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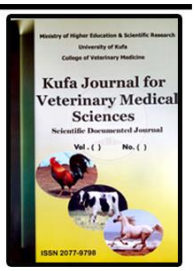

Histopathological study of effects phenobarbital in Goats

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Abstract

In this data was done to demonstrate the administration of phenobarbital compounds & showed histopathological effects. In this study fourteen of local goats were divided into two groups (each group seven animals) for 60 days. First one were treated phenobarbital injected with 35 mg \kg.B.W.,twice daily ,second group act as control group. These animals were examined internally and externally during adaptation period. After end experimental period scarified the animals, necropsy, preparation of slid by routine technique and examined by light microscope, there are showed different histological changes into tissue of animals treatment with phenobarbital such as degeneration of epithelial cells lining of renal tubules of kidney and thyroid gland congested of central vein with fibrosis in liver ,vacuolated of mucosal layer of rumen, small intestine and pancreas, atrophyseminiferous tubules of testis and lymph node.

Key word:- Pathology,phenobarbital, ,liver kidney,pancrease, , , rumen, small intestine, lung, , testis, and sciatic nerve.

دراسة نسيجية مرضية لتأثير الفينوباربيتول في الماعز(capa hircus)

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الخلاصة:

تم اخذ اربعة عشر من الماعز المحلي وقسمت الحيوانات الى مجموعتين كل مجموعة تحتوي على سبعة حيوانات المجموعة الاولى بالفينوباربتول 35 ملغم / كغم من وزن الجسم بمعدل جرعتين يوميا لمدة 60 يوم والمجموعة الاخرى تمثل مجموعة السيطرة وبعد انتهاء مدة التجربة تم اجراء الصفة التشريحية تحضير السلايدات من الاعضاء بواسطة التقطيع النسيجي الاعتيادي وفحصها تحت المجهر الضوئي حيث ظهرت التغيرات المرضية النسيجية على الكثير من الاعضاء وجود التنكس النسيجي للخلايا المبطنة لكل من الكلية ووجود الاحتقان في الاوعية الدموية للغده الدرقية ووجود التلف في نسيج الكبد ووجود التفجي في الخلايا المبطنة للكرش والامعاء والبنكرياس كما اوضح الفحص المجهري ووجود الضمور في النسيج الخصية والغدة اللمعينة

Introduction:-

Phenobarbital(PB) is anticonvulsants compound which is depended into Barbiturates, Hydantoins, Oxazelidones, Succinamides, Glutarimide group, Acetyl urease, Acidifying agents,Benzodiazepins and Bromide(1).Phenobarbital is a long-acting , antiepileptic drug (AED) and a popular choice in many industrialized countries(2).PB is white powder, molecular

weight 232.2 g\mole,chemical structure C12H12N2O3 (3). (4), it work by depressing the central nervous system(4,5,6).This group of drugs (PB), control the brain activity and phenobarbital tend to act on two GABA it is neurotransmitter that has nerve- calming properties and (PB) increase this neurotransmitter(7)and it used to help calm or sleep during periods of anxiety(drawls symptoms),hallucinations, or twitching (8).(PB)has been used prenatally and postnatal to prevent and treat hyperbilirubinemia(familial non-hemolytic, non-obstructive jaundice),to prevent intraventricular hemorrhage at birth(9,10). PB also can cause drowsiness in some infants who were exposed in utero, adequate weight gain and developmental milestones, especially in younger(11) There are reports that is sure liver paraoxanase and arylestrase activities were increase in rats orally treated with phenobarbital, the semi researchers found that (PB)caused decrease in brain tissue superoxide dismutase activity(9,12,13).(PB) is chemical compound known to effect on the endocrine system through different pathways, it is effect on urinary bladder lead to make cyst or hydronephrosis unilateral, missing one lobe of prostate, alopecia of skin limbs, coagulating of seminal vesicles glands with leaked fluid, severe allergic reactions (rash, hives, itching, difficulty breathing, tightness in the chest, swelling of mouth, face and lips(14,15), experimental method was given basal diet containing 0.05% PB for 32 weeks of rats male showed that PB is a tumor promoter in the liver, thyroid gland and urinary bladder(16).Phenobarbital is increased protein synthesis in the mitochondria and its morphological shape changes in liver of rat (17).Phenobarbital a unique ability to induce the microsomal enzymes which means that chronic exposure to (PB) makes the liver more efficient removing other toxins other medications that will not work well with phenobarbital include Chloramphenicol (an antibiotic), estrogens, cardiac beta-blockers,and quinidine(heart rhythm medicine), theophylline(an air way dilator)…etc.(18,19).Phenobarbital induce hyaline membrane disease and fluctuating cerebral blood flow lead periventricular hemorrhage(2o).

