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Histochemical analysis of stomach, liver and kidney tissues in local dogs following hydrochloric acid – induced acidification

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Abstract

Metabolic acidosis is an acid-base imbalance associated with several disorders in different organs, our study elucidate the effects of acidosis on stomach, liver and kidney in local dog by histological and histochemical. local dogs were divided into four groups: a control group and three experimental groups treated with hydrochloric acid (75 mmol), HCL (150 mmol) and HCL (300 mmol) respectively. Treatment duration was set for 15 days, with tissue samples collected for analysis.Histomorphological evaluations showed significant changes in the targeted organs architecture, including gastric sloughing, fibrosis and inflammatory cell infiltration.The hepatic tissue exhibited necrosis, dilation in portal vein and thrombosis with inflammatory cell infiltration and fibrosis. The renal tissue show glomeruli shrinkage with tubular atrophy and cystic dilation. Histochemical analysis revealed decreased PH levels , increase lactic acid levels and elevated liver enzymes with rising of serum levels of urea and creatinine, indicating cellular damage.

Keywords: metabolic acidosis – HCL – stomach – liver – kidney –PH – lactic acid – liver enzymes – urea – creatinine

Abbreviations:

HCL : hydrochloric acid

H&E: hematotoxilen and eiosen stain

MMOL : milimoles per liter

ALT : alanine aminotransferase

AST : aspartate aminotransferase

1. INTRODUCTION

Metabolic acidosis has been found to have diagnostic, therapeutic, and prognostic implications in human medicine The metabolic acidosis considered a significant acid-base inequity that happens when the nonvolatile acids accumulated or the loss of bicarbonate surpasses the body's buffering capacity. It comprises a complex relationship between different organs, mainly the liver, kidneys, and muscles , which effort together to reestablish acid-base homeostasis [1-2]. One of the important influences of metabolic acidosis is the disturbance of nitrogen metabolism in splanchnic organs . For example, the liver practices reduced urea synthesis due to declined activity of urea cycle enzymes [2]. Metabolic acidosis can be classified into two chief types: organic acidosis, characterized by the buildup of organic anions like lactic acid (subsequent in an increased anion gap) and hyperchloremic acidosis, which rises due to electrolyte imbalances[3-4].Metabolic

acidosis has contrary effect on a range of body functions[5]. Metabolic acidosis can occur in three primary scenarios: as a primary acid-base disorder associated with a corresponding pH decrease, as a compensatory response to primary respiratory alkalosis (resulting in a higher-than-normal pH), or as part of a mixed disorder in conjunction with respiratory acidosis or alkalosis. Given these complexities, pH alone is insufficient as a diagnostic tool, necessitating comprehensive acid-base analysis. Blood gas analysis has become an essential diagnostic and monitoring tool in clinical settings, particularly in critically ill patients [26] .

MATERIALS AND METHODS:

In this study, 20 healthy local dogs aged 1.5-3 months old and weighing 7-11 kg were used . The dogs purchased from the local market of Karbala. Food and water are accessible. Dogs were divided to 4 groups, 5 animals for each group and as follows, group one served normal slain as control group. Group 2 treated wih dose of 75 mmol of HCL injection via vein for 10 days. Group three treated with dose of 150 mmol of HCL injection via vein for 10 days .Group four were given 300 mmol of HCL via vein for 10 days. After completing the experimental period, each animal was sacrificed. The animals were anesthesiad with ketamine and after dissection of abdominal cavity . Then targeted organs were removed and the samples collected. The the samples were fixed in 10% formalin solution. After dehydration by passing tissue through a series of alcohol solutions, were cleared in xylene and were embedded in paraffin (Merck, Germany).Then the specimen were embedded .Then sample were sectioned at 5 µm thickness using microtome (Leica, Germany).The final step was staining sample with Hematoxylin and eosin (H &E) and Masson trichrome (MT) (Merck, Germany).Data were analyzed by one-way ANOVA. In all tests, $p \leq 0.05$ was considered as statistically significant

Ethical approve

This investigation was conducted in the anatomical facility of the University of Karbala's College of Veterinary Medicine under reference number UOK.VET. AN. 2024.094

RESULTS:

Histomorphological findings

The current study elucidate sloughing on the gastric internal surface , as well as partial cell necrosis from hydrochloric acid administration, as well as interstitial fibrosis.The histomorphological findings increased with increasing dosage of HCL in figures (2,3,4,5,6,7,23,24,25). As for hepatic tissue in the treated groups showed signs of necrosis, inflammation and cellular vacuolation with edema, as well as thrombosis and dilation of the portal vein. Fibrosis was also noted, indicating a fibrogentic response.our investigations showed that raising the dose HCl resulted in elevated histological changes in figures (9,10,11,12,13,14,27,28,29) . On the other side renal alterations appears as shrinkage of glomeruli and congestion, tubular atrophy, dilation and necrosis with thrombus , dilation in bowman capsule, and mononuclear cell around glomeruli with fibrosis. As the HCl dosage was increased, the alterations in the renal tissue became more pronounced in figures (16,17,18,19,20,21,31,32,33). The immuonohistochemical staining shows positive expression in all targeted organs in figures (35,36,37,34,35,36,37,38,39,40,41 ,43,44,45).

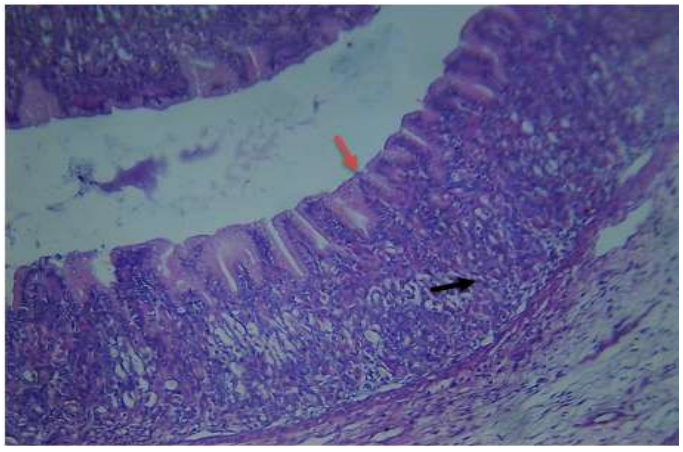
The histochemical analysis

The current study showed, after inducing acidity conditions in the experimental dogs, a significant decrease in PH levels on the seventh and tenth day from the start of the experiment compared to the animals in the control in table (1). On the other hand lactic acid levels increase, it was found that the concentration of 300 M was significantly higher than the rest of the concentrations of the groups (2) . The liver enzymes (AST-ALT) levels increased significantly in dogs induced with acidosis. It was also noted that the rates of increase gradually increased in concentrations in the 75, 150, and 300 mM groups tables (3-4). The kidney function

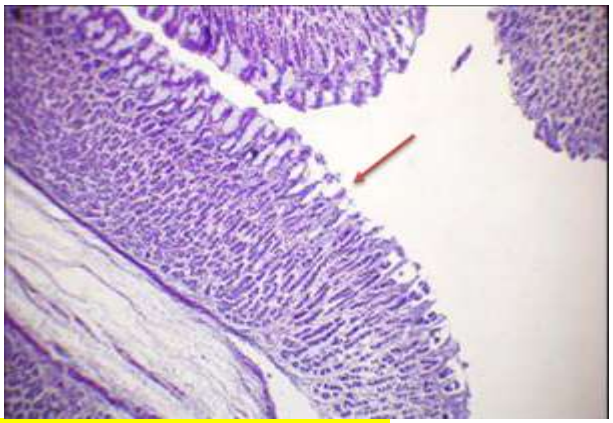
test demonstrate that creatinine and urea levels increased significantly in dogs induced with acidosis. Additionally, it was observed that the 75, 150, and 300 mM groups' rates of concentration increase rose progressively (5-6).

DISCUSSION:

The results of this study showed that the gastric epithelial surface sloughed and infiltration of inflammatory cell with in mucosa due to metabolic acidosis with different concentration with H&E staining. The fibrosis appeared in masson trichrom staining. Our results approved with Mullane and Cathcart [9-10]. In the hepatic tissue appearance necrosis , inflammation and cellular vacuolation additionally thrombosis along side dilation of central vein with fibrosis due to oxidative stress that induced hepatic injury, which are similar to other researchers[9-13] . further studies demonstrated parallel with our findings [19-20] renal alterations as shrinkage of glomeruli and tubules, atrophy, cystic dilation, and hypercellularity with interstitial fibrosis. The immuonohistochemistry MDA staining revealed positive expression in all organs of experiment The levels of PH decreased due to metabolic acidosis [22] on the other hand lactic acid levels increased due to abnormal accumulation of lactic acid in the blood [23] The liver enzymes (AST-ALT) elevated owing to the indicating significant academia and the elevation lead to liver injury[24] kidney function test (urea and creatinine) rose attributable to acidosis indicates liver damage and hepatic necrosis [21-25]



Figure(1): Photomicrograph section of control stomach dog group showed normal epithelia(red arrow) with normal gastric gland(black arrow) (H&E stain 10X)



Figure(2):Photomicrograph section in the stomach of exposed dog to 75 mmol concentration of HCL at 15 days showed mild sloughing of tissue (red arrow) (H&E stain 10X)

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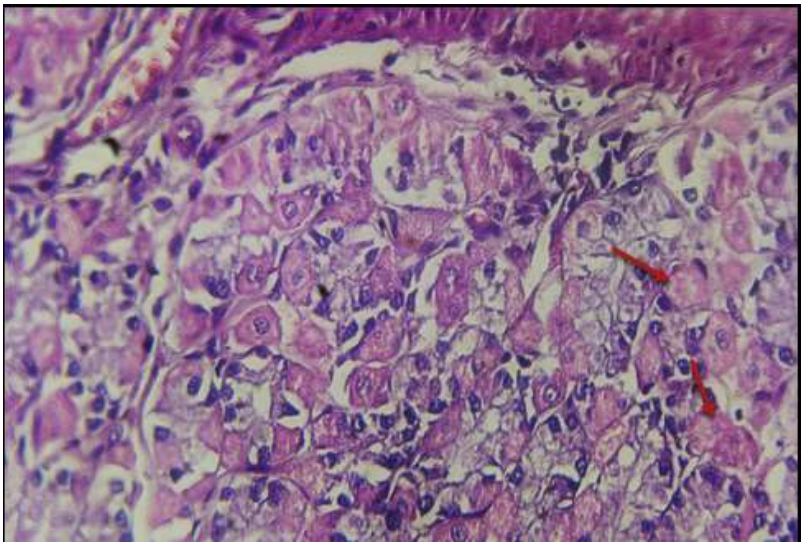

Figure(3):Photomicrograph section in the stomach of exposed dog to 75 mmol concentration of HCL at 15 days showed partial cell necrosis (red arrows) (H&E stain 40X)

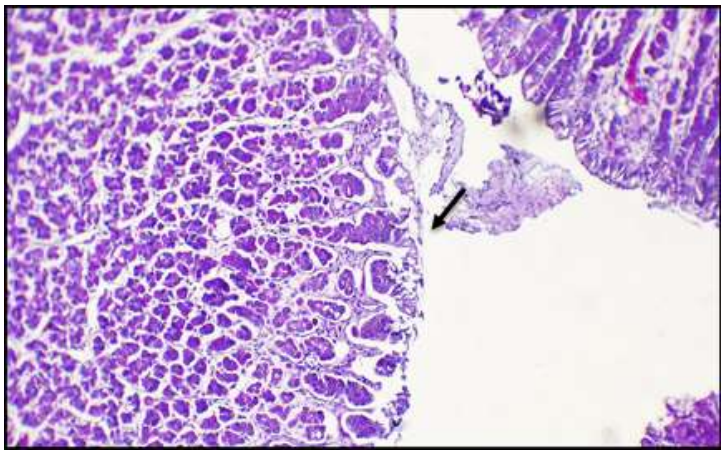

Figure (4): Photomicrograph section in the stomach of exposed dog to 150mmol concentration of HCL at 15 days shows sloughing (black arrow) (H&E stain 10X).

