CLINICAL AND HISTOPATHOLOGICAL INVESTIGATION OF IVERMECTIN TOXICITY IN PIGEONS

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(Received 23 November 2009 , Accepted 14 December 2009)

Keywords; liver, kidney**,** ivermectin**.**

ABSTRACT

The aim of this study was to investigate the clinical signs and histopathological changes of acute toxicity of ivermectin in the centeral and peripheral nervous system liver, kidney, pancreas and heart of pigeons after s/c injection with ivermectin .Eighteen bird were divided into three equal groups.Group A were injected with 8mg,group B were injected with 10 mg and group C served as control group.The results showed markedy reduced of water and food consumption ,somnolence and death of treated pigeons.Nervous signs were restlessness, ataxia, un steady gait, tremor and recumbent. The histopathological changes included degeneration of nerve fibers of spinal cord and sciatic nerve .Degeneration , necrosis and vacuolation were noticed in liver, kidney and heart,as wll as proliferation of bile duct was also seen in liver.

INTRODUCTION

Ivermectin is an antiparasites medication and is it effective against most common intestinal worms,most mice and som lice.While normaly used to treat animals ,it is also prescribed to human to treat infestation of *srongyloides stercoralis*.(1).

It is effective against all kinds of internal and external live stock and poultry parasites,including internal parasites such as nematode,pinworm,filarial,trichinella spiralisand external parasites such as mite, louse, tick, flea, fly, maggot, larva, used in rabbit, chickens, goose, cat, fox and other wild animals.It has good clinical efficacy to treatment of pig scabies rabbit scabies,ring worm and scabies of rabbit ,chickens knee mite,(2).It is slso used to treat internal parasites (*Ascaridia gall*i) of infected white leghorn chicks at dose of 0.3-1mg/kg bw for 10 and 35 days.

Ivermectin exert their anti-parasitic activity via the activation of glutamate-gated chloride channel present un the invertebrate nerve and muscle cells(4,5), and /or trough the effect on gamma amino butyric acid (GABA) receptors(4,6,7),leading to paralysis and death of target organisms.In the vertebrates , ivermectin can produce GABA-mimetic effect agonist

at GABA receptors,stimulating the release of GABA, or through other mechanisms(6,8,9).Mammals ,however,are less susceptible to the toxic effects of ivermectin because GABA-mediated nervous occure in the nervous system (CNS) and ivermectin do not ready cross the blood –brain barrier(BBB;6).

Ivermectin is a semi-synthetic derivative of one of the avermectins , a groupm of macrocyclic lactones produced by the soil bacterium *Streptomyces avermitilis*(10).Peneteration of the blood –brain barriers occurs in releatively high doses ,with brain levels peaking between two and five hours after administration .Symptomas seen in a range of mammalian species are CNS depression ,consequent ataxia,as might be expected from potentiation of inhibitory GABA-ergic synapse(11).

Aim of this study was to investigate the clinical signs and histopathological changes of acute toxicity of ivermectin of pigeons.

MATERIALS AND METHODS

Rock dove pigeons(*Culumba livia*) purchased from local market in basrah province ,with average body weight of (250-400)gm were used in this study .They were reared in cages (100x100x 80) in poultry unit /at the college of veterinary medicine Basrah university .and treated with ivermectin after 7 days of their rearing.

Primary trails were conducted to determine the maximum tolerated dose through using different doses till reaching 8mg and 10 mg/kg body weight of ivermectin . Eighteen birds were divided into three groups ,Group A were injected s/c with 8mg /bird of ivermectin ,while birds in group B injected s/c with 10 mg of ivermectin and the group C served as control group .Clinical signs were recorded .Tissue samples were taken from spinal cord ,sciatic nerve ,liver,pancreas and kidney to study the histopathological changes

Representative tissue samples were taken and fixed in 10 neutral buffered formalin .After prolonged washing in tap water the sections of tissues were dehyderated in ascending grades of alcohol and then cleared in xylin . Paraffin section of 5 μm thickness ,were cut and stained with heamatoxylin and eosin(13) .