Material and methods:-

Experimental Animals:-

Fourteen adult healthy male of local goats were selected from market in Basra were aged between 9-12 months and weight about 25-35kg put in college farm of the veterinary college of Basra University. The animals were examined by clinical signs with internal and external parasites examination by using Ivermectine drug.

Experimental Design:-

The total numbers of 14 male goats were divided randomly into 2 groups, the first group was treated with 35 mg\kg B.W of phenobarbital twice daily for2 months by injected . but ,the second group act as control group.

Histopathological Examination:-

The specimen were taken from animals after necropsy after ending the experimental periods, these organs include (liver, kidney, spleen, rumen, small intestine, pancreas, thyroid, lymph node, testis, nerve, skin) which were fixation in 10% formalin, dehydration was done by passing the specimens upgrading concentration of ethanol, than infiltrated two times with xylene, embedded in paraffin and cutting about thickness 5um by microtome and stained with Hematoxylin and eosin and then examined by light microscope (21).

Results:-

There is such clinical signs in this study present after injected phenobarbital

including dullness, increase body weight, and drinking a lot of quantities of water.

Histopathological study :-

1- LIVER:There are investigated aggregation of fibrocysts around portal duct and perivascular tissue, there are Hemosiderin pigmented into hepatic tissue swelling the cells due to degeneration of hepatic cells figure (1), some of cells are necrotic, congestion of central vein with fibrosis and hyperplasia of epithelial cells lining of portal duct figure(2,3) .

2- RUMEN:-there were clear vacuolated of epithelial cells of mucosal layer, increase amount of collagen fiber in sub mucosal layer figure (4), and there is white space in the muscular layer figure (5).

3- SMALL INTESTINE:- there are changes in intestinal tissue example vacuolated of epithelial cells of villa with proliferation of it ,there were excessive of inflammatory cells with hemorrhage and spaces of edema figure (6). but, there were fibrosis as well as inflammatory cells and new capillaries in submucosal layer ,there were different empty white space into the muscular layer figure (7).

4- SPLEEN:-When we examined the section of spleen there are thinking with vacuolated of capsule and hemorrhage area of splenic tissue figure (8),as well as narrowing of arteriole lumen due to thickening of its wall figure (9).

5- PANCREASE:-After ending of phenobarbital injected period showing degeneration of acini epithelial cells and the islets of Langerhans with amount of edema figure (10).

6- THYROID GLAND:-In the present study there was atrophy of some acinia of this gland and there edematous fluid perivascular with infiltration of inflammatory cells as well as vacuolated of epithelium cells lining of acinia figure (11) with hyperplasia some other epithelial cells figure (12).

7- LUNG:-Showing hyperplasia of epithelial cells of bronchiol ,dilaited of alavolar figure (13,14).

8- LYMPH NODE:-In this research there were atrophy of lymphoid follicle tissue or separated lymphocyte figure (15), infiltration of fatty cells, congestion of blood vessels in lamina properia with fibrosis figure (16).

9- Kidney:- Show swelling epithelial cells of renal tubules and there were space surrounded by one layer of flat cells which was full with pink fluid these are present as cyst shape into the tissue. In other section there are vacuolation in epithelial cells of proximal renal tubules with glomerulus and cellularity of jackstay part figure (17).Some of renal tubules are small in size due to atrophy with necrotic area figure (18).There is hemorrhage of interstitial tissue,desquamates of epithelial cells into lumen of renal tubules which lead to close to each other figure (19,20).

TESTES:-

Phenobarbital injected for long time appeared congestion of blood vessels and suppression of spermatogenesis in the semineferous tubules (21),some of epithelial cells were necrostic (22),sever vacuolated of semineferous tubules cell and present due to accumulation of nuclei as multinucleated of spermatic giant cells(23).

EPIDYDIMUS:-

Sever atrophy of duct (24) and there were less hyperplasia of epithelial cells lining (25).