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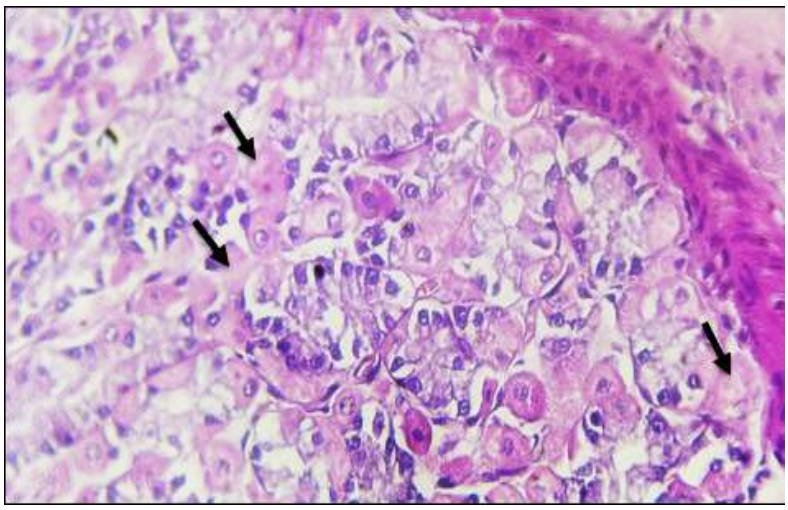
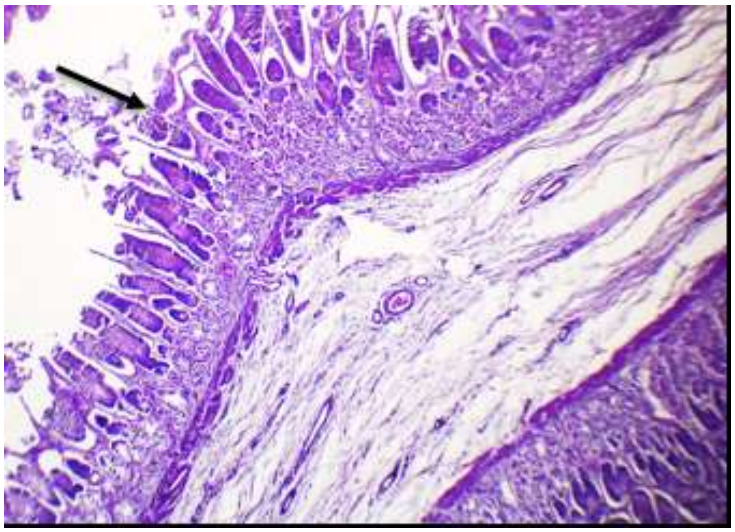
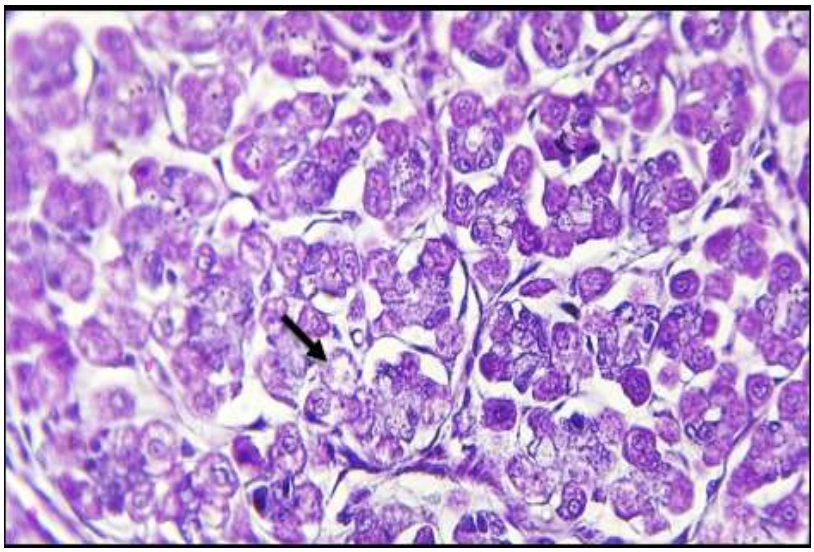


Figure (5):Photomicrograph section in the stomach of exposed dog to 150mmol concentration of HCL at 15 days shows partial cell necrosis (black arrow) (H&E stain 40X).



Figure(6):Photomicrograph section in the stomach of exposed dog to 300mmol concentration of HCL at 15 days showed increase sloughing (black arrow) (H and E stain 10X).



Figure(7:Photomicrograph section in the stomach of exposed dog to 300mmol concentration of HCL at 15 days showed necrosis of parietal cell with cystic dilation (black arrow) (H and E stain 40X).

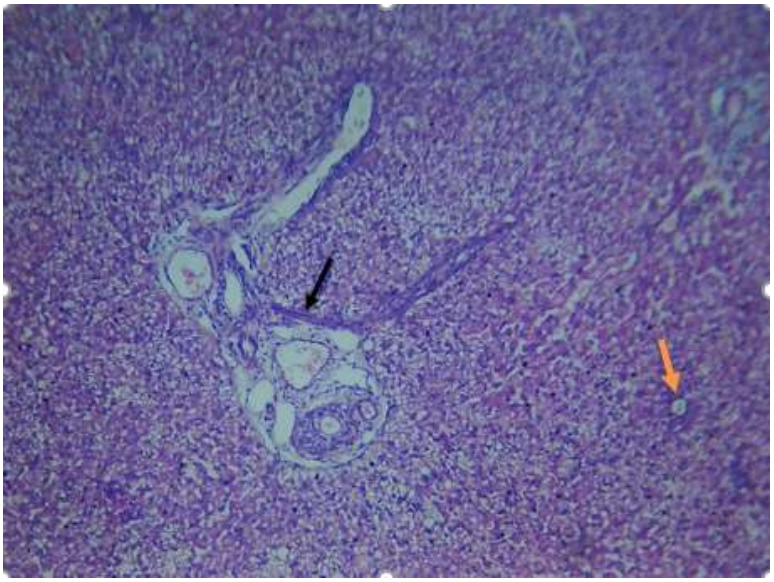
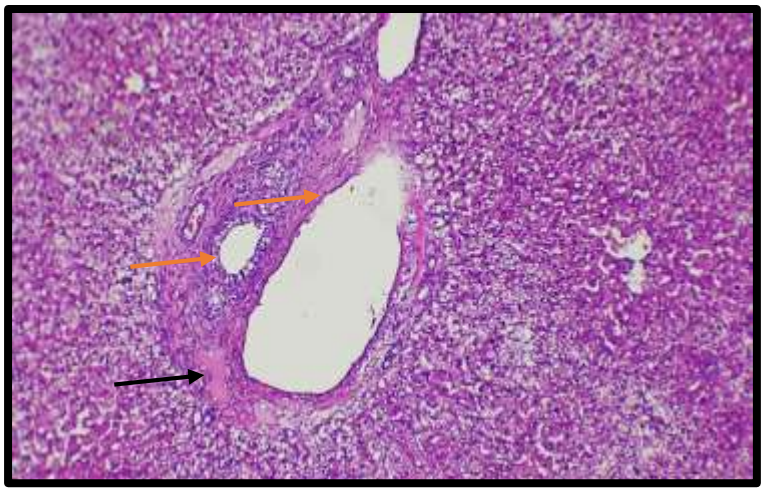
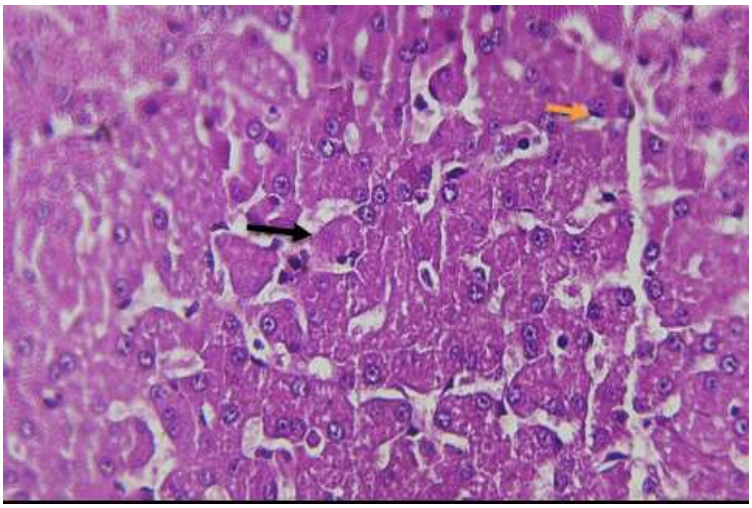


Figure (8): Photomicrograph section of control liver local dog group showed normal portal area (black arrow) with normal central vein (orange arrow) (H&E stain 10X)



Figure(9):Photomicrograph section in the liver of exposed dog to 75mmol concentration of HCL at 15 days showed Edema substance (black arrow) dilated of portal vein& bile duct(red arrow) (H&E stain 10X).



Figure(10):Photomicrograph section in the liver of exposed dog to 75mmol concentration of HCL at 15 days showed Endothelial cells (orange arrow) with necrotic lesion that nuclear karyolitic (black arrow) (H&E stain 40X).