RESULTS AND DISCUSSION

A-Clinical signs

Clinical sings of ivermectin toxicity included ataxia ,sedation ,tremor ,coma ,somnolence and listlessness were developed 4 hours post s/c injection of 8 mg ivermectin /kg bw.Five bird of group A were deaed after 48 hour of dosing .These results in the line with that of (14) who mentioned the same clinical signs in falcon(*Falco rusticolus*).The group B exihibited more sever clinical signs than that of group A .All bird of group B were died after

40 hour of dosing with 10 mg ivermectin /kg bw. The same results were recorded in chickens (15).

These results attributed to high doses of ivermectin or mutation in p-glycoprotein which can allow ivermectin to pass through the blood – brain barrier to cause neurotoxicity in animals (15), manifesting diarrhea ,depression ,ataxia,coma, tremor and death(16,17). In this study the signs of ataxia ,tremors,sedation ,somnolence and coma were in agreement with (18) who observed that the feed and water consumption were markedly reduced .Bradypnea ,ataxia ,sedation ,coma and death occurred with the highest dose of ivermectin in chickens .This result was in line with that of (16) who recorded that dose –releated toxicity was also found in chickens,

Ivrmectin ,given ton rat IV at dose of 4 mg /kg produced moderate incoordination ;6 mg /kg induced a state rresembling anaesthesia which began one minute after injection and lasted for four to five hours .Higher doses caused death in most type of animals due to respiratory depression (11).Four of eight dog given 2mg /kg/day developed tremors,ataxia ,anorexia and become dehydrated (12).

B-Histopathological examination;

Pigeons injected s/c with 8 mg of ivermectin were showed histopathological changes either in peripheral nerve (sciatic nerve) or in spinal cord as degenerate nerve fiber of both ,these results conflicted with(15) who did not report any histological cganges in chickens.Young animals are generally more sensitive to the toxicity of ivermectin.A kitten was reported to exhibit toxicosis afterb receiving subcutaneous administration of 0.3 mg/kg ivermectin(7).Animals deficient in p-glycoprotein a component of the blood brain barrier are also more sensitive to ivermectin toxicity than animals with normal p-glycoprotein level(14,15).Solvents and additives of commercial avermectins (hexanol,butylated hydroxytoluene) may enhance the toxicity as well(19).Adverse effects of ivermectin therapy are not un common and most of them appear within 48 hour of initiating therapy(20,21.22).

The present study revealed ,area of hepatic necrosis in group B and hepatic cell degeneration with marked vacuolation of hepatocytes in group A.These results were in disagreement with those of(15) who did not report any histological changes in chicken injected s/c with ivermectin. This may be explained by the fact that pathway and primarily ivermectin is metabolized in the liver via oxidative , and excreted in the feces while less than 5% of ivermectin is excreted in the urine. A very large numbers of etiological agents are capable of causing necrosis such as medications (23).

The study revealed ,no evidence of effect of ivermectin in the pancreas. The results revealed ,vacuolation of renal cortical tubules .The present study exhibited bile duct proliferation and dilatation and congestion of artery in myocardial muscles .These results were in disagreement with that of (15).There is no previous study releated to this work.