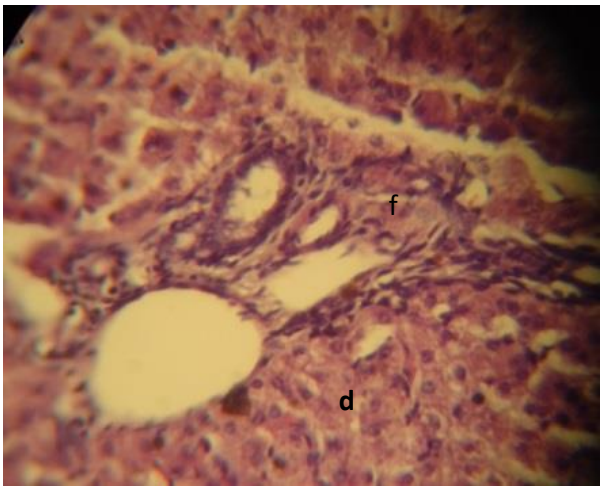


Figure (1):-section of liver treated with PB note degeneration of hepatic cells(d)and fibrosis(f)x10 H&E.

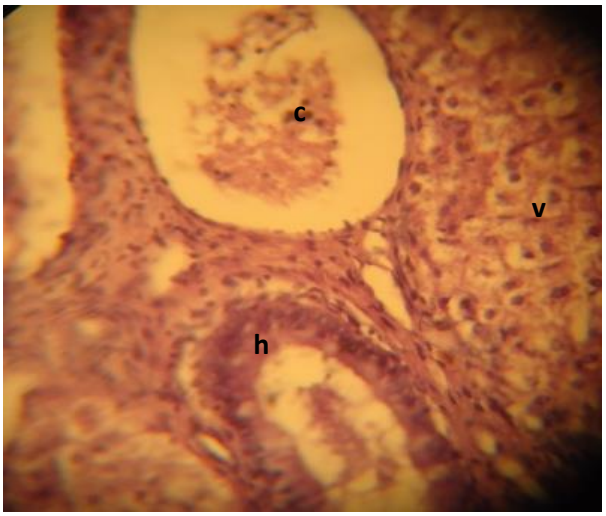


Figure (2):- section of liver treated with PB note congestion of portal area(c),hyperplasia of epithelial duct(h) and vacuolated hepatic cells(v).x10 H&E.

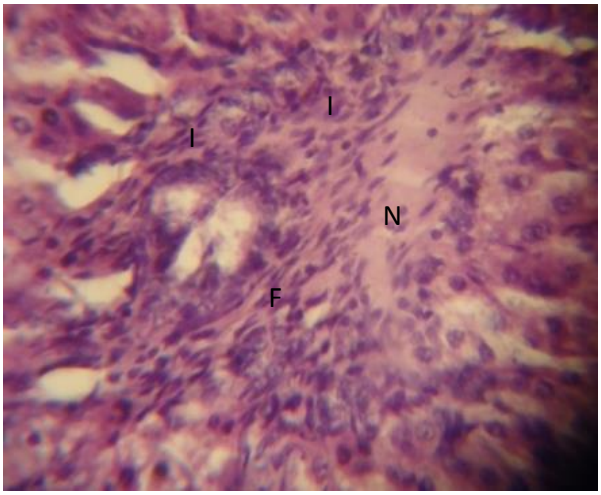
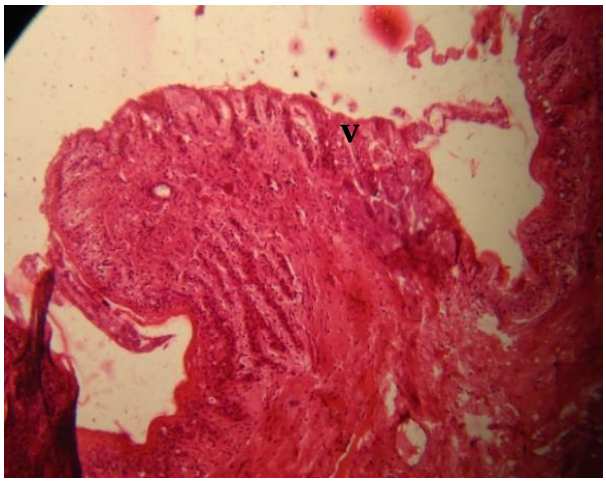
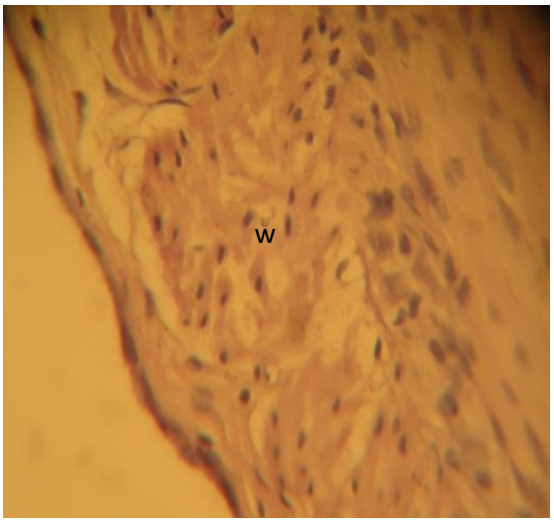