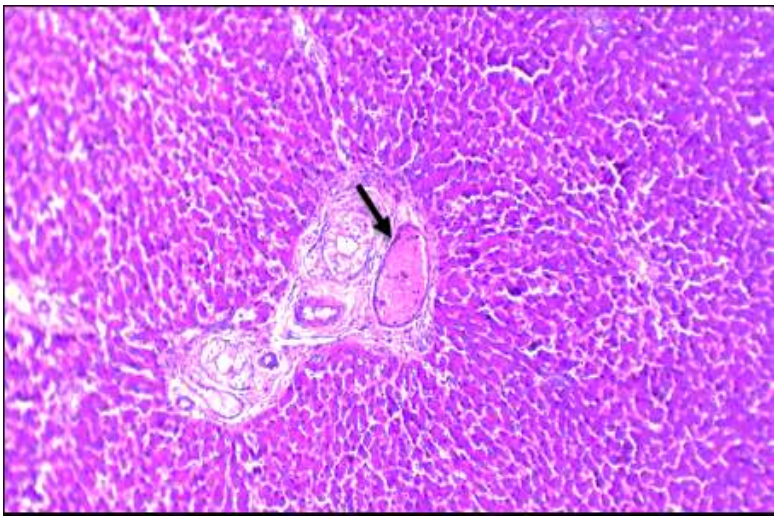


Figure (11):Photomicrograph section in the liver of exposed dog to 150mmol concentration of HCL at 15 days showed thrombus (black arrow) (H&E stain40+10X).

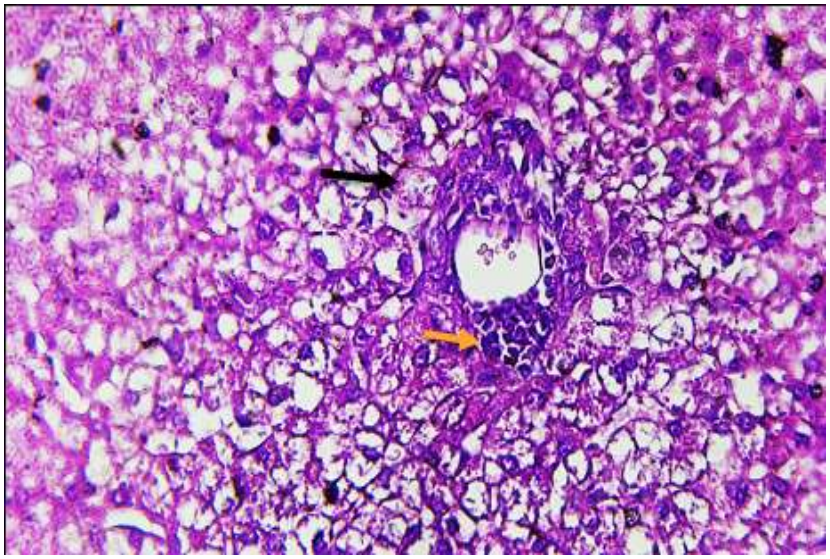


Figure (12): Photomicrograph section in the liver of exposed dog to 150mmol concentration of HCL at 15 days showed mono nuclear cell around central vein (orang) with necrotic lesion of hepatocytes (black)(H&E stain40X).

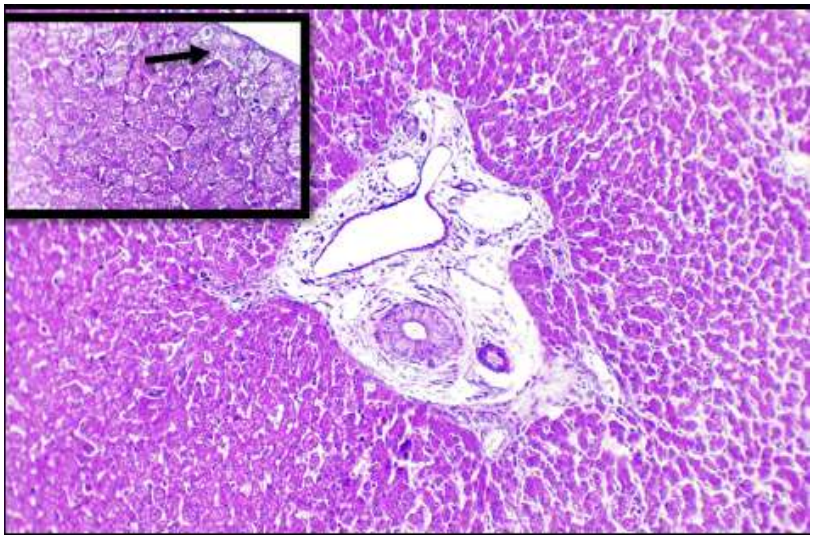


Figure (13):Photomicrograph section in the liver of exposed dog to 300mmol concentration of HCL at 15 days showed vacuolations (black arrow) (H and E stain40+ 10X).

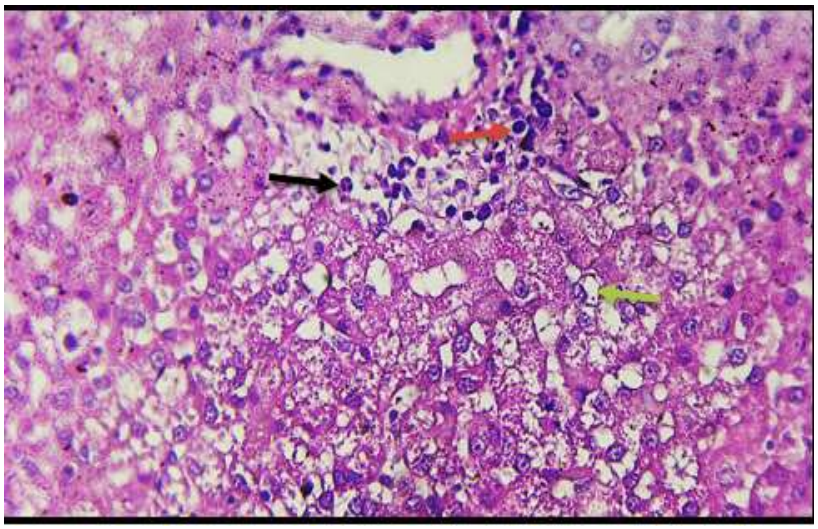


Figure (14):Photomicrograph section in the liver of exposed dog to 300mmol concentration of HCL at 15 days showed Perivascular mononuclear cells (red)& neutrophils(black) infiltration with vacuolation of hepatocytes(green) (H and E stain40X).

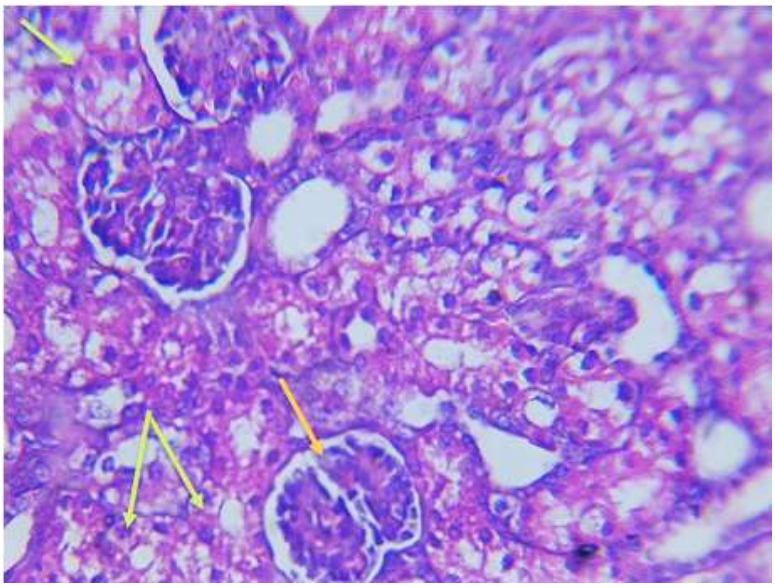


Figure (15):Photomicrograph section of control kidney local dog group showed normal glomeruli (orange arrow) with normal tubules (green arrow) (H&E stain 10X)

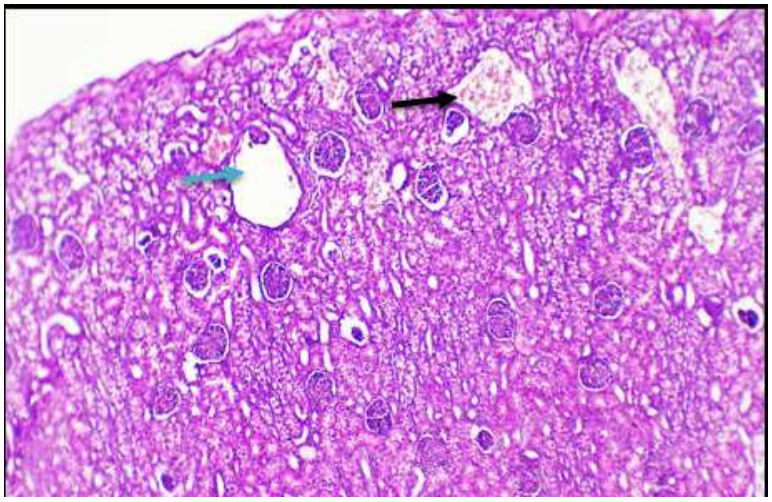
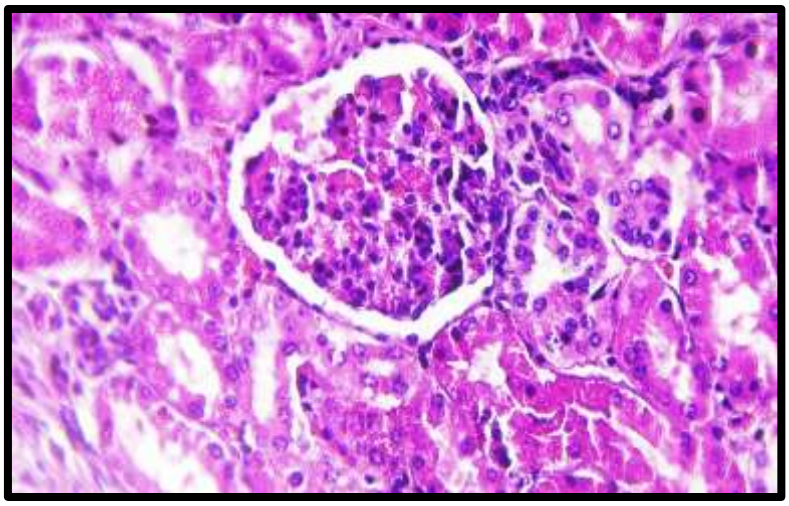
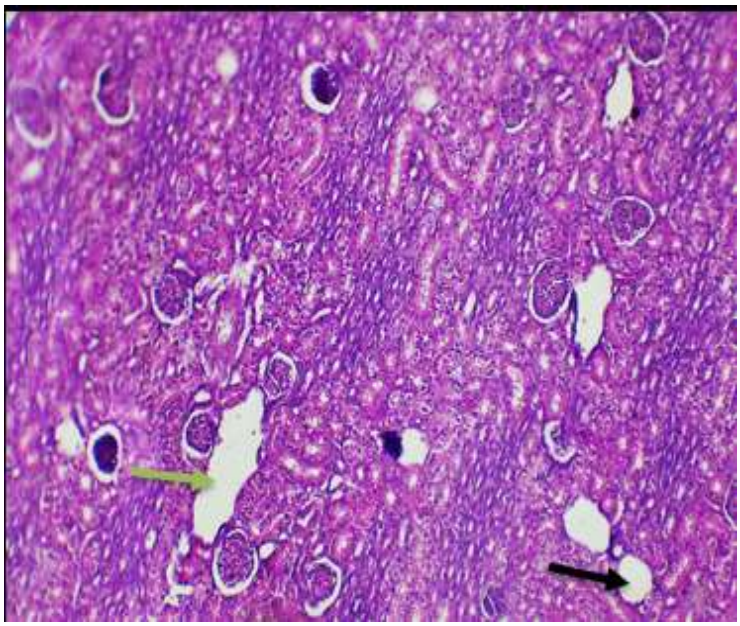


