THE EFFECT OF ARABIC GUM ON THE HISTOPATHOLOGICAL CHANGES ON DIABETES MELLITUS EXPERIMENTALLY INDUCED IN RATS

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Keyword: Rat, Arabic gum, Alloxan.

ABSTRACT

Forty eight albino rats were used to investigate the effect of Arabic gum on renal, hepatic and Pancreas hitological parameters in alloxan induced diabetes mellitus.

The animals were randomly distributed into four groups, each group 12 animals, the first group was regarded as normal healthy control, the second group was regarded as diabetic control, the third group was received Arabic gum 15gm/kg/day for two week, the fourth group diabetic rats treated with Arabic gum for two week.

This study showed that functionally diabetes related organs such as renal hepatic and Pancreas showed diabetes related pathological changes and these revealed a noticeable tendency for melioration in histophathological changes in renal hepatic and pancreas tissues.

INTRODUCTION

Diabetes Mellitus (DM) is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid and protein metabolism which causes hyperglycemia resulting from insufficient insulin secretion, insulin action or both **[1, 2**]. affecting at least 10% of the population, worldwide. Complications of DM include hypertension, atherosclerosis, microcirculatory disorders, retinopathy, nephropathy, neuropathy and angiopathy [3]. Hyperglycemia can cause oxidative stress, which, in turn, may result in cellular tissue damage. The harmful influence of diabetes on metabolism of tissues and organs is well known Likewise, uncontrolled hyperglycemia can lead to disturbances in the structure and function of organs [4].

Many hypoglycemic agents, such as the biguanides and sulfonylureas, are used alone or together with insulin to treat this disease, however these medications can cause serious side effects, motivating a search for safer, more efficacious agents to control diabetes [5].

Studies showed that numerous extract obtained from plants are effective in reducing glycemia, causing fewer side effects and with lower cost than the usual antidiabetic agents [6]. The majority of the plants that are used in popular medicine for treatment of DM have been shown to possess biologically active chemical constituent such as alkaloids, flavonoids, phenolic substances, and other constituents, that can be used as new hypoglycemic agents [7].

Arabic gum (Ag)is a branched-chain, complex polysaccharide, either neutral or slightly acidic, found as a mixed calcium, magnesium and potassium salt of a polysaccharidic acid. Ag has been shown to have an adverse effect on electrolyte balance and vitamin D in mice, and to cause hypersensitivity in humans.[8]In Middle Eastern countries Ag is widely used in the treatment of patients with chronic kidney disease and end-stage renal disease [9].

Alloxan has been widely used to produce experimental diabetes mellitus syndrome. It causes necrosis of pancreatic β-cells and induces free radicals which play a relevant role in the etiology and pathogenesis of both experimental and human diabetes mellitus [10]. Moreover, widespread lipoid deposits throughoutthe exocrine tissue, and loss of β–cells [10].Therefore, they are predominantly vulnerable to oxidative stress resulting in the suppression of insulin gene transcription, glucose-stimulated insulin secretion and even producing apoptosis [11].

The aim of this study is to investigate the effectiveness of the Arabic gum (Ag) in the reduction of pathological changes of alloxan induced diabetes on rat kidney, liver and pancreas.

MATERIAL AND METHODS

In this studyadult male albino rats were obtained From Mosulmedical college as 40-50 days old, weighting between 250-300 gm, the animals were housed under standardlaboratorycondition (14 hrs:10 hrs light and dark) in a roomwith controlled temperature at 22±2℃ duringthe experimental period. water and food (standard commercial rats diet) were provided ad libitum.

Alloxan was obtained from Sigma-Aldrich Corp, St Lous, Mo, USA.

Arabicgum was obtained from Dar Savanna Ltd., Khartoum, Sudan.

Experimental design:

The duration of experiment is two weeks, the animals were divided in to 2 groups the half of animal was killed after (1) week and the other half were killed after (2) week.

Diabetes mellitus was induced in rats using diabetogenic substance alloxan monohydrate by a single intrapretonialinjection of freshly prepared in normal saline solution of alloxan (100mg/kg/B.W.) in 24 hrs fasting animal.This dose of alloxan was previously tested and proven to increase blood glucose level above 200 mg/dl were considered as diabetic [12].Forty eight male rats were randomly divided into four groups (12 rats in each):

Group 1: Control: rats of this groupreceived theregular diet and drinking water.

Group 2:Diabetic control: rats of this groupreceivedalloxan 100mg/kg/B.W. intrapretonial (i.p.) injection.

Group 3: Rats of this groupreceivedArabic gum (Ag) 60gm/l in drinking water which is equivalent to 15 gm/kg/B.W./day orally by using stomach tube.

Group 4: Alloxan diabetic rats treated with Arabic gum (Ag)15 gm/kg/B.W./day orally by using stomach tube.

Autopsy procedures:

Animal were anesthetizedwith ether inhalation, then killed by cervical dislocation and immediately after death, kidney, liver and pancreaswere fixed in 10% neutral buffer formalin, embedded in paraffin, sectioned at 5 Mm and stained with haemotoxylin-eosin (H+E). Lightmicroscope was evaluate the lesions [13].

RESULT

Histopathological changes ingroupanimalsreceivedalloxan 100mg/kg /b.w

Kidney: kidney sections after 1 week of the study showed, histological changes in the renal glomeruli dilation ofBowmaṅsspace as a result of shrinkage of glomerular tuft, as well as the clarity of vascular changes are severe congestion of blood vessels found in the interstitial tissue andbetween the renal tubules.. In addition tothickening in the blood vessels walls and dilation in renal tubules (figures 1, 2). However, after 2 weeks of the study, showed increased sloughing of renal tubular epithelial cells, sever necrosis, increased congestion and thickening in the blood vessels walls, Also deposition of eosinophilic material between renal tubules has been seen (figures 3, 4).

liver: liver sections after1 week of the study showedmild coagulation necrosis of hepatocytes especially surrounding the central veins in addition to dilation of central veins and sinusoid (figure 5), but after 2 weeks of the study thrombi in central vein and blood vessels in portal vein and massive necrosis in hepatocyte were observed (figure 6).

Pancreas: pancreas sections after 1 week of the study revealed atrophy in endocrine islet of langerhans, swelling, degenerative changes and necrosis also to oedemabetween lobules of exocrine part of pancreas (figure7). after 2 weeks of the study showed severswelling, thickening in blood vessels, with congestion of blood vesselsbetween pancreas lobes, sever necrosis of β-cell and vacuolation has been seen (figures 8, 9).

Histopathological changes ingroupanimalsreceivedArabic gum (Ag) 15 gm/kg/day

Kidney: kidney sections after 1 week of the study showednecrosis, swelling of epithelial cells lining renal tubules, congestion of blood vessels and dilation in bowman's space due to shrinkage of glomerular tuft (figure 10). However, after 2 weeks of the study, sever necrosis, vacuolationof mesangialcells and dilation of bowman's space(figure 11).

liver:liver sections after1 week of the study revealed degeneration changes represented by vacuolar degeneration, sinusoid dilationand simple coagulation necrosis of hepatocyte (figure 12). However, after 2 weeks of the study increased necrosis, mild focal infiltration of inflammatory cells Also thickening in liver capsule were observed (figure 13).