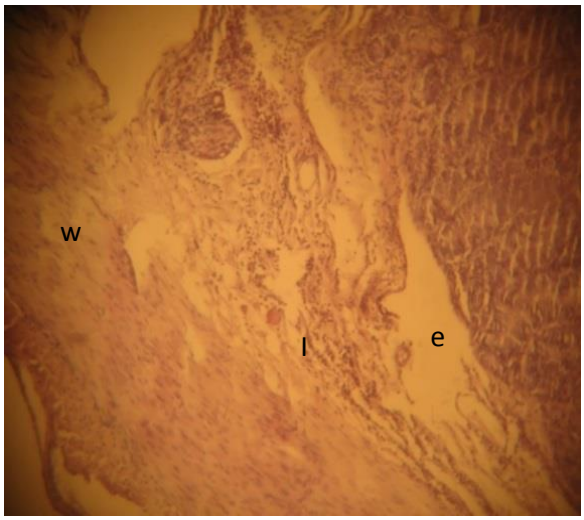
Figure (3):-section of liver treated with PB note necrotic area(n) , fibrosis(f) and inflammatory cells (I) x10 H&E.



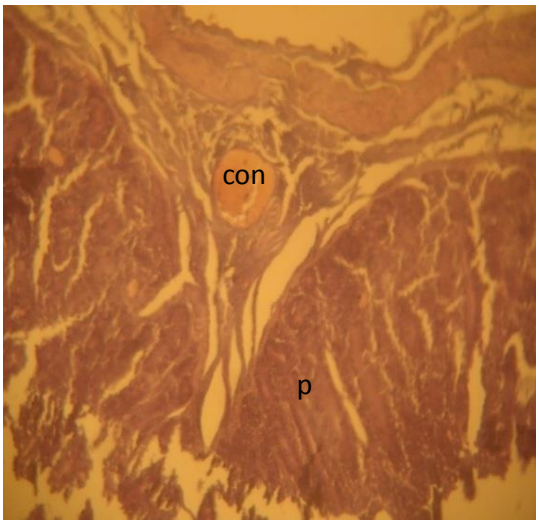
Figure(4)section of rumen treated with PB show sever vacuolated (v) epithelial cells lining mucosal layer .10x H&E .



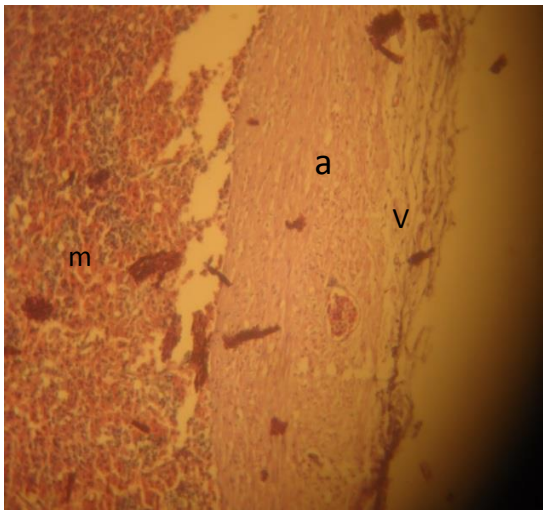
Figure(5)section of rumen treated with PB show vacuolated in myocytes of muscular layer(w).40x H&E .



Figure(6)section of intestine treated with PB show edema(e), inflammatory cells in submucosal layer(I) and white space in muscular layer(w)).x10 H&E .



Figure(7)section of intestine treated with PB show proliferation of epithelial cells (p)and congestion of blood vessels(con).x10 H&E .



Figure(8)section of spleen treated with PB show sever thickening of capsule(a) hemorrhage(m) and vacuolated(V). x10 H&E .