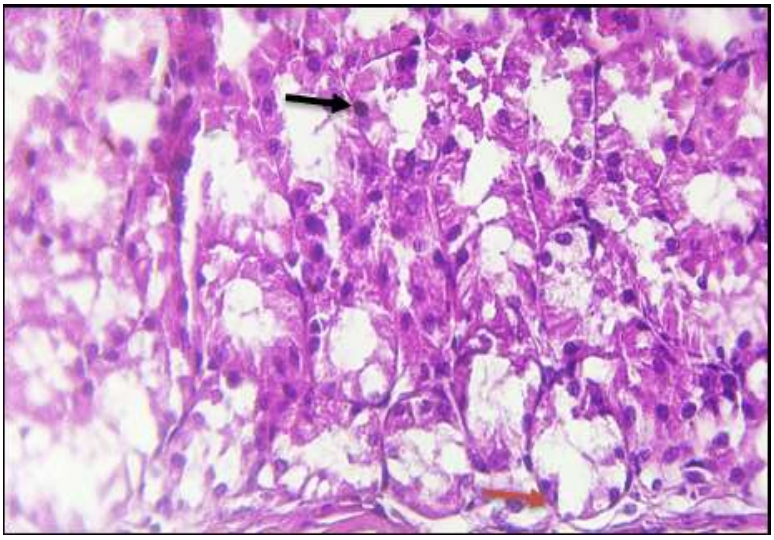
Figure (16):Photomicrograph section in the kidney of exposed dog to 75mol concentration of HCL at 15 days showed congestion of blood vessels(black) & shrinkage of glomeruli with dilation of Bowman's space (blue) (H&E stain 10X).



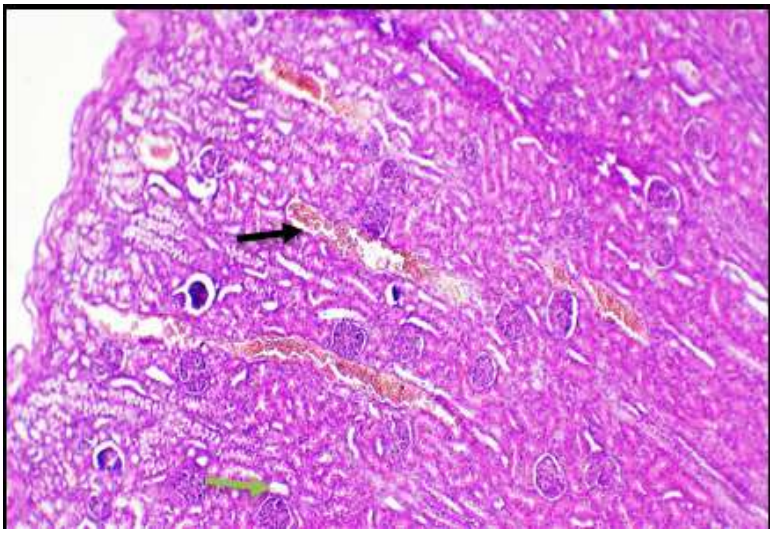
Figure(17):Photomicrograph section in the kidney of exposed dog to 75mol concentration of HCL at 15 days showed of MNCs mainly macrophages concentrated around glomeruli (black arrows) focal MNCs aggregation (H&E stain 40X).



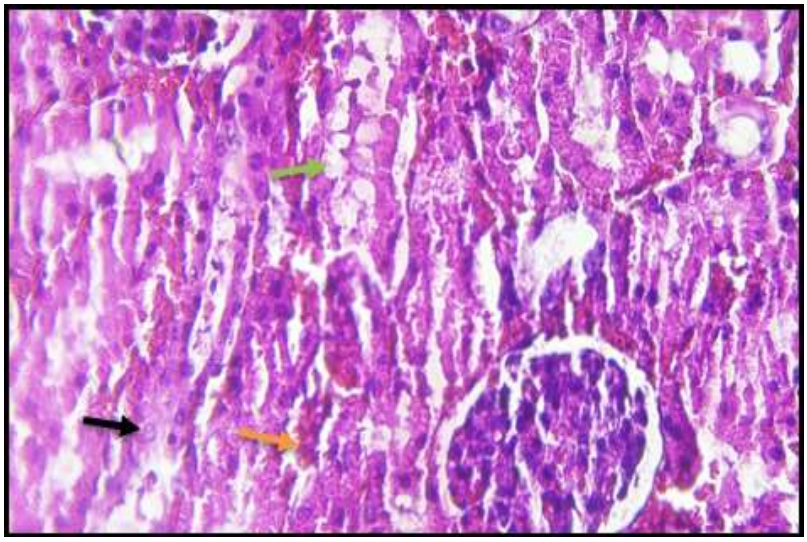
Figure(18):Photomicrograph section in the kidney of exposed dog to 150mmol concentration of HCL at 15 days showed tubular dilation(green) with absence of glomerular (black arrow) (H&E stain10X).



Figure(19):Photomicrograph section in the kidney of exposed dog to 150mmol concentration of HCL at 15 days showed Diffuse Tubular necrosis (black arrow) & single cell necrosis in sub capsular region(red arrow) (H and E stain 40X).



Figure(20):Photomicrograph section in the kidney of exposed dog to 300mmol concentration of HCL at 15 days showed thrombus formation (back) with tubular atrophy(green) (H&E stain10X).



Figure(21):Photomicrograph section in the kidney of exposed dog to 300mmol concentration of HCL at 15 days showed interstitial hemorrhage(orange arrow) & tubular vacuolation(green arrow) with necrosis in epithelial lining tubules (black arrow) (H and E stain 40X).

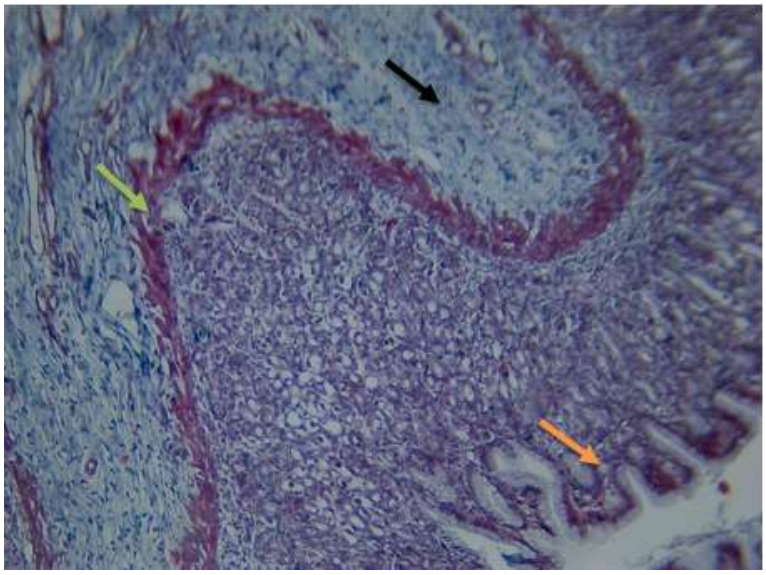
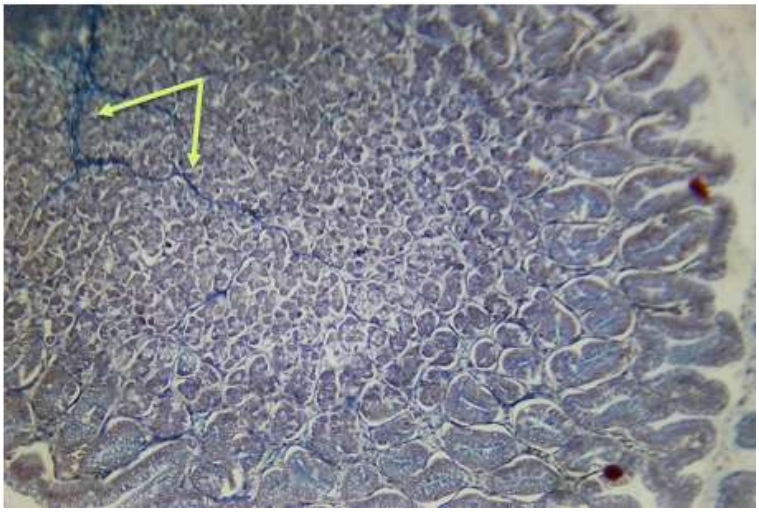


Figure (22): Photomicrograph section of control stomach local dog group normal gastric pits (arrow orange) muscularis mucosae (green arrow) sub mucosa (black arrow) (Masson Trichrome stain 10X)



Figure(23):Photomicrograph section in the stomach of exposed dog to 75 mmol concentration of HCL at 15 days post showed interstitial fibrosis with collagen fiber (green arrows) (Masson Trichrome stain 10X)