Pancreas: pancreas sections after 1 week of the study showed normal acini and zymogene granule but after 2 weeksof the experiment atrophy of islet Langerhans, oedema between lobes and swelling in acini has been seen (figure 14).

Histopathological changes ingroupanimalsreceived alloxan and Arabic gum (Ag) 15 gm/kg/day:

Kidney: kidney sections after 1 week of theexperiment revealed a slight Improvement compared with the group treated with alloxan only (figure 15). while, after 2 weeks of the study showed slight improvement of the histological changes represented by necrosis and shrinkageglomeurl tuft (figure 16).

Liver: liver sections after 1 week of theexperiment showedimprovement of liver but withvacuolar degeneration of hepatocyte (figure 17). But after 2 weeks of the studymeliorating of liver picture with coagulation necrosis in hepatocytes (fig 18).

Pancreas:pancreassections after 1 week of theexperiment showedslight improvement of the histological changes revealed necrosis of islet langerhans cells andswelling in acinicell. While, meliorating in pancreatic tissue picture was observedafter 2 weeks of the experiment.

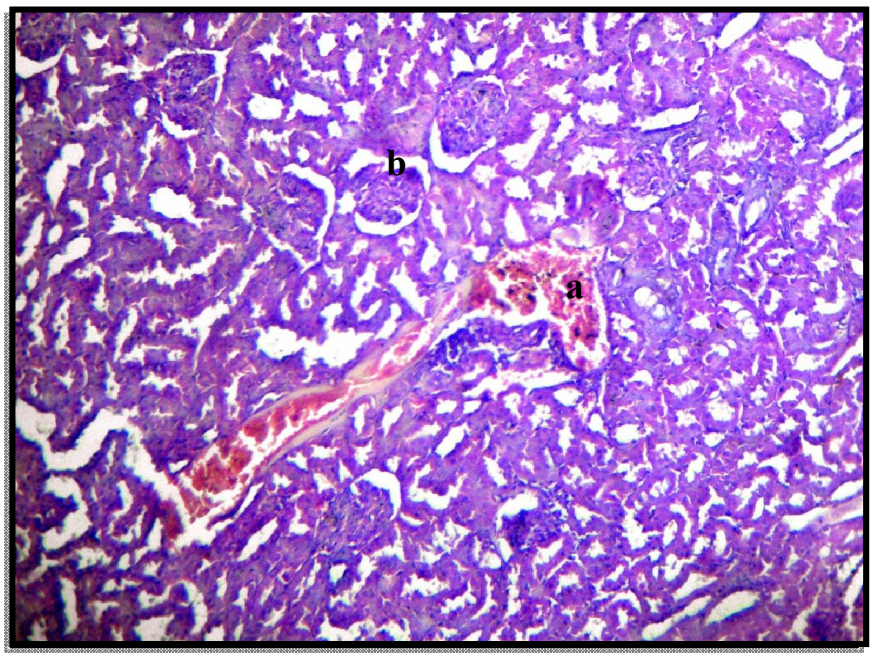

Fig .1: histological section of rats kidney treated with alloxan for one week , showed, sever congestion (a) and dilation ofBowman'sspace(b) .H&E, 68X.

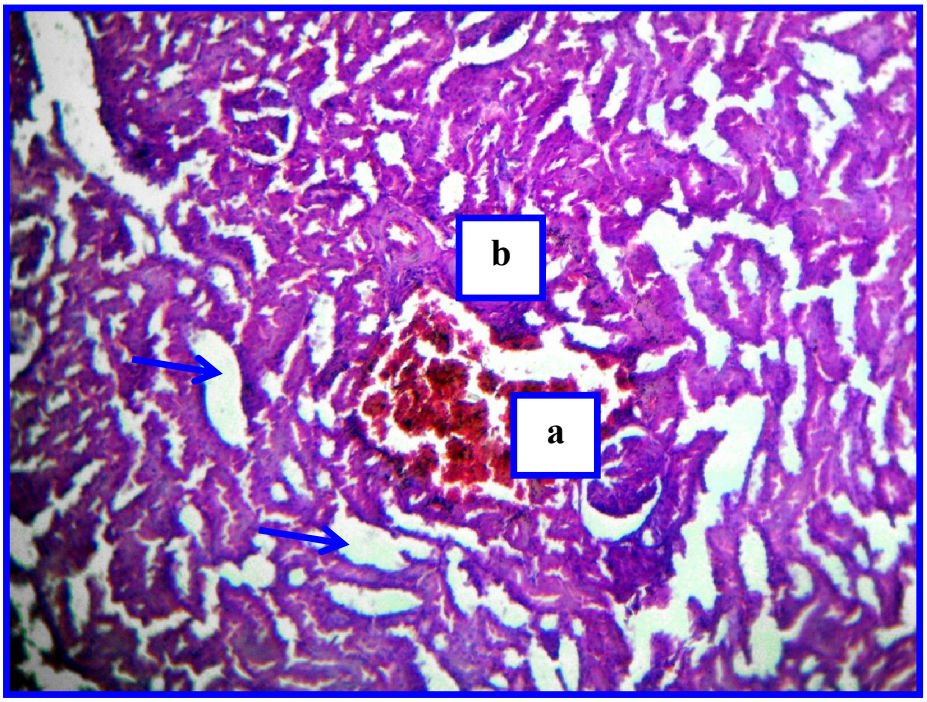

Fig . 2: histological section of rats kidney treated with alloxan for one week , showed, congestion of blood vessels(a), thickening in the blood vessels walls (b)and dilation in the lumen of renal tube (arrows). H&E, 68X.