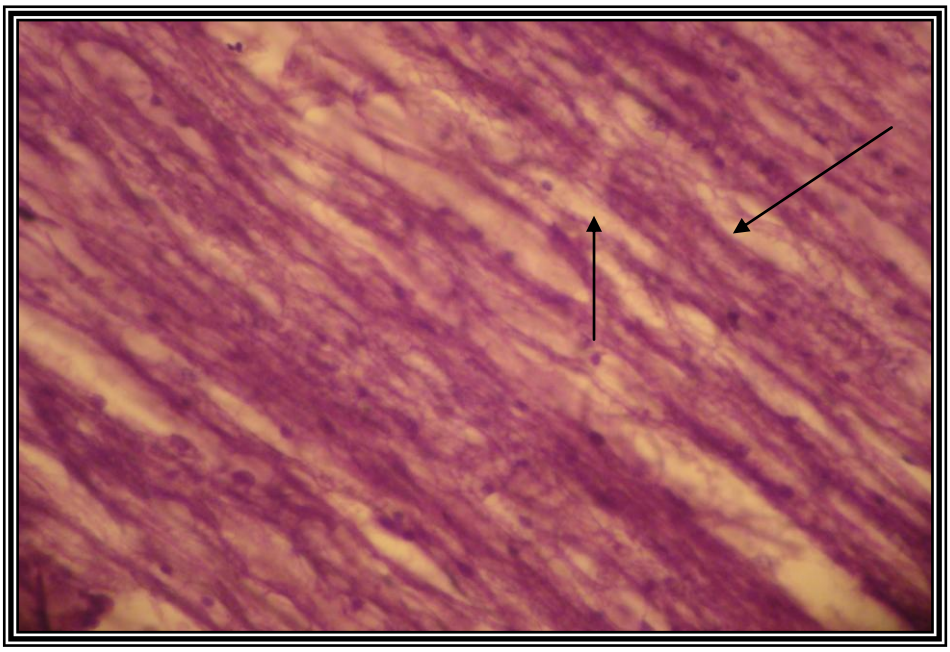


Fig.(1) Group A. Sciatic nerve. Longitudinal section . degenerate and vacuolated nerve fibersx200

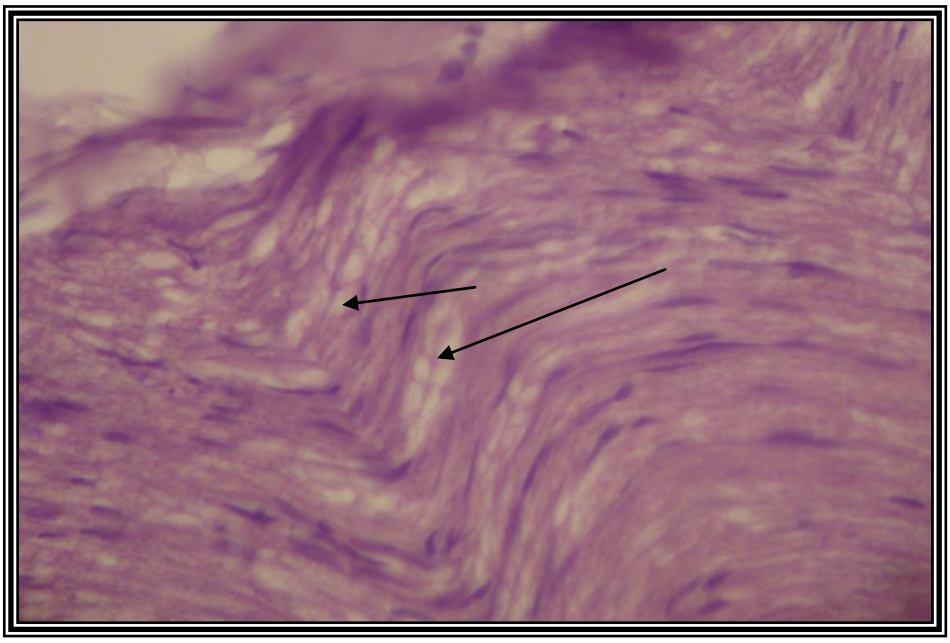


Fig. (2): Group B. Sciatic nerve .Longitudinal section . Vacuolated and degenerate nerve fibers.X200.