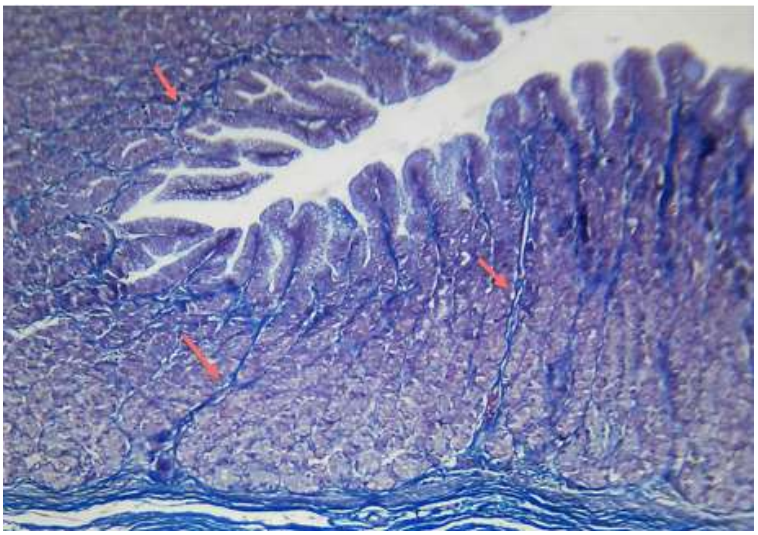
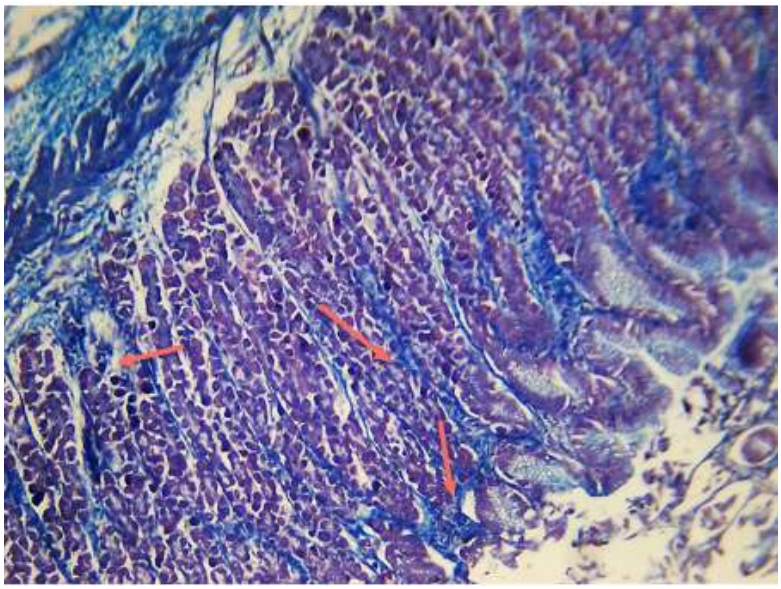


Figure (24): Photomicrograph section in the stomach of exposed dog to 150mmol concentration of HCL at 15 days showed fibrosis expansion (red arrow) that blue color (Masson Trichrome stain 10X)



Figure(25):Photomicrograph section in the stomach of exposed dog to 300mmol concentration of HCL showed extending fibrosis (red arrow) that blue in color (Masson Trichrome stain 10X).

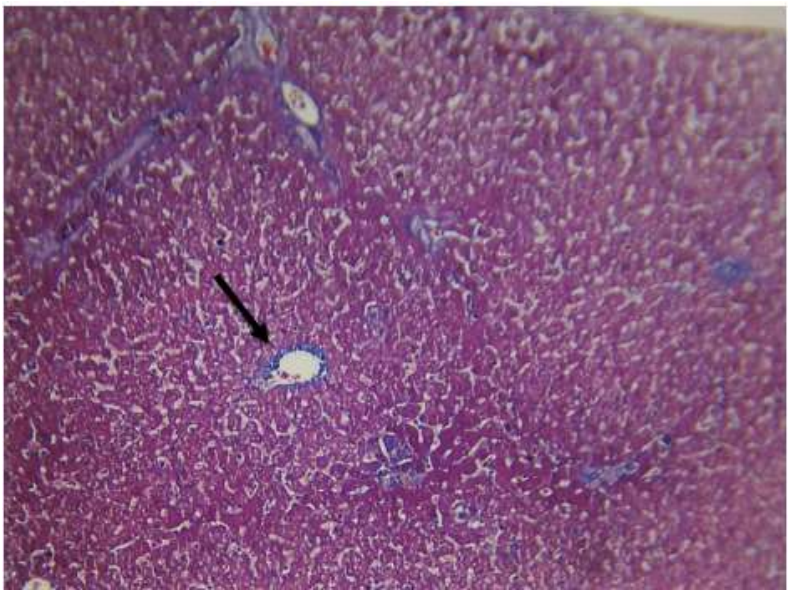
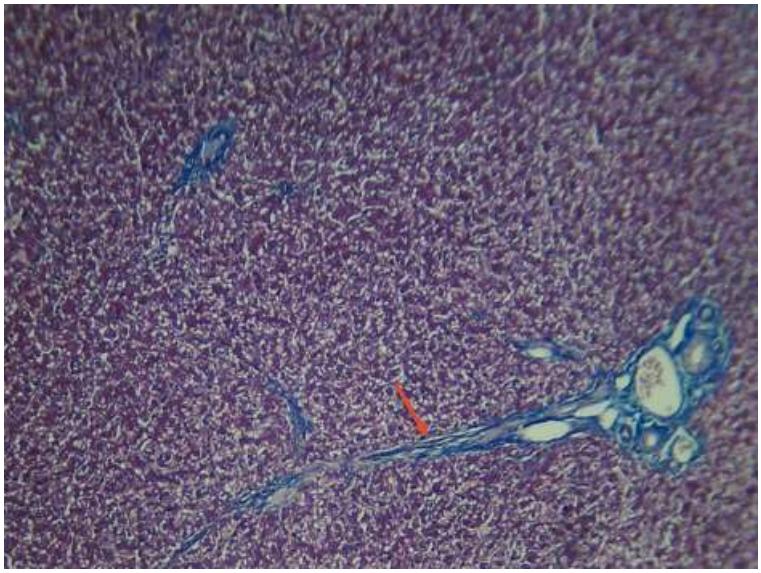


Figure (26):Photomicrograph section of control liver local dog group normal central vein with normal collagen fiber around central vein (black arrow) (Masson Trichrome stain 10X)



Figure(27):Photomicrograph section in the liver of exposed dog to 75 mmol concentration of HCL at 15 days showed fibrosis (red arrow) (Masson Trichrome stain 10X).

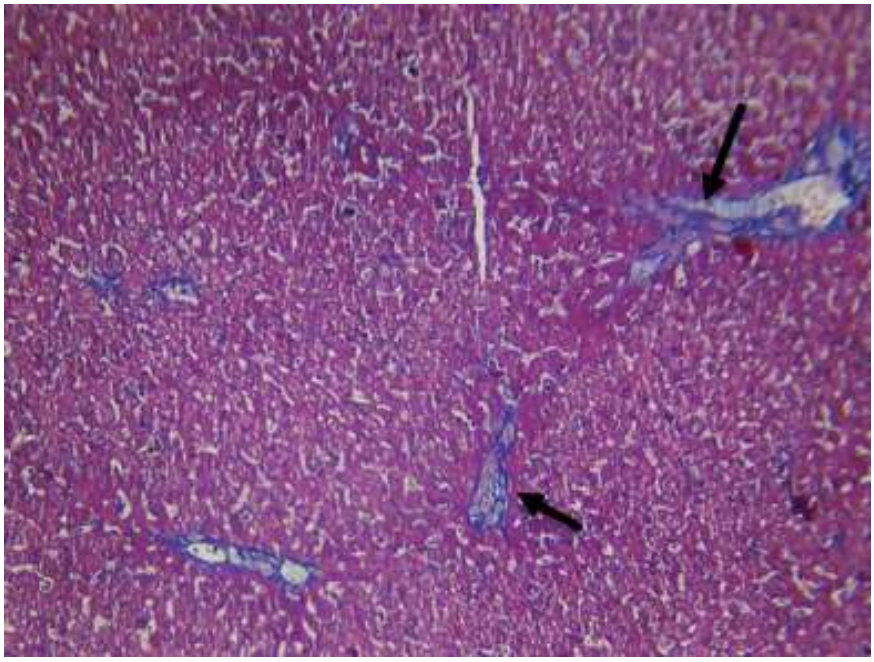
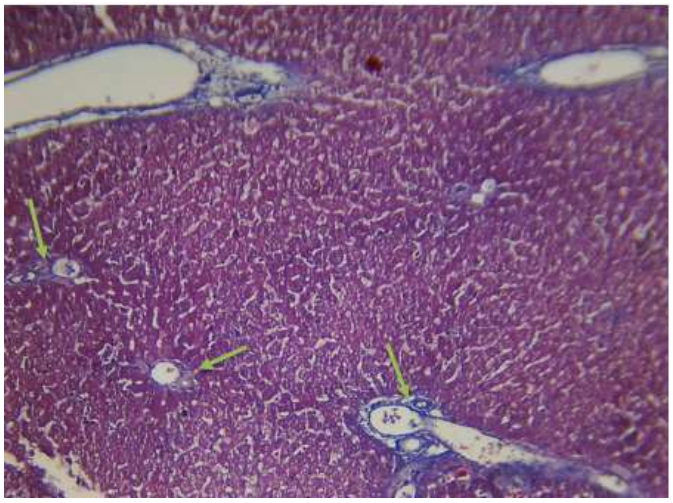


Figure (28):Photomicrograph section in the liver of exposed dog to 150mmol concentration of HCL at 15 days showed perivascular fibrosis (black arrow) (Masson Trichrome stain 10X).



Figure(29):Photomicrograph section in the the liver of exposed dog to 300mmol concentration of HCL at 15 days showed collagen fiber deposition around dilated central vein (green arrow) (masson trichrome stain 10X).

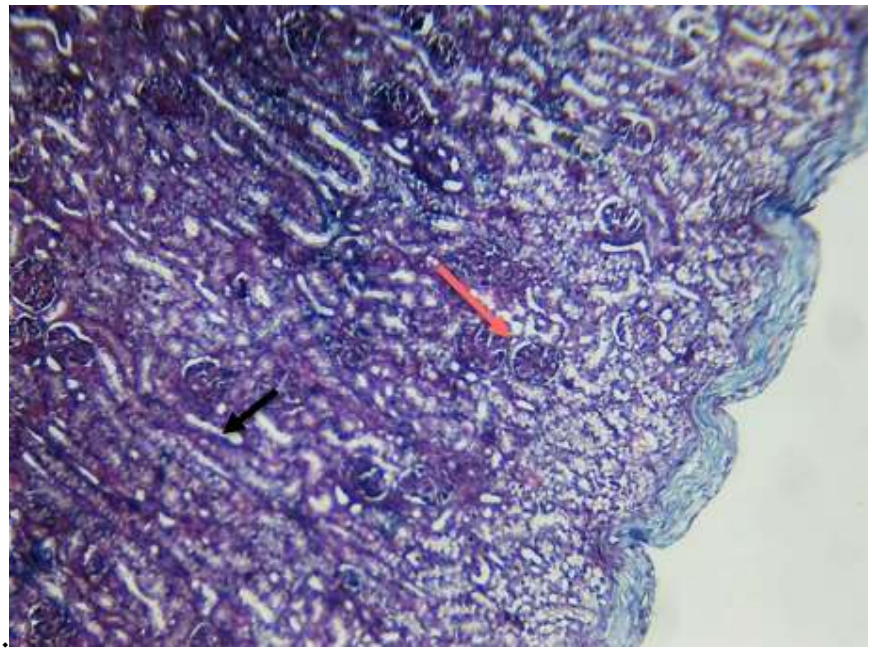


Figure (30):Photomicrograph section of control kidney local dog group normal glomeruli (red arrow) normal tubules(black arrow) (Masson Trichrome stain 10X)