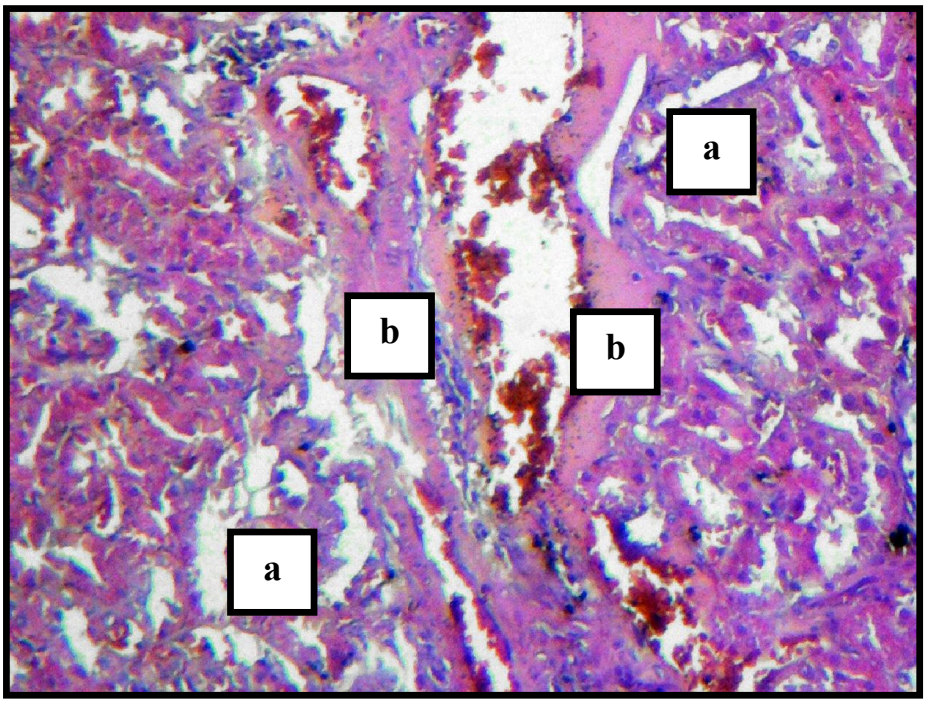

Fig .3: histological section of rats kidney treated with alloxan fortwo week , showed, sloughing of epithelial cells lining renal tubules (a) thickening the blood vessel wall and depeosition of eosinophilic material (b). H&E, 115X.

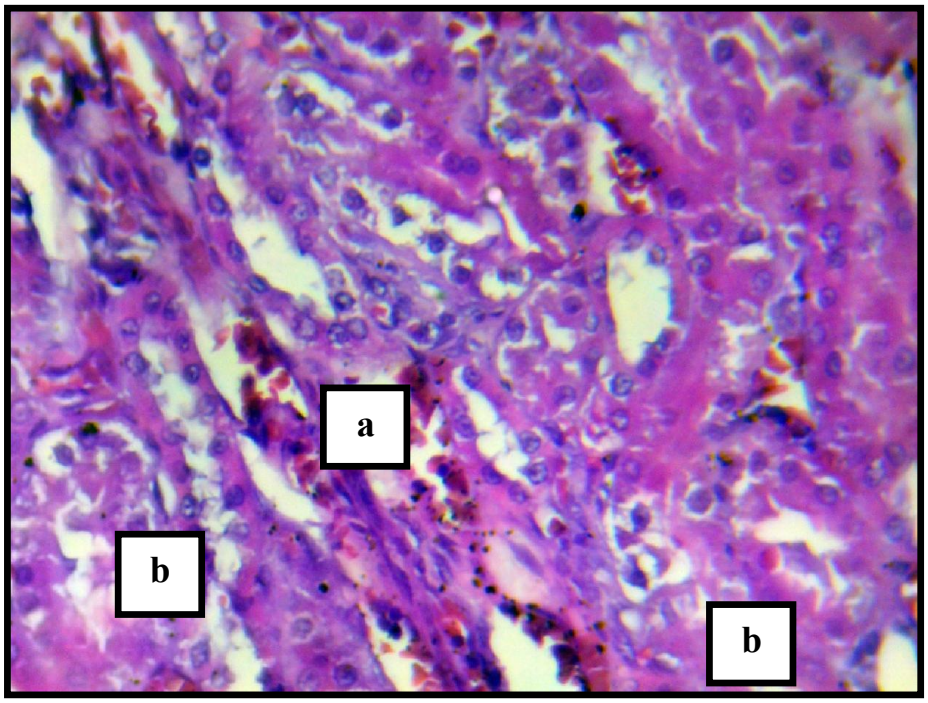

Fig .4: histological section of rats kidney treated with alloxan for two week , showed, congestion ofblood vessels(a) sever necrosis (b) . H&E, 115X.

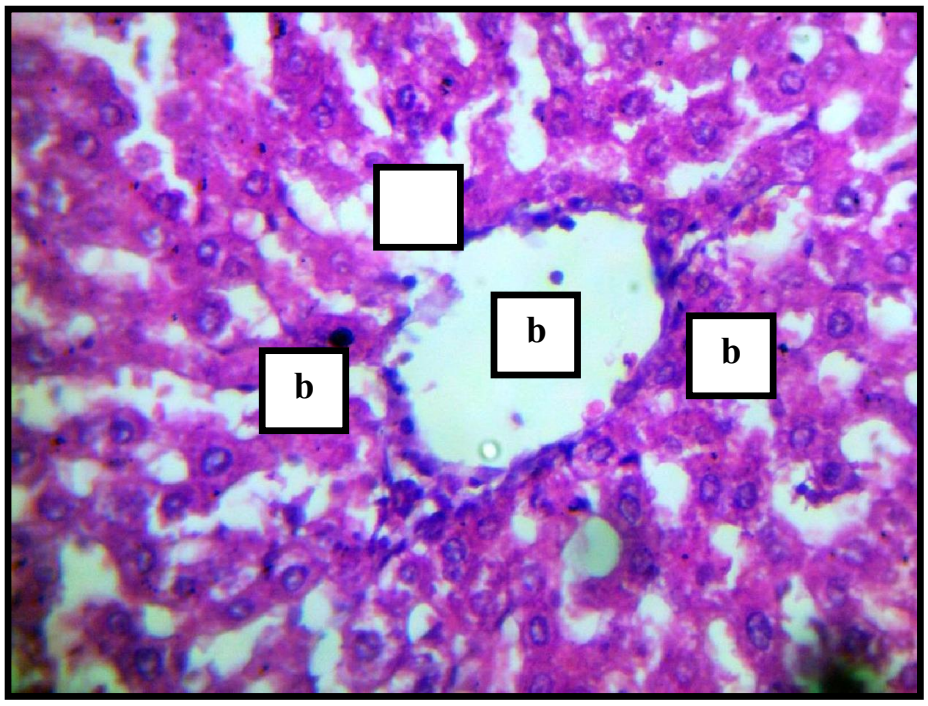

Fig. 5: histological section of rats liver treated with alloxan for one week , showed, coagulation necrosis (a), dilation of central vein andsinusoid (b). H&E, 240X.