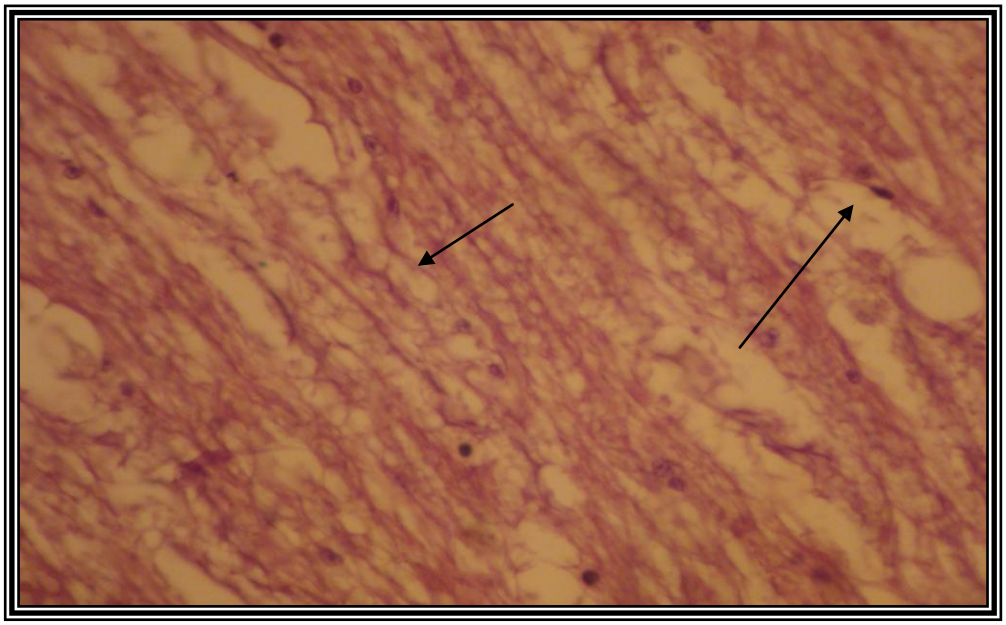
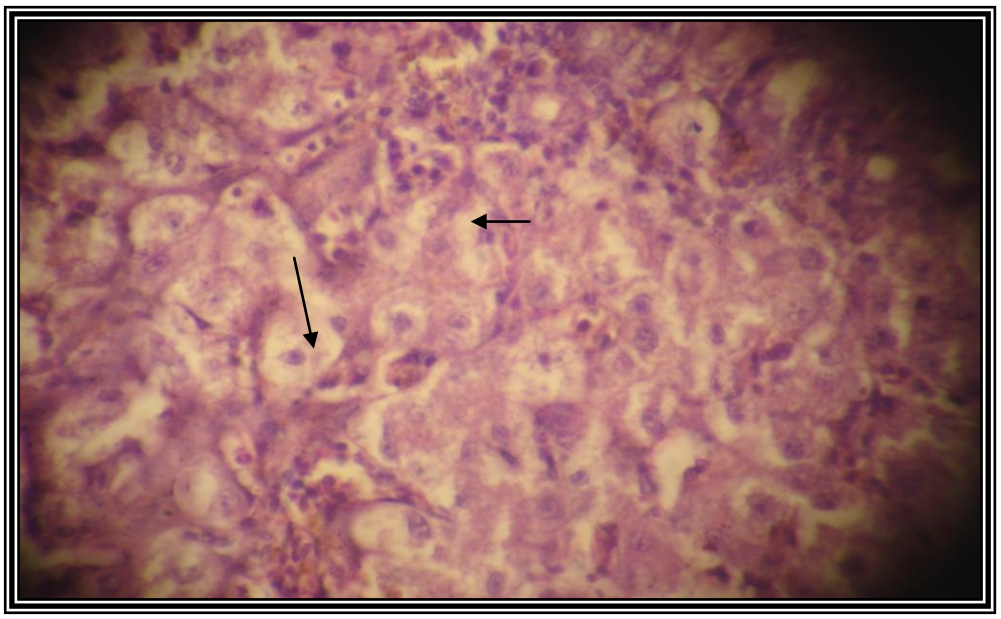
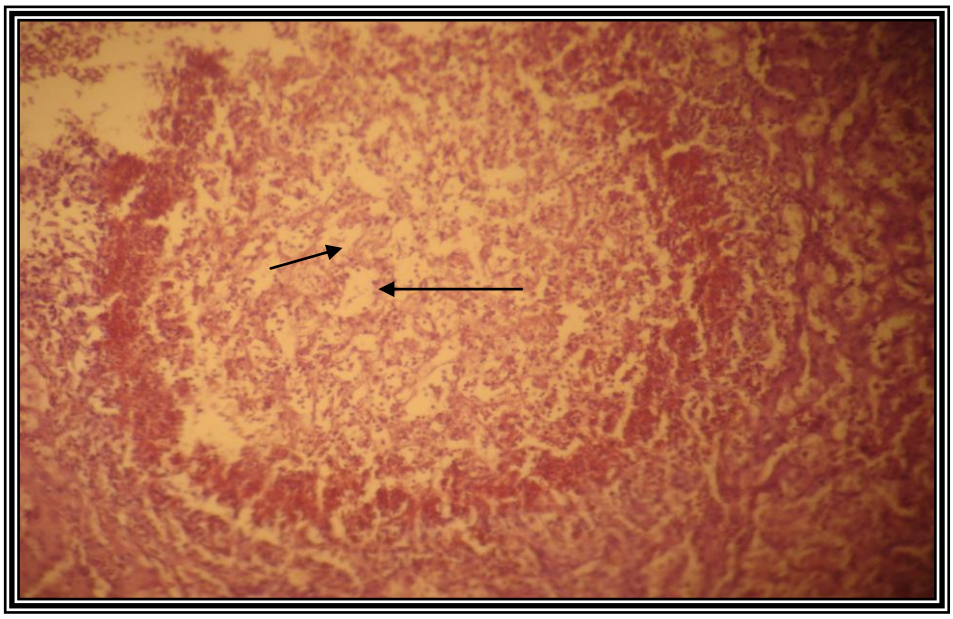