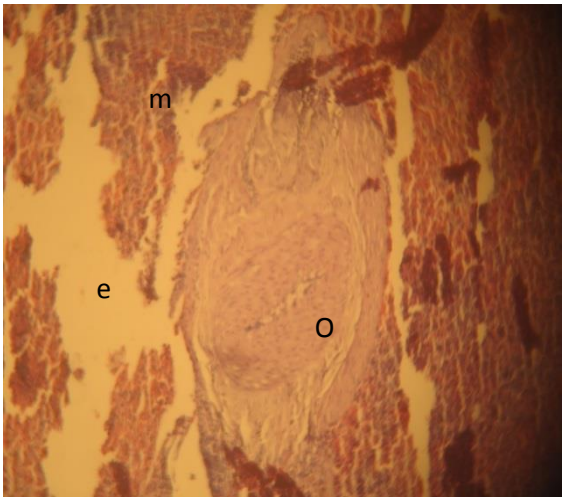
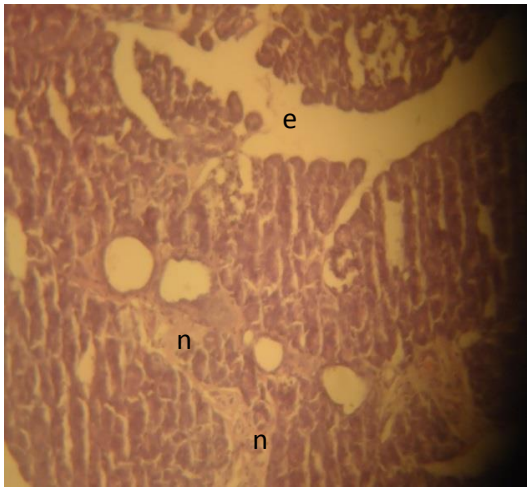
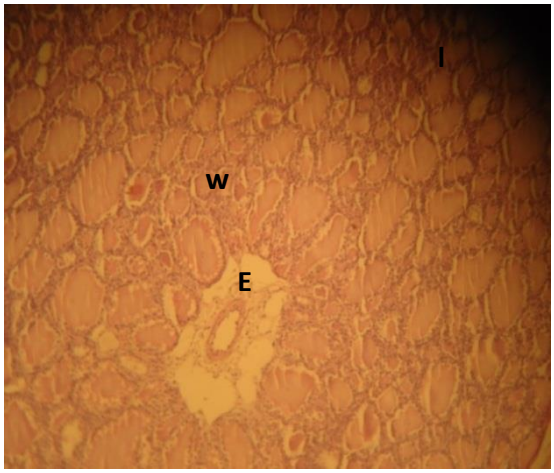


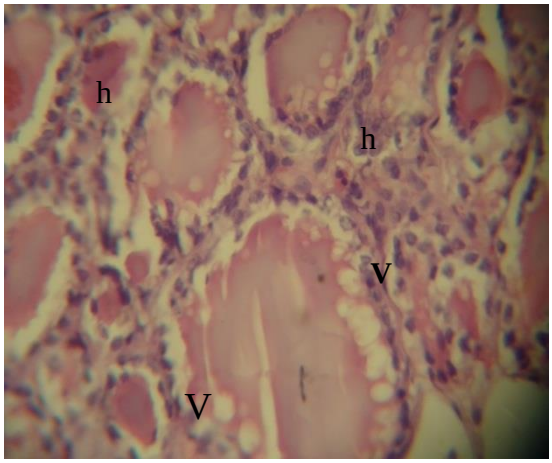
Figure (9)section of spleen treated with PB show narrowing of arteriole (o),edema (e) and hemorrhage(m) x10 H&E



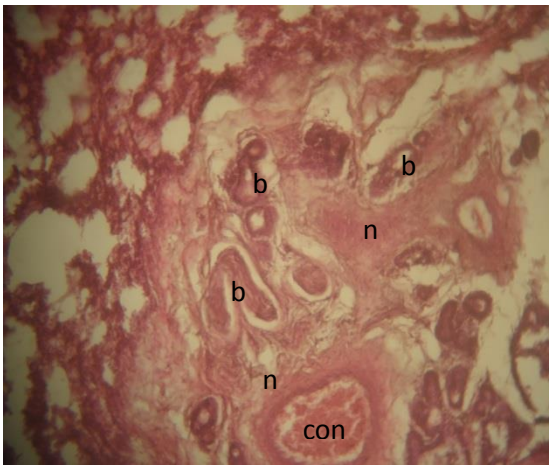
Figure(10)section of pancreas treated with PB show edema(E)and necrotic area (n).10X H&E.