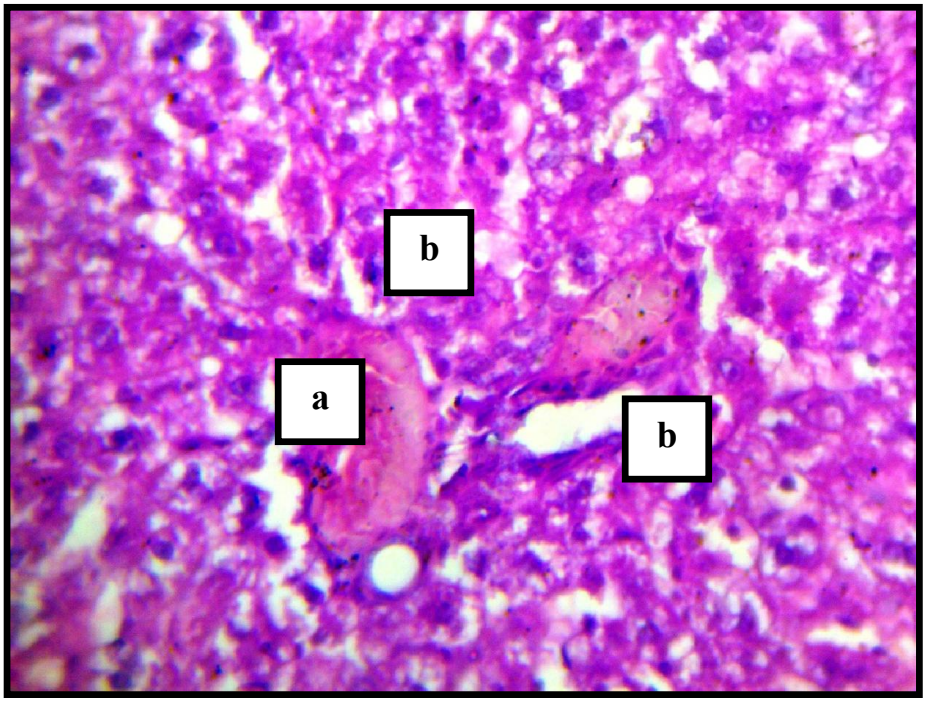

Fig .6: histological section of rats livertreated with alloxan fortwo week , showed, thrombi in blood vessels (a), and massive necrosis (b), H&E, 200X.

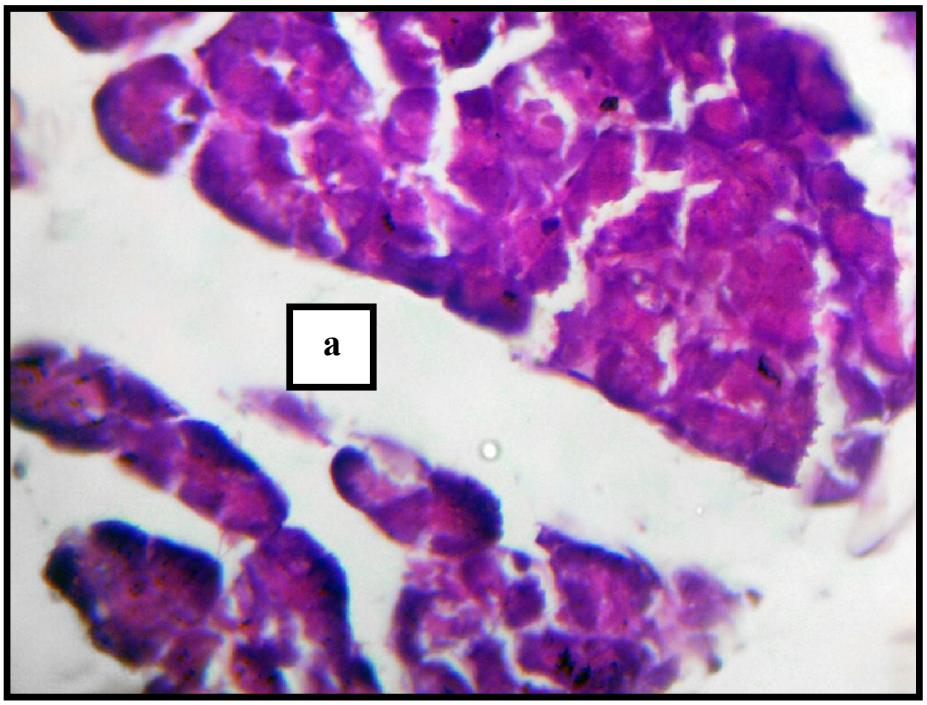

Fig .7:histological section of rats pancreastreated with alloxan forone week , showed, oedema between lobules of exocrine part of pancreas (a), H&E, 115X.

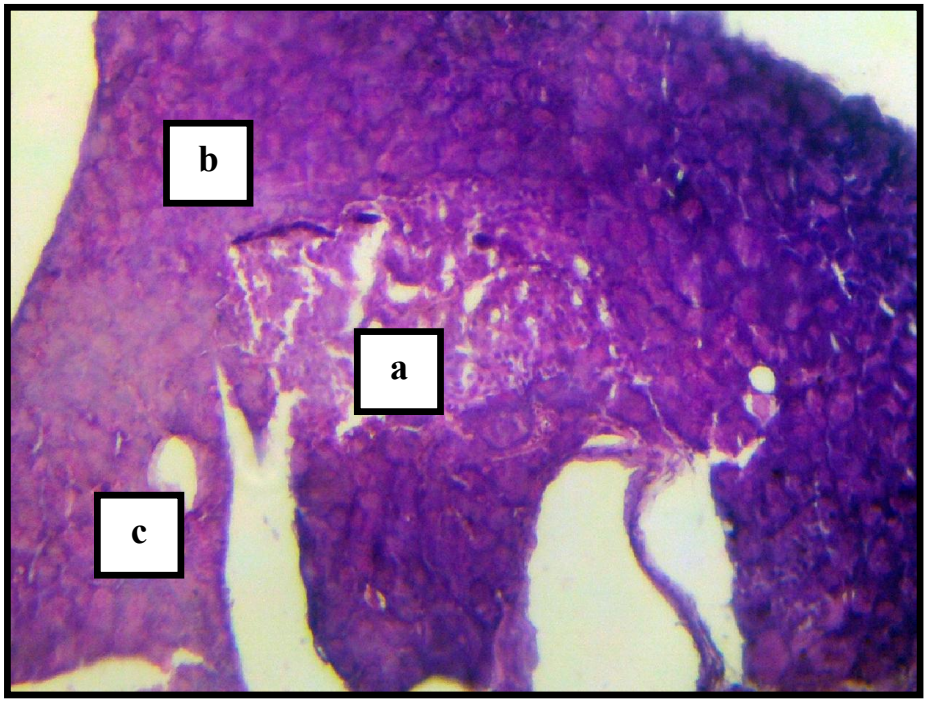

Fig .8: histological section of rats pancreastreated with alloxan fortwo week , showed, necrosis of B cells (a) swelling of the cell lining acini (b), and with congestion of blood vessels (c). H&E, 68X.