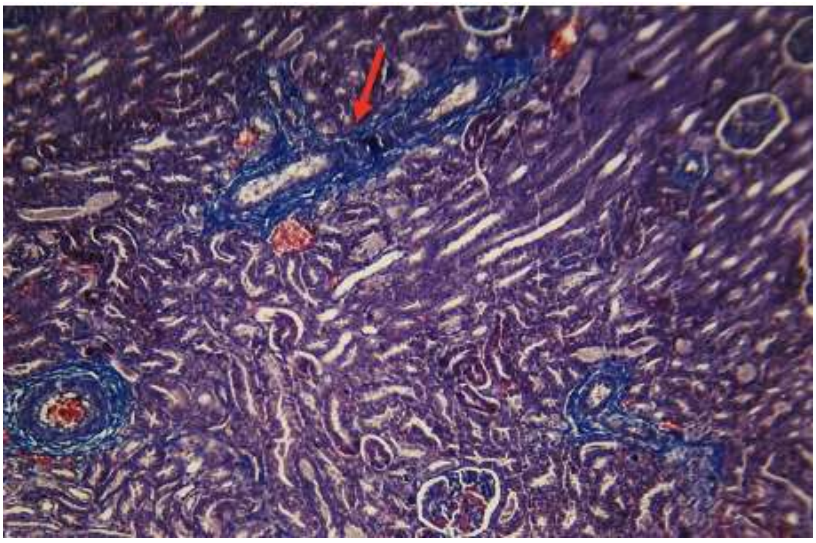


Figure (31):Photomicrograph section in the kidney of exposed dog to 75mmol concentration of HCL at 15 days showed perivascular fibrosis (red arrow) (Masson Trichrome stain 10X)

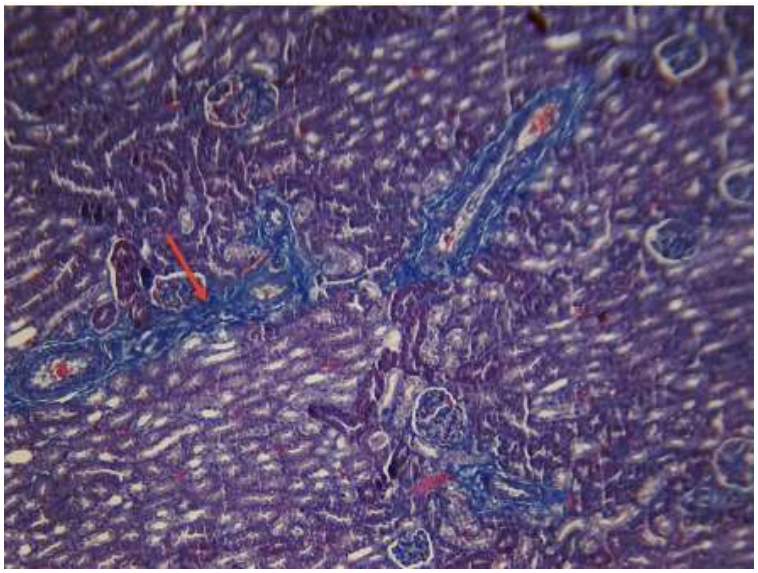


Figure (32):histopathological section in the kidney of exposed dog to 150mmol concentration of HCL at 15 days showed perivascular fibrosis (red arrow) (Masson Trichrome stain10X).

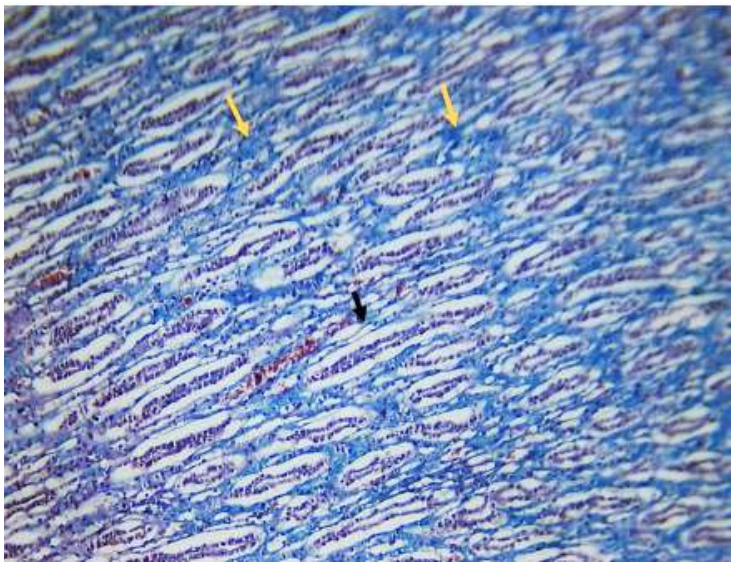


Figure (33):Photomicrograph section in the kidney of exposed dog to 300mmol concentration of HCL at 15 days showed interstitial fibrosis (orange arrows) with tubular atrophy (black arrow) (Masson Trichrome stain 10X).

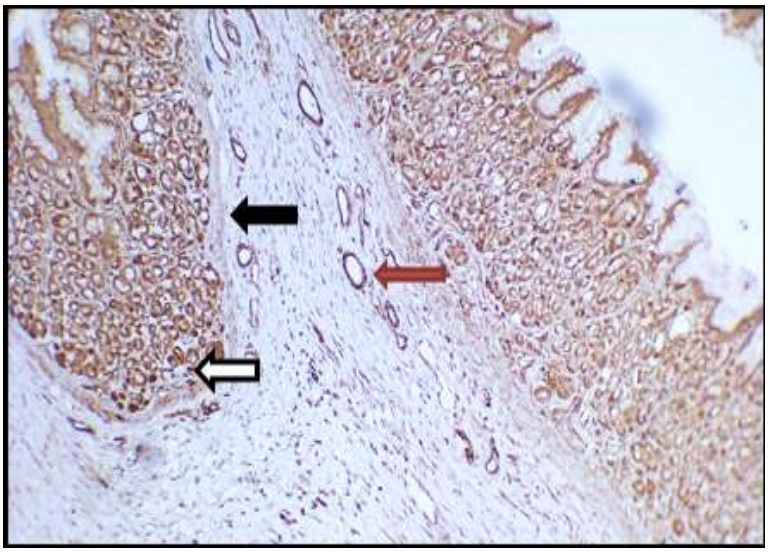


Figure (34):Immunohistochemistry analysis of MDA in formalin fixed stomach sections of normal control dogs at 15 days of experiment. Representative photomicrographs demonstrate the presence of MDA immunoexpression in mucosal glands(white arrow) muscularis mucosa (black arrow)&with intimal blood vessels in sub mucosa(red arrow) (MDA immunostaining X10).

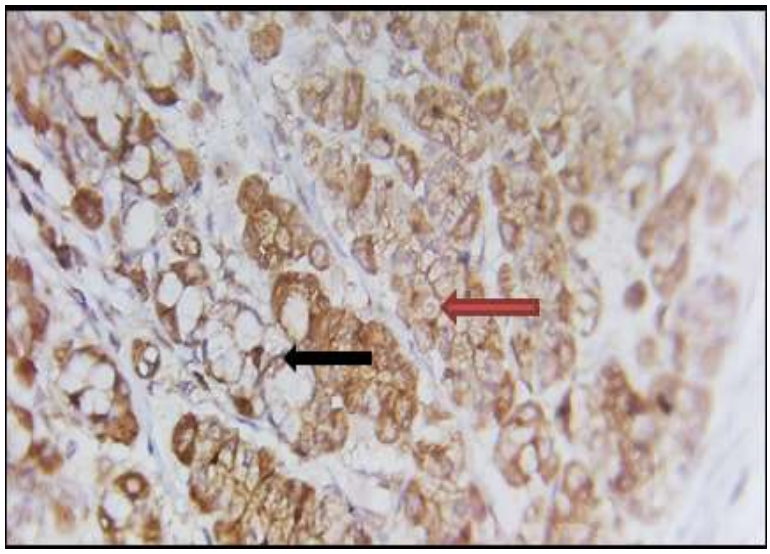
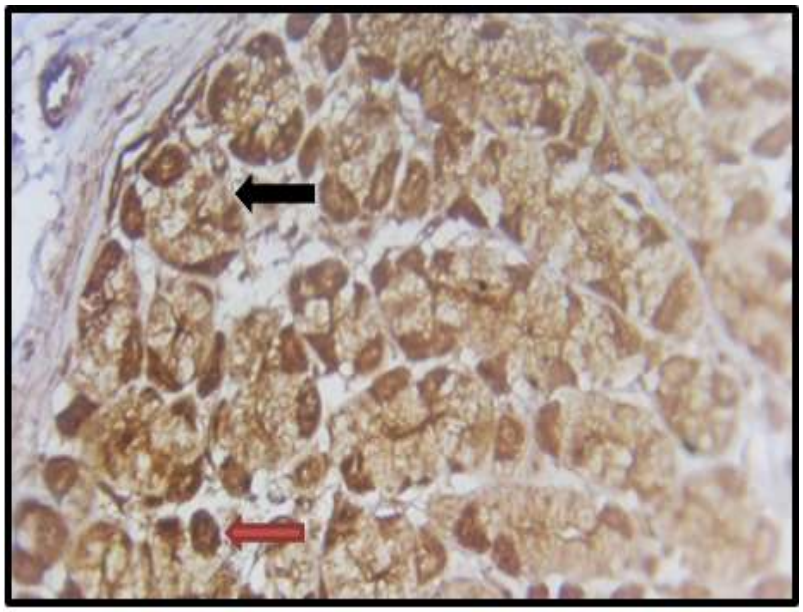
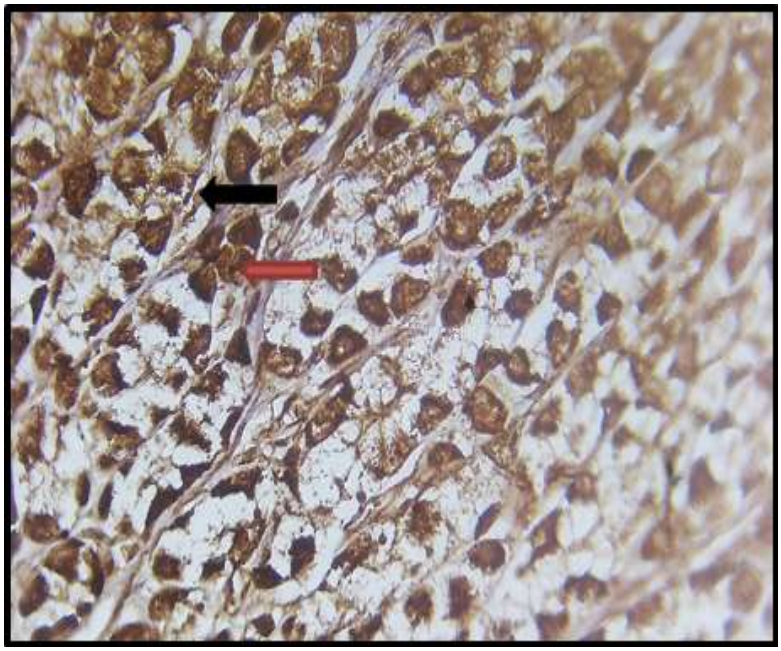


Figure (35):Immunohistochemistry analysis of MDA in formalin fixed stomach sections of 75mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing mild expression of MDA in small intracytoplasmic vesicles(black arrow) with cytoplasm & nuclear cell (red arrow) in mucosal glands (MDA X40).



