hemorrhages, necrosis along with infiltration of inflammatory cells in the interstitium.

The above findings are in accordance with Ellakany *et al.* [8] who reported that congestion, tubular degeneration, and areas of hemorrhage in kidney after administered with enrofloxacin at 10 mg/kg bw through drinking water for five days in broiler chicken. Sureshkumar *et al.* [9] reported that degeneration of tubular epithelial cells with haemorrhagic areas, cytoplasm of swollen tubular epithelial cells and filled with eosinophilic material were observed in the toxicity of enrofloxacin administered at 10mg/kg bw via drinking water for five days in poultry birds. Nada and Shawi [10] reported that nephrosis, cell swelling of the epithelial lining and coagulative necrosis of renal tubules observed after the administration of ciprofloxacin at 25 mg/ kg and 50 mg/ kg bw in rats.

Histopathology of the Heart

In control group (Group I) section of heart showed normal architecture of cardiac muscle fibers (Fig.7). The sections of the heart did not reveal any histopathological changes on day 0,7,14,21, 28 in Group II and day 0,7,14 in Group III of the experimental birds.

In group III, section of heart showed mild congestion, hemorrhages in cardiac muscle (Fig. 8) and mild myocardial degeneration and infiltration of inflammatory cells between cardiac muscle fibres (Fig. 9) respectively on day 21 and 28 of the experimental period.

Microscopically heart of Group III experimental birds showed mild congestion, hemorrhages, myocardial degeneration and infiltration of inflammatory cells in cardiac muscle.

The above findings are in accordance with Nada and Shawi, [11] who reported that mild degree of congestion, perivascular infiltration of mononuclear cells in the cardiac muscle was observed after administration of 50 mg/kg ciprofloxacin compared to control groups in juvenile rats.

CONCLUSION

The experimental birds were administered with levofloxacin at the dose rate of 10 mg/kg bw and 20 mg/kg bw respectively directly for 28 days in dual purpose chicken. The levofloxacin showed the histopathological changes at low and high doses of the levofloxacin produced in low dose on day 21, 28 and in high dose on day 14, 21, 28 in the kidney samples and Levofloxacin on high dose at 20mg/kg bw showed histopathological changes in heart tissue samples. The present study showed that the levofloxacin at the dose rate of 10 mg/kg bw and 20 mg/kg bw for 28 days produced toxicological effects in both low and high doses in kidney and heart muscle of the dual purpose chicken.

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