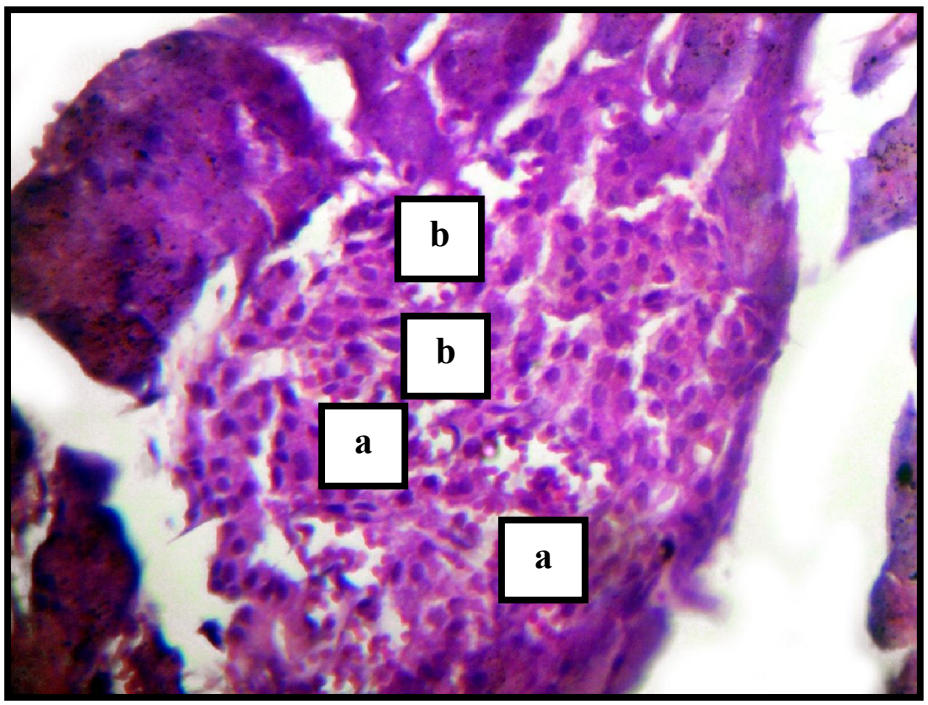

Fig. 9: histological section of rats pancreastreated with alloxan fortwo week, showed sever necrosis of B cell (a), and vaculation (b). H&E, 240X.

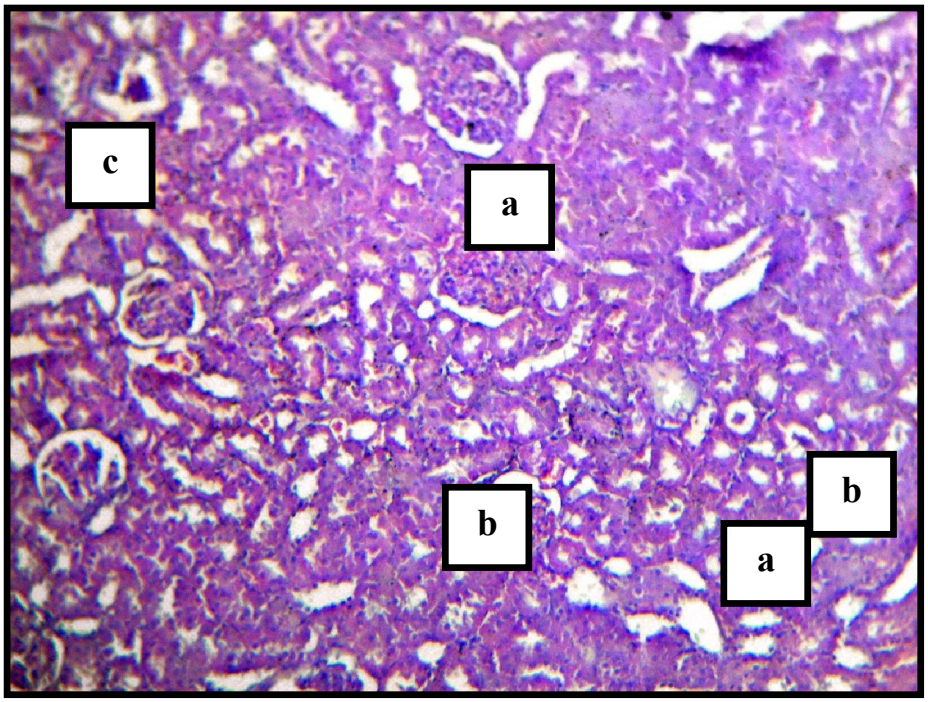

Fig .10:histological section of rats kidney treated with Arabic gum for one week, showed, severe swellingof epithelial cells of renal tubules (a), shrinkage of glomerular tuft and dilation in Bowman's space (b). and congestion of blood vessels (c) H&E, 100X.

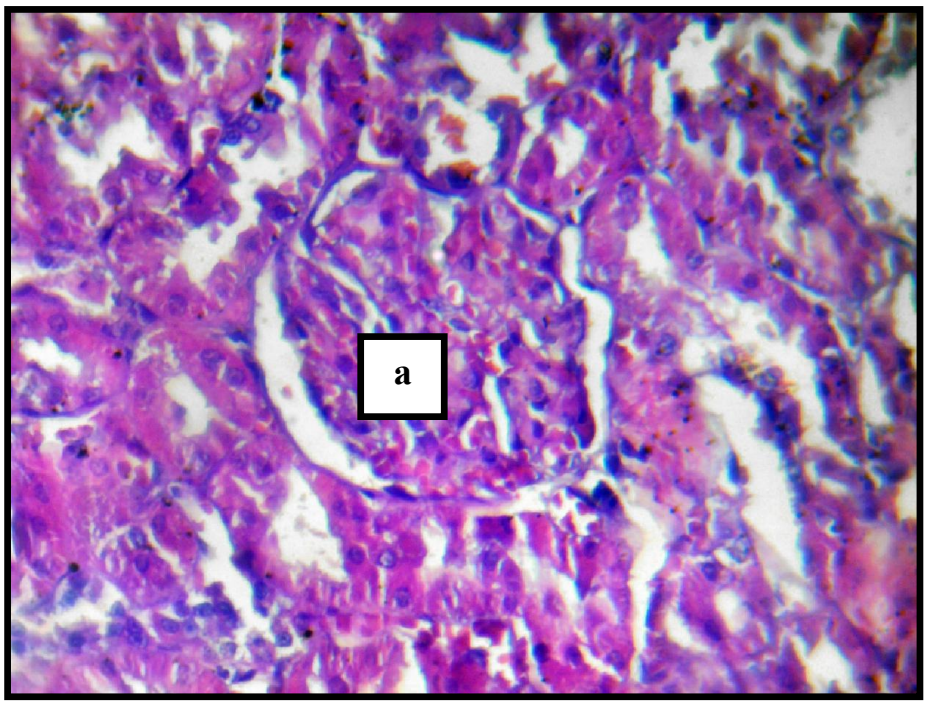

Fig. 11: histological section of rats kidney treated with Arabic gum fortwo week , showed, vacuolation of mesangialcells (a). H&E, 200X.