Fig.(3) Group A Spinal cord. Longitudinal section .degenerate and vacuolated nerve fibers x200



Fig(4) Group B . liver .transverse section. degeneration X200



Liver.Transvers section. necrosis X200. Fig(5):Group A.

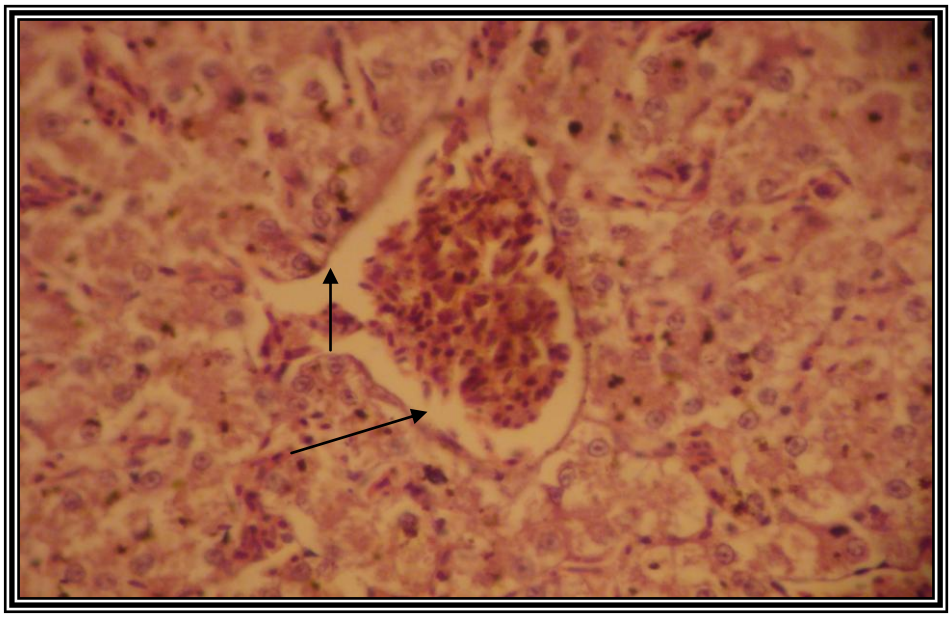


Fig.(6):Group B. Liver .transverse section. necrosis. X200.