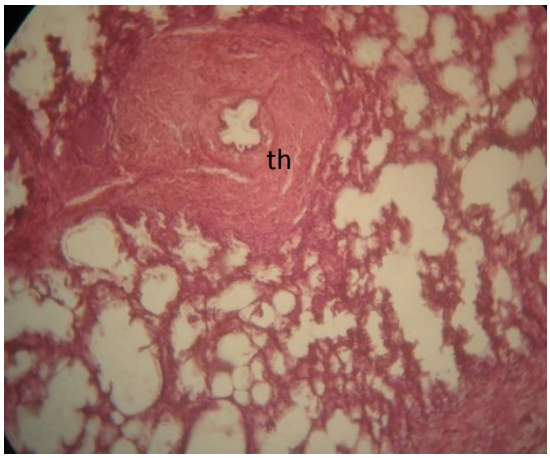
Figure(11)section of thyroid treated with PB show perivascular edema(E)and atrophy some acini(M)x10 H&E .



Figure(12)section of thyroid treated with PB show hyperplasia(h) and vacuolated(v) of epithelial cellsx10 H&E.



Figure(13)section of lung treated with PB show necrotic area(a) congestion of blood vessels(con)narrowingofbronchioles(b).10 x H&E.



Figure(14)section of lung treated with PB show thickening of bronchiole wall and dilated of alveoli (th).10x H&E.

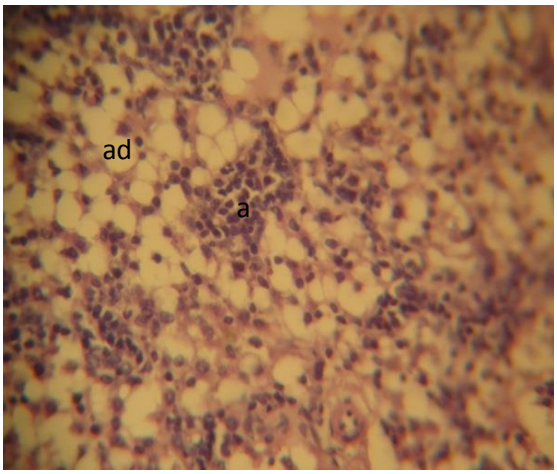


Figure (15)section of lymph node treated with PB show atrophy of lymphoid follicle (a) and adipose tissue (ad).10xH&E.

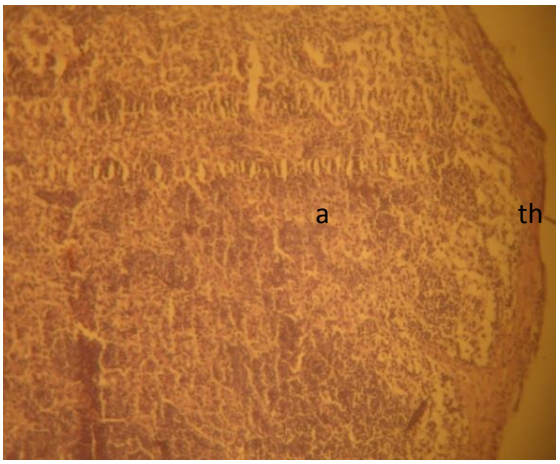


Figure (16)section of lymph node treated with PB show thickening of capsule(th)and atrophy lymphoid follicle(a).4x H&E.

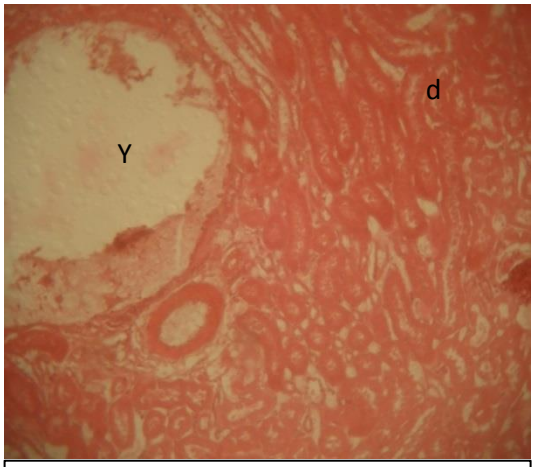
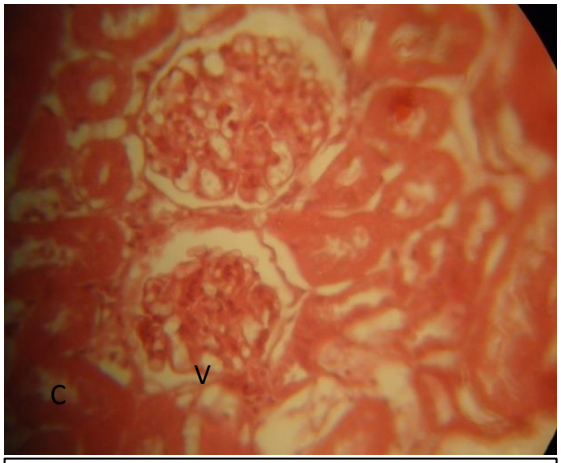
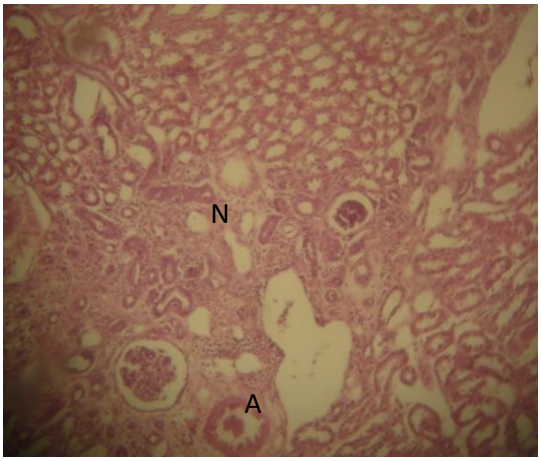