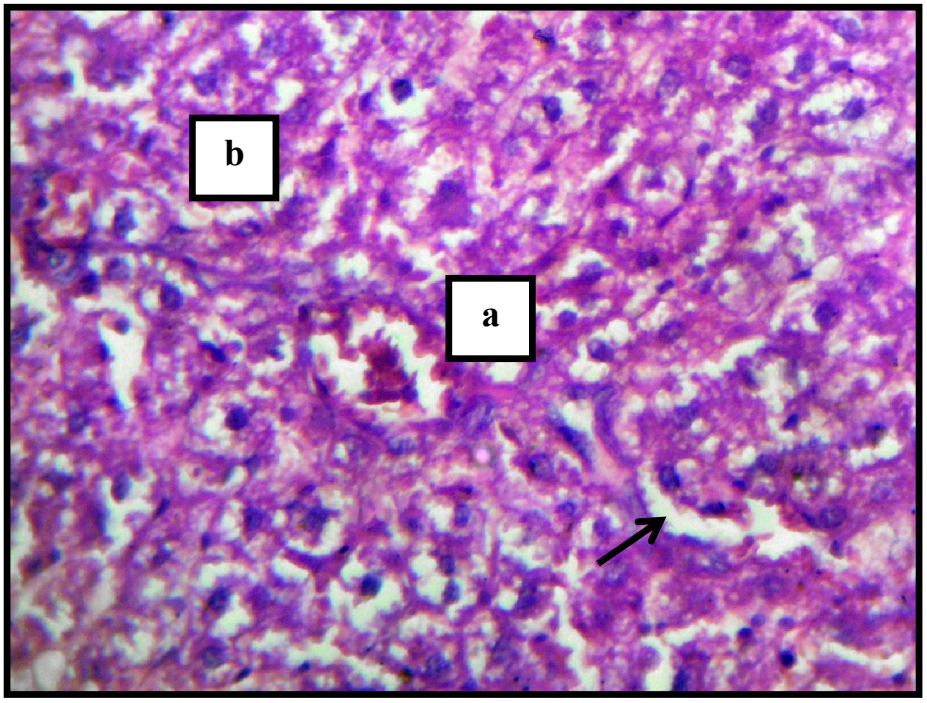

Fig. 12: histological section of rats liver treated with Arabic gumforone week , showed coagulation necrosis (a) vacuolar degeneration(b) and dilation of sinusoid(arrows). H&E, 115X.

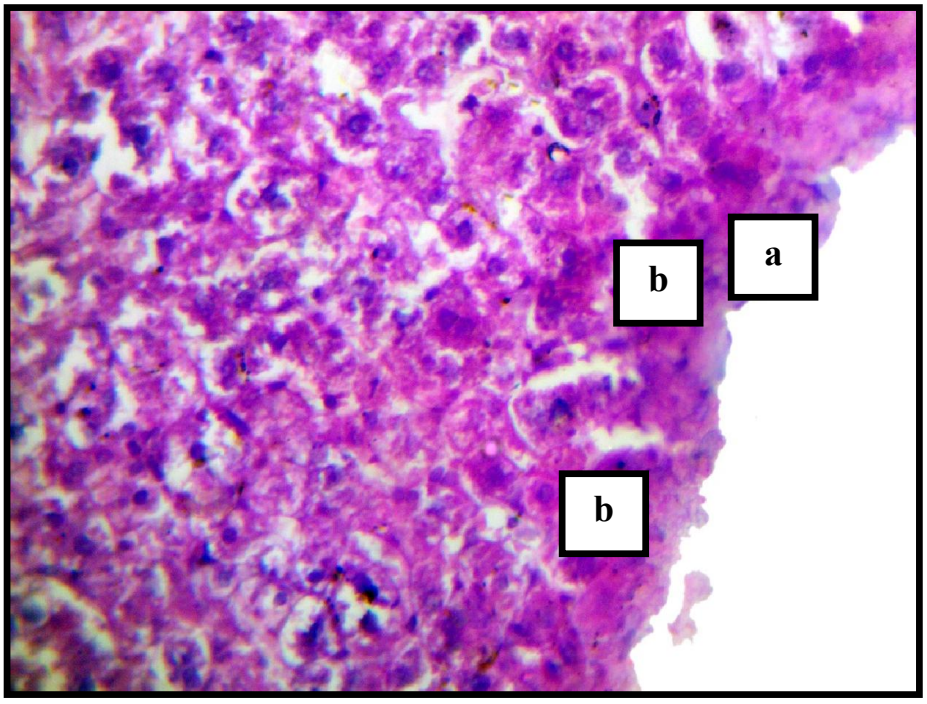

Fig .13: histological section of rats livertreated with Arabic gum fortwo week, showed, thickening in liver capsule (a)and necrosis hepatocyte (b). H&E, 240X.

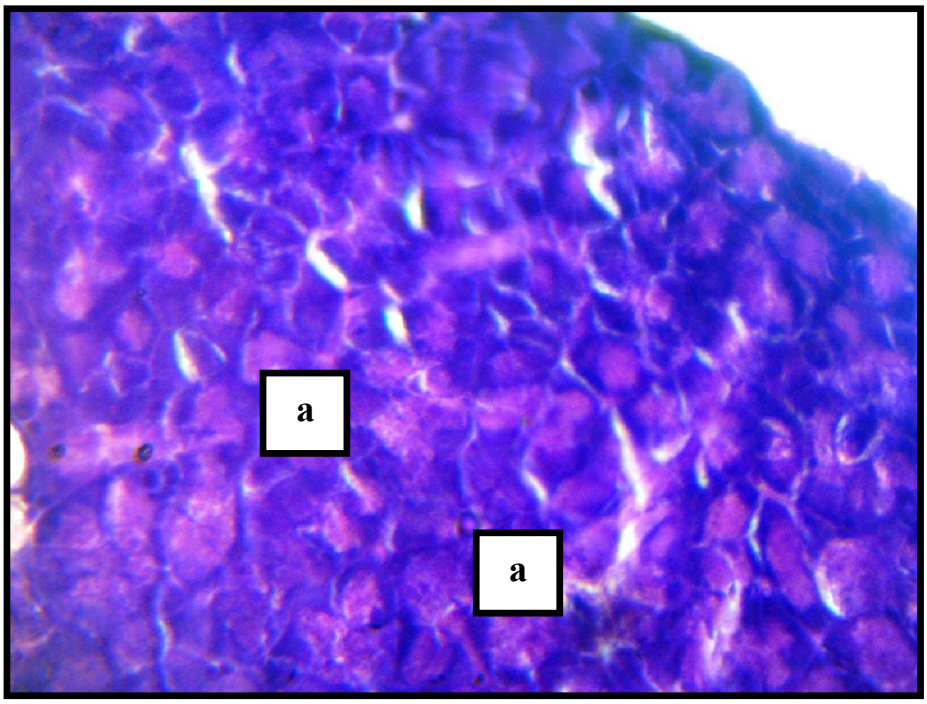

Fig. 14: histological section of rats pancreastreated with Arabic gumfortwo week , showed, swelling acini cells (a). H&E, 165X.