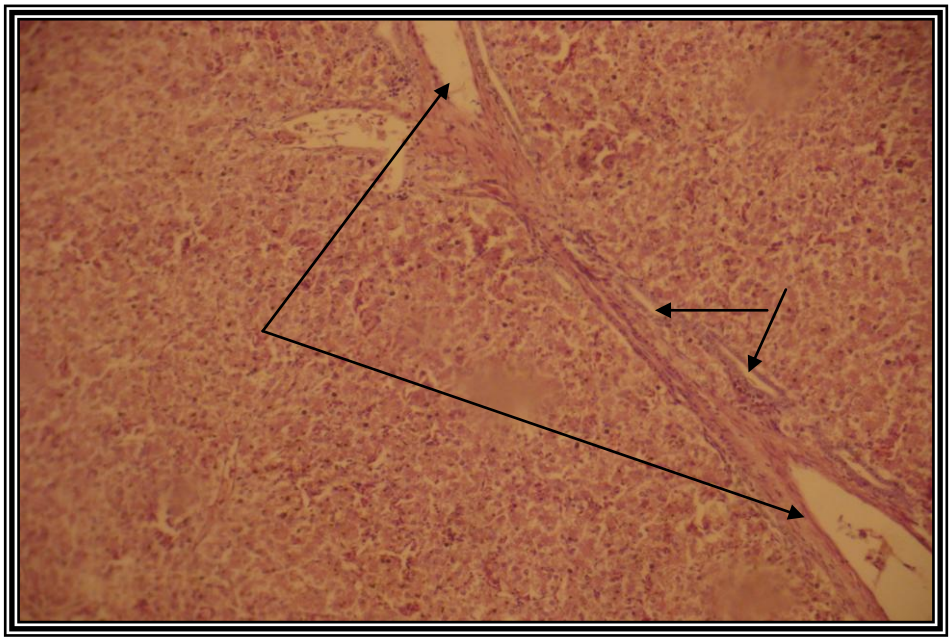


Fig. (7) Group B . Liver.portal vein dilatation, Bile duct proliferation.X200