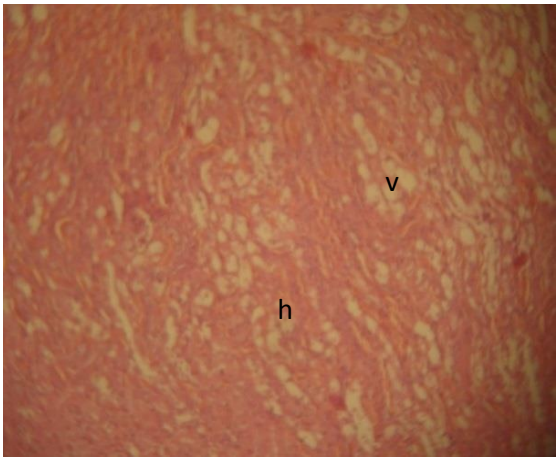
Figure (17):-section of kidney treated with PB note degeneration cells(d) and cyst(y) x10 H&E.



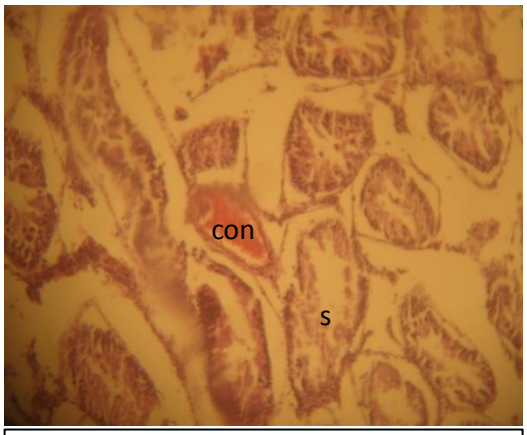
Figure(18)section of kidney treated with PB note vacuolated of epithelium cells of renal tubule with glomerulus(v) and cellularity of jackstays (c) x10 H&E.



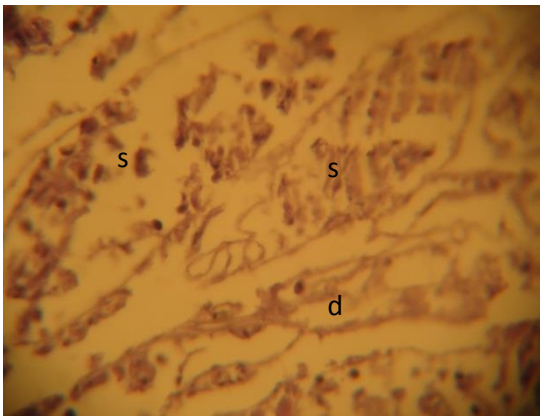
Figure(19)section of kidney treated with PB note atrophy of renal tubule(A) and necrotic area(N) x10 H&E.



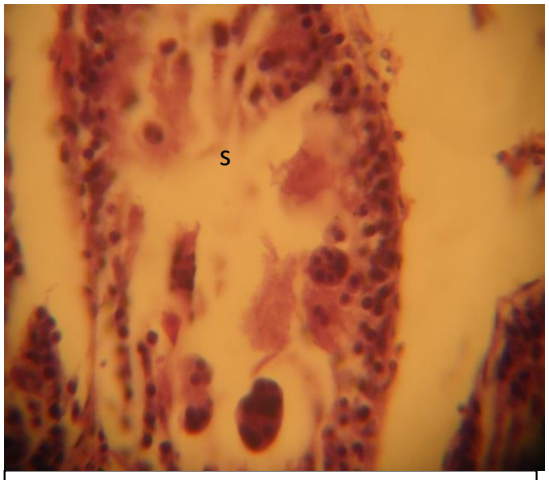
Figure(20)section of kidney treated with PB note vacuolated of epithelium cells(v) and hemorrhage in interstitial tissue(h). x10 H&E.