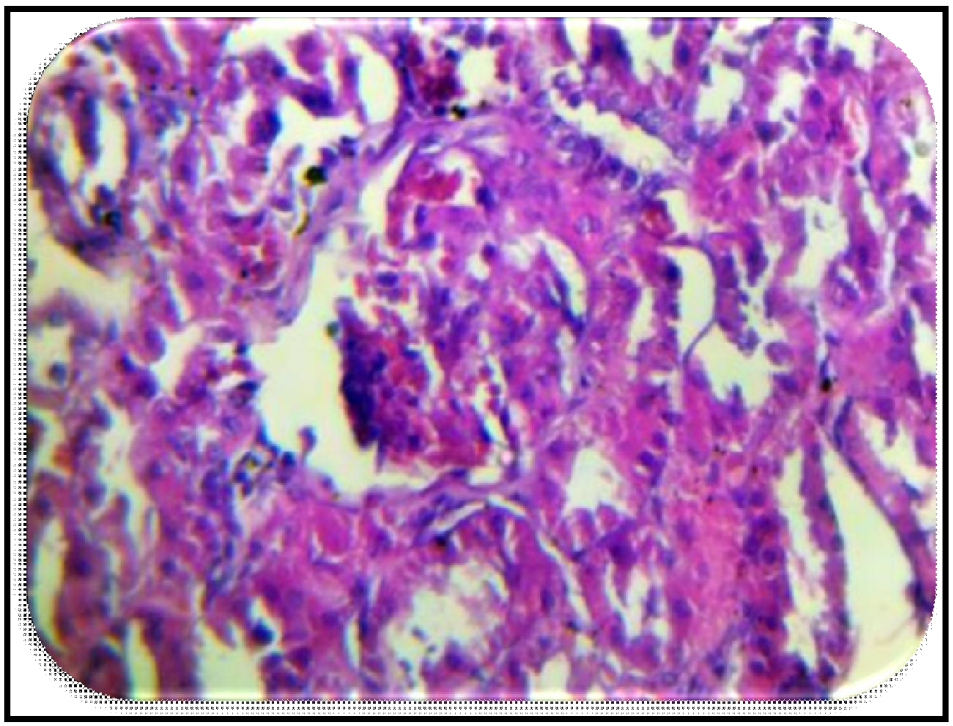

Fig. 15: histological section of rats kidney treated with Arabic gum &alloxan for one week, revealed, a slight improvement of kidney picture. H&E, 240X.

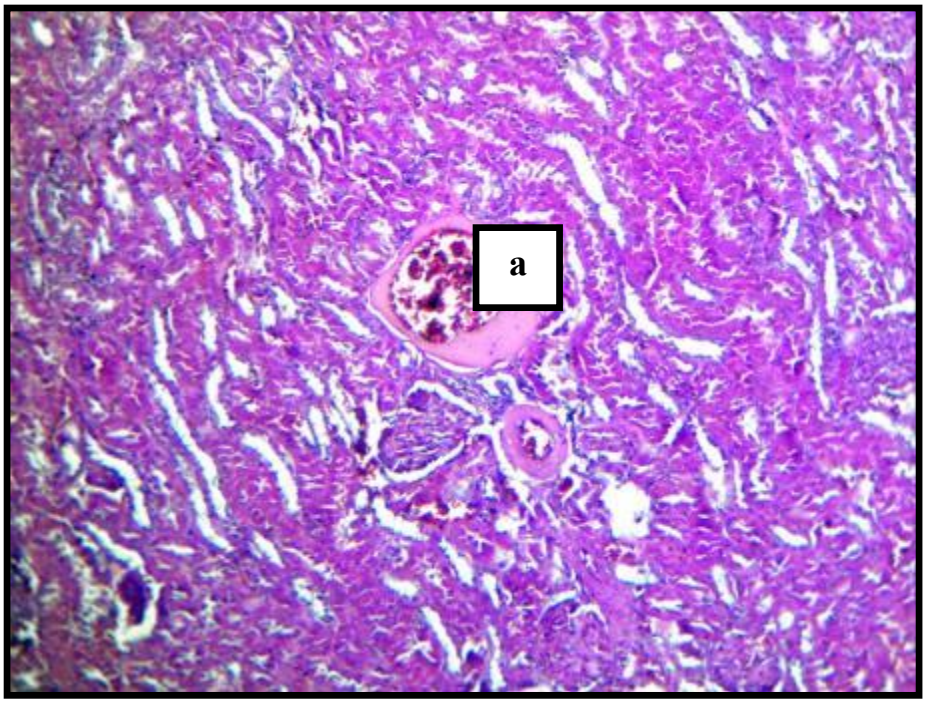

Fig. 16: histological section of rats kidney treated with Arabic gum & alloxan fortwo week , showed, thrombus (a). H&E, 100X.

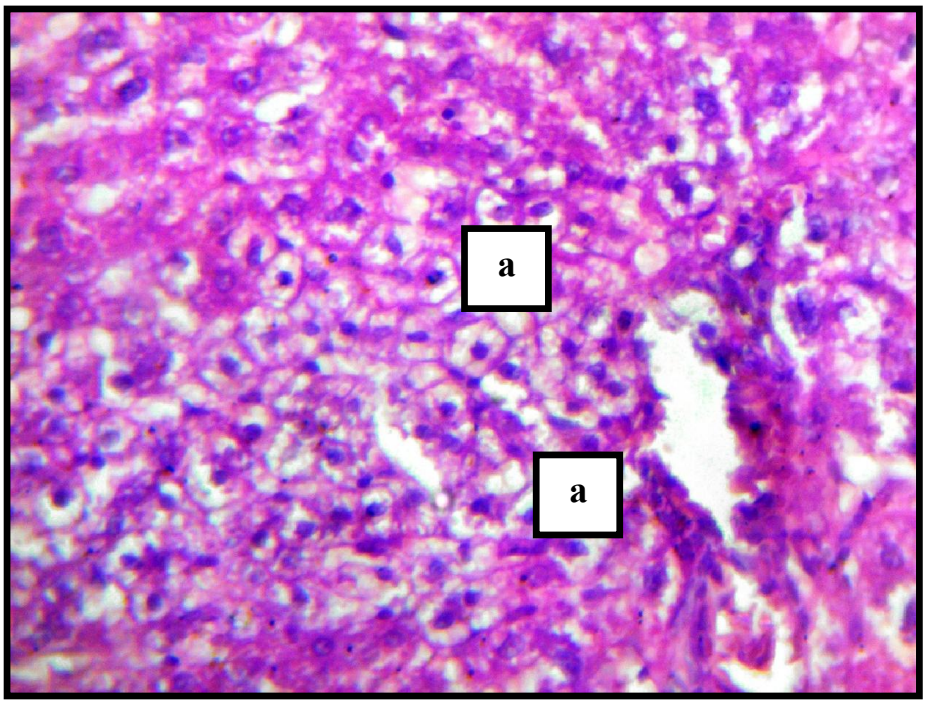

Fig .17: histological section of rats liver treated with Arabic gum&alloxan forone week , showed, vacuolar degeneration (a), H&E, 240X.