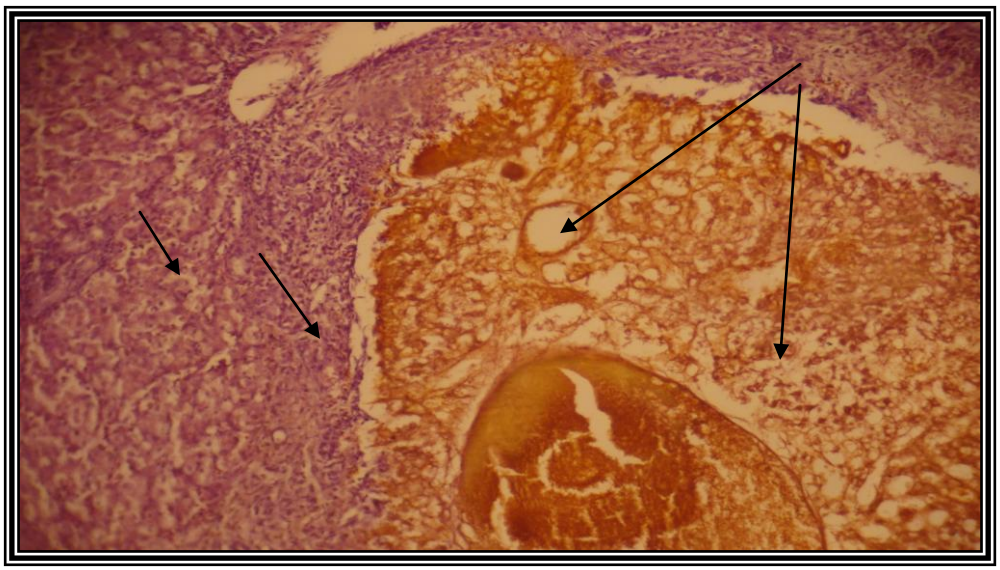
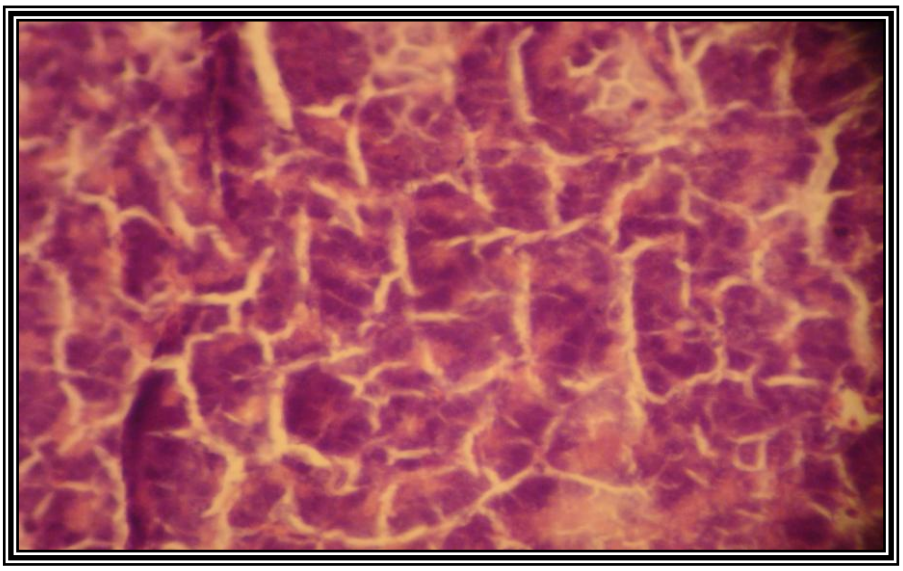
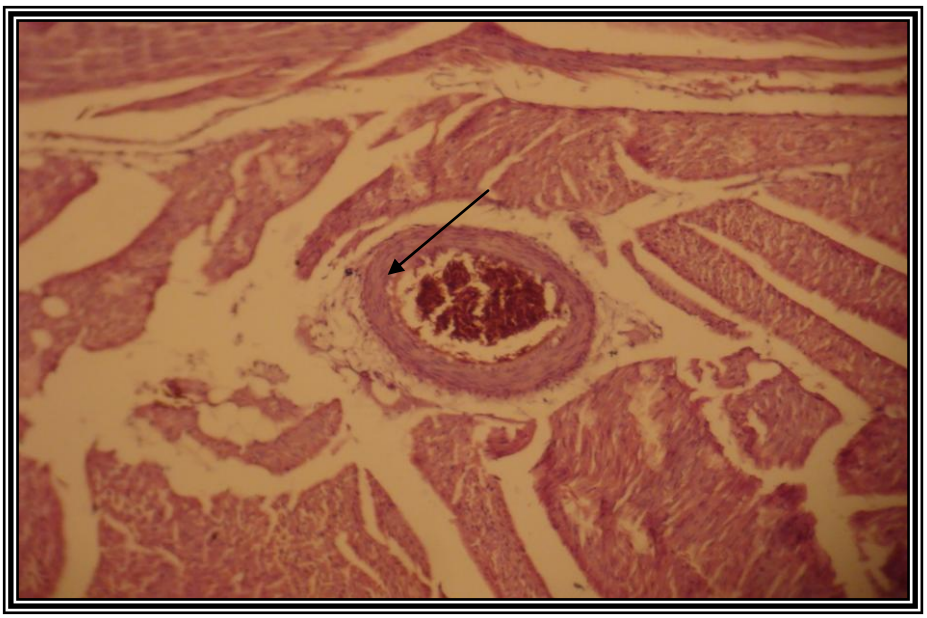