Figure(36):Immunohistochemistry analysis of MDA in formalin fixed stomach sections of 150mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing moderate expression of MDA in small intracytoplasmic vesicles(black arrow) with nuclear & cytoplasm cells(red arrow) in mucosal glands (MDA X40).



Figure(37):Immunohistochemistry analysis of MDA in formalin fixed stomach sections of 300mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing strong expression of MDA in small intracytoplasmic vesicles(black arrow) with nuclear & cytoplasm cells(red arrow) in mucosal glands (MDA X40).

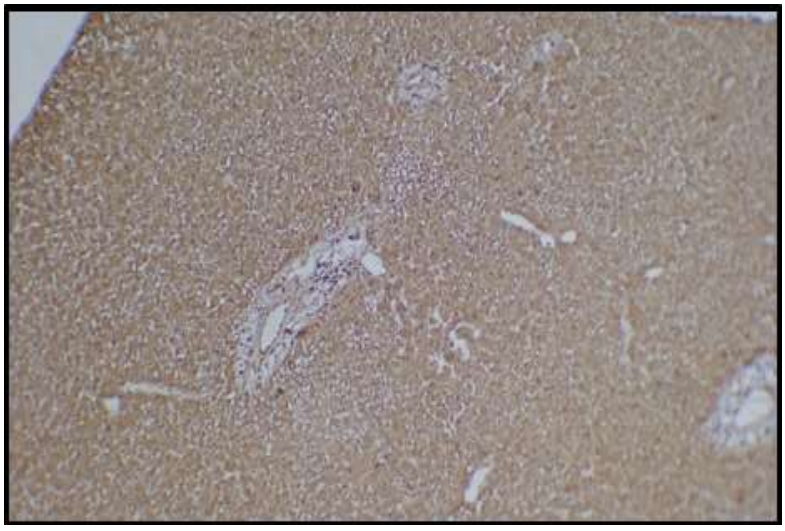


Figure (38): Immunohistochemistry analysis of MDA in formalin fixed liver sections of normal control dogs at 15 days of experiment. Representative photomicrographs demonstrate the presence of MDA immunoexpression (MDA immunostaining X10).

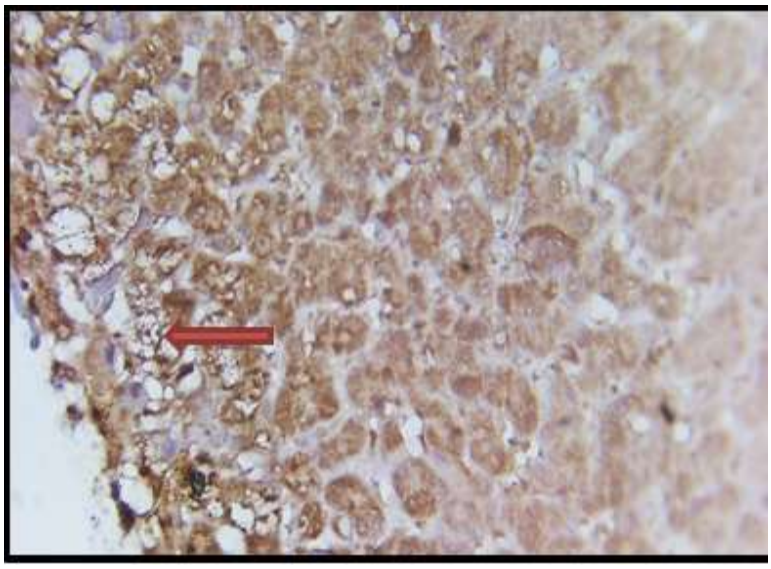


Figure (39): Immunohistochemistry analysis of MDA in formalin fixed liver sections of 75mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing mild expression of MDA in small granules close to steatosis vacuoles or intracytoplasmic vesicles (red arrow) (MDA immunostaining X40).

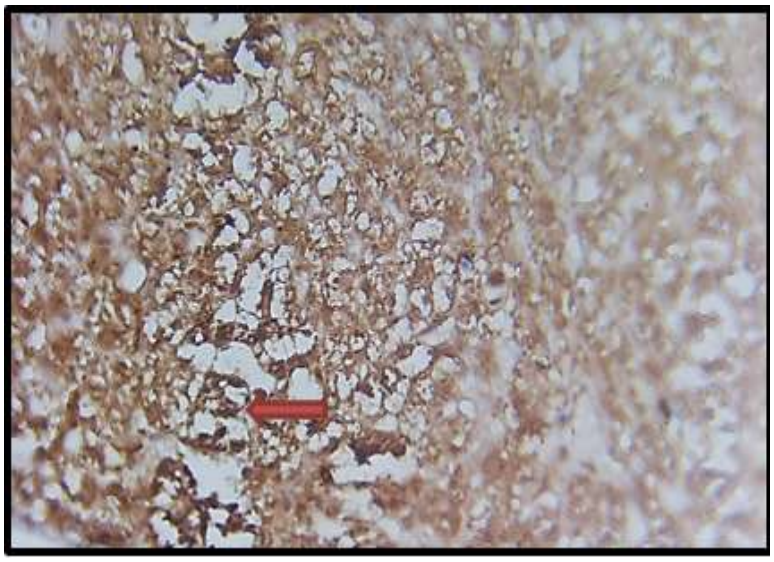


Figure (40): Immunohistochemistry analysis of MDA in formalin fixed liver sections of 150mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing moderate expression of MDA in small granules close to steatosis vacuoles or intracytoplasmic vesicles (red arrow) (MDA immunostaining X10).

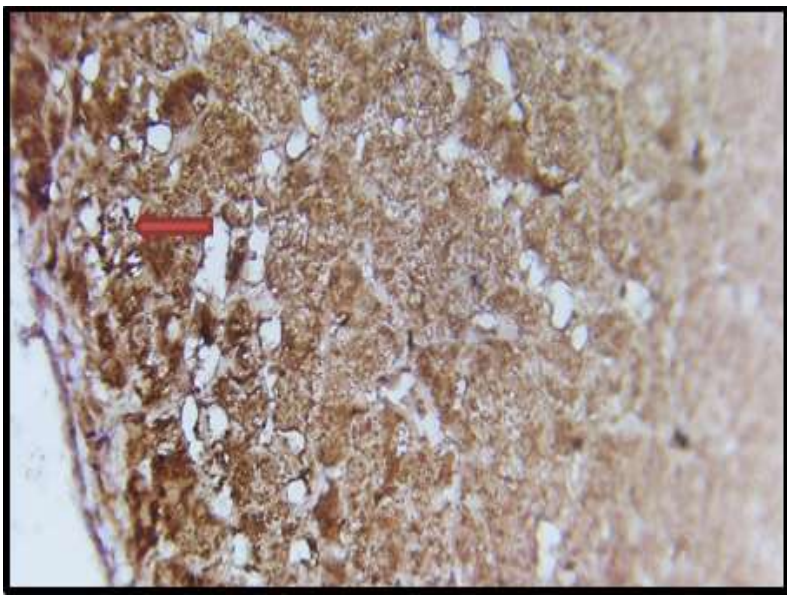


Figure (41): Immunohistochemistry analysis of MDA in formalin fixed liver sections of exposed dog to 300mmol concentration of HCL at 15 days experiment. Representative photomicrographs showing strong of MDA immunoexpression in small intracytoplasmic vesicles (red arrow) (MDA immunostaining X10).

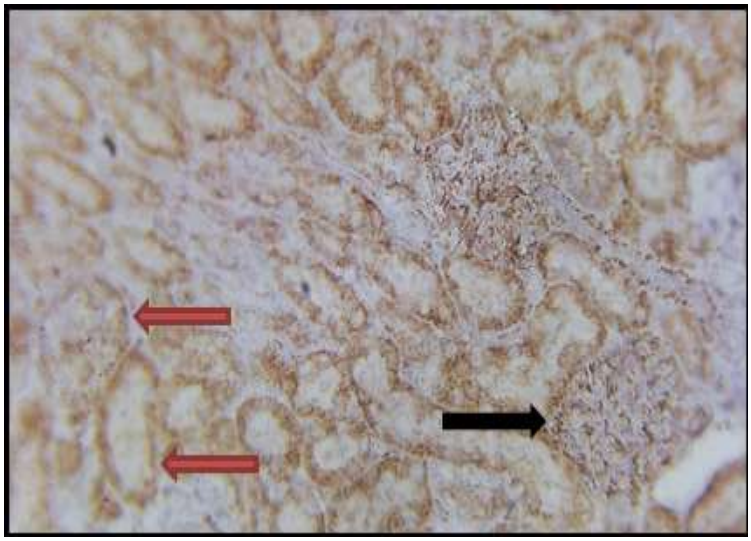


Figure (42): Immunohistochemistry analysis of MDA in formalin fixed kidney sections of normal control dogs at 15 days of experiment. Representative photomicrographs demonstrate the presence of MDA immunoexpression in mesangial area of glomeruli (black arrow) with tubular epithelial cells (red arrow) (MDA immunostaining X40).

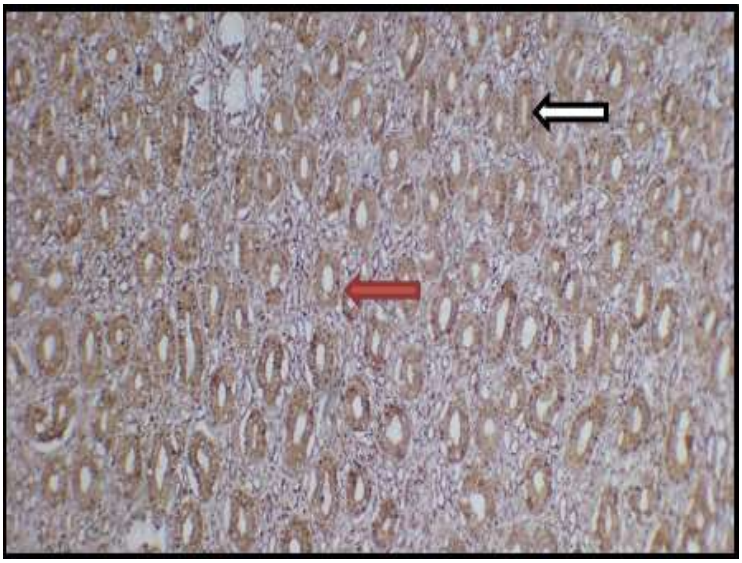


Figure (43): Immunohistochemistry analysis of MDA in formalin fixed kidney sections of 75mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing mild expression of MDA in collecting ducts in middle medullary area (red arrow) & interstitium (white arrow) (MDA immunostaining X10).