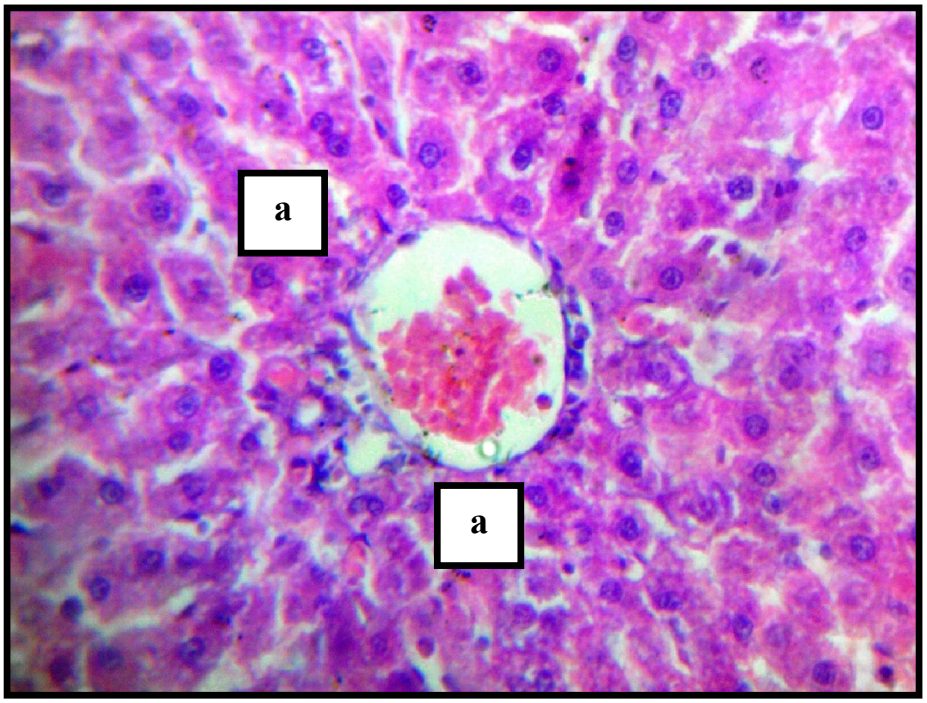

Fig .18: histological section of rats livertreated with Arabic gum and alloxan fortwo week, showedcoagulation necrosis (a). H&E, 240X.

DISCUSSION

The major characteristics of diabetes mellitus are polydipsia, polyurea, polyphagia, weight loss, muscle weakness and hyperglycemia [14].Alloxan, a beta cytotoxin, destroys beta-cells of islets in the langerhans of pancreas resulting in a decreased endogenous insulin secretion leading to a decreased utilization of glucose by body tissues [15]. This results in the elevation of blood glucose level, decreases protein content, and increases levels of cholesterol and triglycerides [16].

Studies in the last several decades have shown that plant and plant based therapies have a potential to control and treat diabetes and its complications [17,18]. They are better than allopathic drugs, which have a lot of adverseside effects [19] for testing antidiabeticpotential of plants, alloxan and streptozotocininduced hyperglycemia in rats is considered to be a good preliminary screening model and is widely used. Alloxan is well known for its selectivepancreatic islet cell toxicity and has been extensivelyused to induce diabetes mellitus in animals [20].

Wadood *et al*.(1989) concluded, albeit without experimental evidence, that Arabica initiated the release of insulin from pancreatic beta cells of normal rabbits.

Previously, experiments were carried out in vitro and in normal human subjects to evaluate alternative food-grade viscous polysaccharides as agents for reducing postprandial hyperglycemia and to assess the relationship between the in vitro and in vivo performance of the polysaccharides[22].Mixtures of different types of gum have been shown to inhibit glucose movement in vitro, and lower postprandial bloodglucose and plasma insulin in human subjects whenincorporated in a drink containing 50 g glucose [22,23]. Infusion of meals containing starch showed that a decrease in the digestion rate of starch in the upper small intestine accounted for part of the effect of viscosity on glycemic response, whereas the main effect of gum was apparently to slow gastricemptying [24].

In diabetic nephropathy in group 2 (diabetic control), the histopathologicalchanges revealed dilation ofBowman'sspaceas result of shrinkage of glomerular tuft, necrosis, congestion and thickening in the blood vessels. The structural changes in kidneys could be attributed to altered metabolism in diabetes [25], and the subsequent effects on the increased renal threshold for hyperglycaemia [26]. Bulut *et al*. (2001) have reported that glomerular capillaries entirely fill the renal corpusclealong with mesangial cell proliferation and hypertrophy inalloxan-induced diabetic rabbits.In diabetic dogs, degeneration of glomeruli and tubular epithelium along with the presence of hyaline casts, mildly sclerotic glomerulus and coagulative necrosis of tubular epithelium has been reported [28]. Further, studies have shownthat good metabolic control is beneficial in slowing the progression of nephropathy in diabetes, and if the duration of diabetes is prolonged before reinstitution of normoglycaemianephropathy is not easily reversed [29,30].Arabic gumhelped in amelioration of renal diabetic changes mainly through the action of GA as an antioxidant has led to the publication of a series of articles by the same group claiming a protective effect of GA against experimental gentamicin and cisplatinnephrotoxicity [9,31]. doxorubicin cardiotoxicity in rats[32].

Histological examinations indicated that the liver of diabeticcontrol rats exhibited disruption of hepatocytes, dilation of central vein and sinusoid, necrotic hepatocytes.Similar structure changes in liver have been reported by[33,28]. Changes in glucose metabolism such as decreased glycolysis, impeded glycogenesis and increased gluconeogenesis in diabetic liver have been reported [34].Treatment of alloxan –induced diabetic rats with Arabic gum resulted in apparent amelioration of

most hepayocytes, the effect ofAg to reduce the damage of hepatic tissue take place due to have abilityto scavenging nitric oxide in order to blocking oxidative stress [35]. Moreover, Ag was found to blockingfunction hepatic macrophage to prevent release nitric oxide [36].

Histopathological examination that revealed degenerative changes of beta cells of islets of Langerhan's induced by alloxan have been experimentally observed in animals [15,26,28].The action of alloxan in the pancreas is preceded by its rapid uptake by the beta cells [37]. Further, in long standing diabetes mellitus congestion and degenerative changes in acini and disorganization of acini has been reported [38].Ag has strong antioxidant properties and major mechanism for the inductionof these toxicities is the generation of free radical [39,40], and Ag was found to decrease production of free oxygen radicals [9].

تأثير الصمغ العربي على التغيرات المرضية النسجية لداء السكري المحدث تجريبياً في الجرذان

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الملخص

في هذه الدراسة تم استخدام ٤٨ من ذكور الجرذان البيض للتحري عن تأثير الصمغ العربي على التغيرات النسجية في الكلية والكبد والبنكرياس في الجرذان المصابة بداء السكري المستحدث بالالوكسان.

تم توزيع الحيوانات عشوائيا إلى اربعة مجاميع بمعدل ١٢ جرذ في كل مجموعة، عدت المجموعة الاولى مجموعة السيطرة، والمجموعة الثانية مجموعة سيطرة مصابة بالسكري، والمجموعة الثالثة، عوملت بالصمغ العربي بنسبة ١٥غم/كغم/ من وزن الجسم يومياً ولمدة اسبوعين، أما المجموعة الرابعة فان الجرذان المصابة بالسكري عوملت بالصمغ العربي وبنسبة ١٥غم/كغم/يوم.

اظهرت الدراسة ان الاعضاء المتأثرة بداء السكري وهي الكلية، الكبد، البنكرياس قد اظهرت تغيرات مرضية نسجية وان هذه التغيرات اظهرت تحسنا واضحا بعد المعاملة بالصمغ العربي.

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