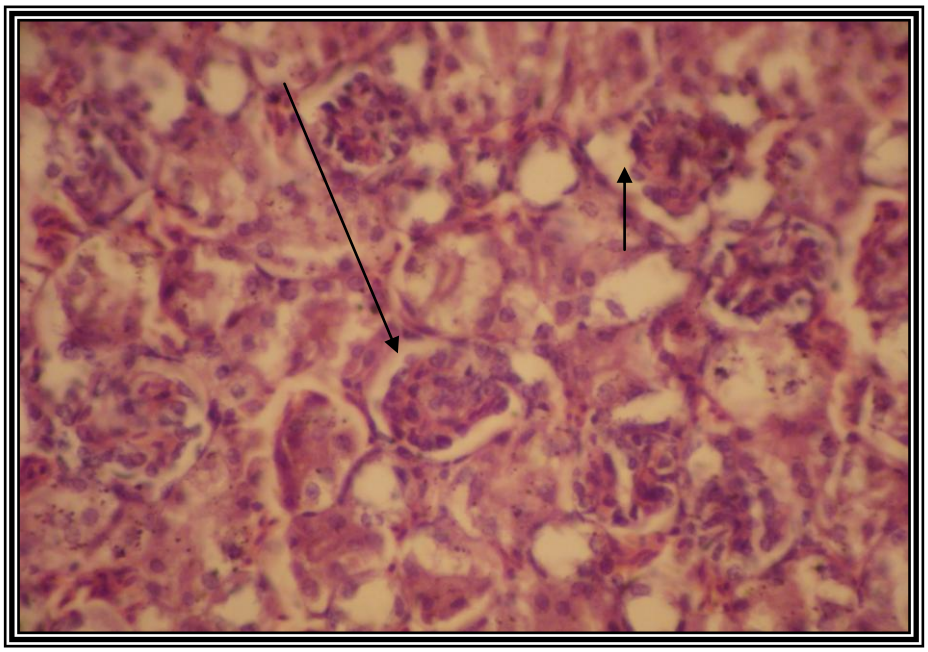
Fig. (9) Group A. Liver . Transverse section a- Congestion b- haemrorrhage. Periportal fibrosis with inflammatory cells. X800.



Fig(10) Group A .Pancreas.longitudnal section. Exocrine and endocrine . There is no evidence of effect on exocrine or endocrine part of the pancrease. X200.



Fig(11): (Group A)Heart-myocardial muscle. Congested artery.X200.



Fig(12): Group A. Kidney. Transverse section. vaculation of renal cortical tubules.200X

دراسة سريريه و نسجية مرضية للتسمم بالايفرمكتين في الحمام .

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الخلاصة

كان الهدف من الدراسة هو تقصي العلامات السريرية والتغيرات المرضية النسجية للتسمم الحاد بالايفرمكتين في الجهاز العصبي المركزي والمحيطي و الكبد والكلية والبنكرياس والقلب في الحمام بعد حقب الايفرمكتين تحت الجلد. قسمت 18 طيرا الى ثلاثة مجاميع متساوية . حقنت المخموعة ا 8 ملغم ،بينما حقنت المجمعة ب 10 ملغم ،اتخدت المجموعة س كمجموعة سيطرة .اوضحت النتائج انخفاض واضح في استهلاك العلف والماء والخمول وموت الحمام المعامل .كانت العلامات العصبية :الترنح والمشية غير المتزنة والرعشة والرقود. تضمنت التغيرات النسجية المرضية تنكس الالياف العصبية للحبل الشوكي والعصب الوركي. لوحظ التنكس و التنخر و التفجي في الكبد والكلية وايضا تكاثر القناة الصفراء.

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