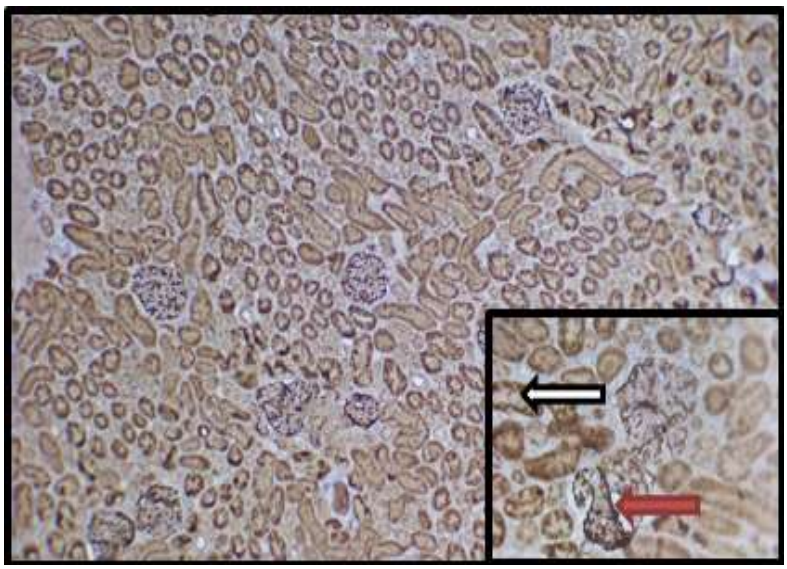


Figure (44): Immunohistochemistry analysis of MDA in formalin fixed kidney sections of 150mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing mild of MDA immunoexpression in granular-like cytoplasmic tubular epithelial cell (white arrow) & mesangial area of glomerular (red arrow) (MDA X40 +10x).

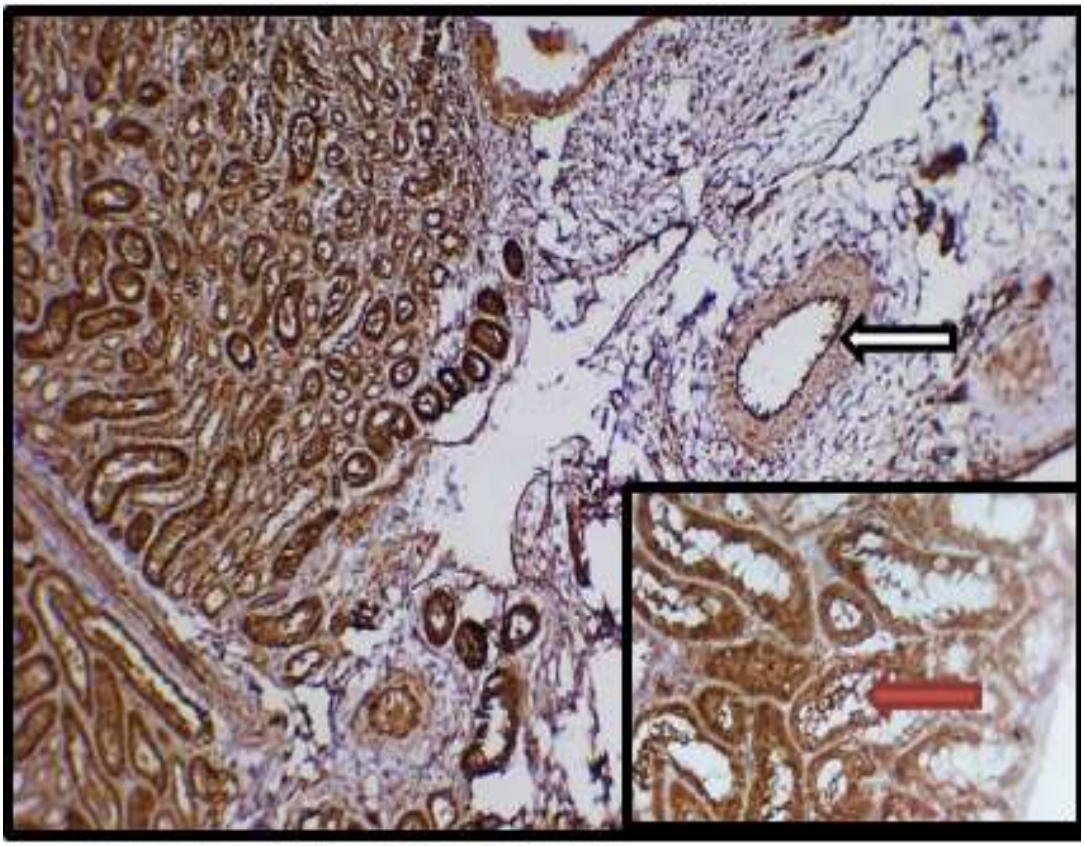


Figure (452): Immunohistochemistry analysis of MDA in formalin fixed kidney sections of 300mmol concentration of HCL at 15 days of experiment. Representative photomicrographs showing strong positive expression of MDA in hypertrophic &vacuolated tubular epithelial cells (red arrow) & intima of arterial walls (white arrow) (MDA X10+40).

Table 1 pH levels in experimental dog.

The current study show, after inducing acidity conditions in the experimental dogs and using intravenous hydrochloride acid, a significant decrease on the seventh and tenth day from the start of the experiment group B(7.37 ±0.018,7.25±0.0158,7.17±0.0158)group C

Groups	0 day	7 day	10 day	Lsd
Group A (normal saline)	7.40 ±0.018	7.38 ±0.017	7.40 ±0.085	0.0623
Group B (75 mM)	7.37 ±0.018	7.25 ±0.0158	7.17 ±0.0158	0.0972
Group C (mM150	7.35 ±0.017	7.272 ±0.017	7.15 ±0.015	0.0252
Group D (300 mM)	7.39 ±0.085	7.272 ±0.067	7.14 ±0.065	0.0453
Lsd	0.0623	0.0531	0.0341	

(7.35±0.017,7.272±0.017,7.15±0.015) and group D (7.39±0.085,7.272±0.067,7.14±0.065)compared to the animals in the control group. On the other hand, it was found that the concentration of 300 M was significantly lower than the rest of the concentrations of the groups showed in table 1

Table 2 lactic acid levels in experimental dog.

Groups	0 day	7 day	10 day	Lsd
Group A (normal saline)	1.5 ±0.015	1.4 ±0.025	1.5 ±0.013	
Group B (75 mM)	1.7 ±0.015	3.624 ±0.025	6.3 ±0.043	0.2187
Group C (mM150	1.4 ±0.025	3.34 ±0.031	6.7 ±0.0077	0.2195
Group D (300 mM)	1.7 ±0.013	3.34 ±0.025	7.3 ±0.0072	0.1918
Lsd 1.23		0.421	0.243	

Table 2 indicate that lactic acid levels increased significantly in dogs induced with acidosis, especially after days 1 and 10, respectively. It was also noted that the rates of increase in this acid gradually increased in concentrations in the 75(1.7±0.015,3.624 ±0.025, 6.3±0.043) 150(1.4±0.025, 3.34±0.031,6.7±0.0077)and 300(1.7±0.013, 3.34 ±0.025, 7.3±0.0072 mM groups.

Table 3 ALT levels in experimental dog.

Groups	0 day	7 day	10 day	lsd
Group A (normal saline)	35.3 ±0.153	37.8 ±0.184	36.7 ±0.144	
Group B (75 mM)	36.3 ±0.153	222 ±0.142	261 ±0.122	0.00266

Group C (mM150	38.66 ±0.184	234 ±0.193	267 ±0.142	0.0287
Group D (300 mM)	35.6 ±0.144	240 ±0.291	264 ±0.158	0.035
Lsd	0.062	0.087	0.066	

Table 4 AST levels in experimental dog.

Groups	0 day	7 day	10 day	lsd
Group A (normal saline)	39 ±0.148	42 ±0.053	35 ±0.114	
Group B (75 mM)	40 ±0.148	105 ±0.118	206 ±0.418	0.0263
Group C (mM150	45 ±0.053	111 ±0.075	210 ±0.024	0.034
Group D (300 mM)	32.9 ±0.114	108 ±0.232	212 ±0.158	0.0293
Lsd	0.0241	0.021	0.051	

Tables 3, 4 indicates that ALT and AST levels increased significantly in dogs induced with acidosis, especially after days 1 and 10, respectively. It was also noted that the rates of increase gradually increased in concentrations in the 75, 150, and 300 mM groups.

Table 5 creatinine levels in experimental dog.

Groups	0 day	7 day	10 day	Lsd
Group A (normal saline)	0.60 ±0.13	0.59 ±0.114	0.61 ±0.130	
Group B (75 mM)	0.58 ±0.13	0.62 ±0.11	0.66 ±0.083	0.0187
Group C (mM150	0.64 ±.114	0.66 ±0.113	0.68 ±0.112	0.0192
Group D (300 mM)	0.64 ±0.130	0.68 ±0.164	0.69 ±0.114	
Lsd	0.023	0.011	0.043	

Table 5 indicate that creatinine levels increased significantly in dogs induced with acidosis, especially after days 0 and 10, respectively. It was also noted that the rates of increase gradually increased in concentrations in the 75(0.58±0.13,0.62±0.11,0.66±0.083)150(0.64±.114,0.66±0.113,0.68±0.112) and 300 Mm(0.64±0.130, 0.68±0.164,0.69±0.114) groups.

Table 6 urea levels in experimental dog.

Groups	0 day	7 day	10 day	lsd
Group A (normal saline)	20.34 ±0.158	19.77 ±0.158	21.43 ±0.321	
Group B (75 mM)	18.32 ±0.158	31.3 ±0.142	33.3 ±0.115	0.0318

Group C (mM150	21.32 ±0.158	33.3 ±0.132	35.3 ±0.116	0.0758
Group D (300 mM)	19.84 ±0.321	24.7 ±0.44	30.7 ±0.26	0.0297
Lsd	0.0121	0.0532	0.0143	

Table6 indicate that urea levels increased significantly in dogs induced with acidosis, especially after days 0(20.34±0.158,18.32±0.158,21.32±0.158, 19.84±0.321)and 10(21.43±0.321,33.3±0.115,35.3±0.116,30.7±0.26), respectively. It was also noted that the rates of increase gradually increased in concentrations in the 75, 150, and 300 mM groups.

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