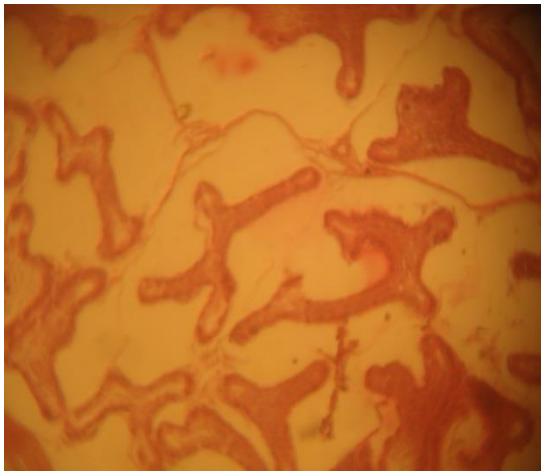
Figure(21)section of testis treated with PB show congestion blood vessels (con)andsuppressionofspermatogenesis (s)x10 H&E



Figure(22)section of testis treated with PB show sever degeneration of testicular cell(d) suppression of spermatogenesis(s)x10 H&E .



Figure(23)section of testis treated with PB show spermatidgiant cell (G) and suppression of spermatogenesis(s)x40 H&E .



Figure(24)section of epididymis treated with PB show atrophy of duct with irregular lumen(arrow).10x H&E.

Discussion:-

The animals were injected by phenobarbital 35mg\kgB.W.twice daily for 2months according to sequences of researches in surgical and pathological department of the college. After experimental period present the goats were increase of thirst by show exhausted a lot of quantity of water in their dishes and dullness with increase appetite in early days but, they were decreasing in last time compare with control group animals which were agree with(15,23, 24,25) due to phenobarbital treatment induction different the individual metabolites and also showed sex-dependency due to phenobarbital treatment were increased of antipyrine metabolites, 3-hydroxymethylantipyrine (HMA),norantipyrine(NORA),4-hyroxyantipyrine(OHA) and 4,4-dihydroxyantipyrine(DOHA).

HISTOPATHOLOGICAL CHANGES:-

The result of phenobarbital injected showed different histological features changes especially into hepatic and kidney tissue due to phenobarbital is known inducer of microsomal enzymes (cytochrome P-450 (cyp), NADPH oxidase, glutathione-S-transferase) which are responsible for the metabolic breakdown of a large number of endogenous and exogenous chemical(26,27). In other side some researchers enplane that Phenobarbital is removed from the body primarily75% by the liver and 25% by the kidney and due to phenobarbital has a unique ability to induce the microsomal enzymes which means that chronic exposure to phenobarbital makes the liver and kidney more efficient removing other toxins, other medications and other materials (3,28)lead to damage in tissue like degeneration in most body organs and tissues as well as there were note necrosis some of cells lead to stimulating the fibrosis as chronic inflammation that agree with (29).Therefore, Toxic ruminates secondary to overeating of phenobarbital as a consequence events, long period of phenobarbital treatment induced degeneration of in epithelial cells of intestine due to the down-regulation of CYP3A in the upper intestine and liver predominantly contributes to the increase in cyclosporine A absorption that agree with (30), vacuolated in testes and pancreas which are well supported with biochemical and enzymatical studies that provide the effect of phenobarbital that agree with(31). glutathione depletion increase mortality and pulmonary lesions (32).phenobarbital is chemical compound known to affect the endocrine system through different pathways and \or mechanisms of action, this assay is expected to detect estrogenic-, androgenic- and thyroid- like activity based on compound-related changes in target organ weight and systemic circulating hormones.there were seen acute passive congestion is seen in spleen due to distention of red pulp by blood, the lymphoid tissues (periarteriolar lymphoid sheathes and splenic follicles are widely separated and replacement by fat tissue or connective tissues, various exogenous and endogenous stimuli lead to activate acute inflammation and then chronic inflammation in the body in which the tissue response consists of the leakage or accumulation of fluid into epithelial cells as response in intestine,rumine,pancrease(33) .

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